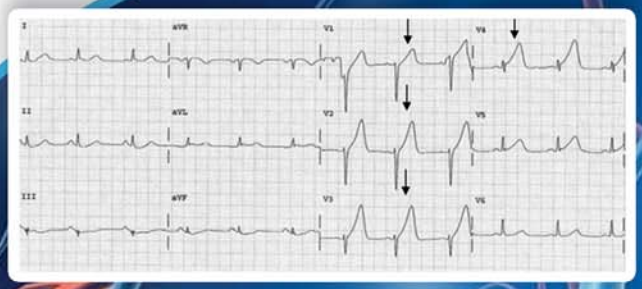
Annual Journal of National IMA AMS Conference

Theme : Acute Coronary Syndrome

27th & 28th October 2023

KOZHIKODE, KERALA

AMSCON 2023



INDIAN MEDICAL ASSOCIATION

ACADEMY OF MEDICAL SPECIALITIES

Head Quarters, Hyderabad, Telangana

Dr Ketan Desai
Chief Patron
Indian Medical Association

Dr. Sharad Kumar Agarwal
National President ,IMA

Dr. Sahajanand PD Singh
Imm. Past National President

Dr. Anilkumar J Nayak
Hony. Secretary General

Dr. R.V Asokan
National President Elect

Dr. Shitij Bali
Hony. Finance Secretary

Dr. Pankaj Mutneja
IMA AMS, Chairman

Dr. Srirang Abkari
IMA AMS, Hony. Secretary

IMA ACADEMY OF MEDICAL SPECIALITIES

NATIONAL CONFERENCE 2023

27th and 28th October 2023

Gateway Hotel Taj Kozhikode

INDIAN MEDICAL ASSOCIATION
ACADEMY OF MEDICAL SPECILAITIES

ANNUAL JOURNAL OF
NATIONAL IMA AMS CONFERENCE
Theme : Acute Coronary Syndrome
AMSCON - 2023

27th & 28th October 2023
KOZHIKODE, KERALA

Dr. Pankaj Mutneja Chairman, IMA AMS
Dr. Srirang Abkari Hony. Secretary, IMA AMS
Dr. Shilpa Basu Roy Hony. Editor, IMA AMS
Dr. Rajiv Ranjan Prasad Executive Editor, IMA AMS

Dr. Sharad Kumar Agarwal National President, IMA
Dr. R. V. Asokan National President Elect, IMA
Dr. Anilkumar J Nayak Hony. Secretary General, IMA
Dr. Shitij Bali Hon Finance Secretary, IMA

IMA PRAYER

May everybody be happy
May everybody be healthy
May everybody be free from pain
May everybody be free from sorrow
May we be the healing cure
Beyond every greed & lure

FLAG SALUTATION

We, the members of Indian Medical Association
Stand here to salute our National Flag.
Its honour and glory shall be our light and strength
And its course shall be our course.
We pledge our allegiance to it and realizing our responsibilities
As the accredited members of this National organization,
We swear we will dedicate everything in our power
To see it fly high in the comity of Nations.
Jai Hind!

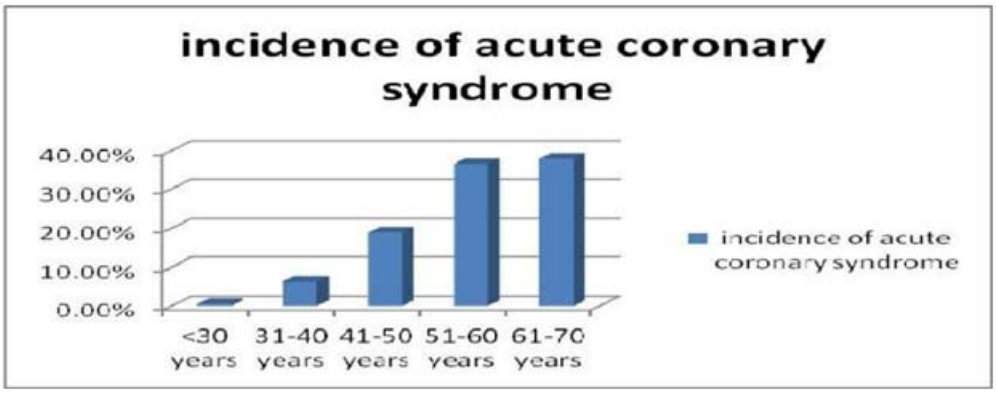
From the Editor's Desk

Dr. Shilpa Basu Roy
MBBS (Hons), MS (General Surgery), MCh (CTVS)
Associate Professor & Consultant Cardiothoracic, Vascular &
Transplant Surgeon, Institute of Postgraduate Medical Education and
Research & SSKM Hospital, Kolkata
E-mail : drshilpa@aol.com +919831480813

In this issue, we welcome you to the *Cardiac Club* of Annals. We are now at your doorstep & we are happy to educate, discuss & help on the core topic- "Acute Coronary Syndrome".

Acute Coronary Syndrome (ACS) is a term that usually means a person is experiencing one of two things namely a small or large heart attack, or the person is suffering severe chest pain called an unstable angina (a heart attack that has not yet occurred but is likely to happen).

A heart attack is further categorized as STEMI (classical elevations in the S-T segment of the ECG taken) and Non-STEMI (usually non specific changes in the ECG with respect to the S-T segment, but a rise in the Cardiac troponins thought to be an earliest marker in cardiac ischaemia). Indian patients with ACS have a higher rate of STEMI (61%) than do patients in high income countries which are ~ (15-25%). India has the highest burden of ACS in the world. The CREATE registry has provided contemporary data on 20,468 patients from 89 centers from 10 regions and 50 cities in India.



For a startup, The three most common risk factors for ACS were smoking (40%), high blood pressure (25%), diabetes (25%), dyslipidemia (10%). Mean age of such patients who suffered from one or more adverse cardiovascular outcomes due to Acute Coronary syndrome was 58 years with a male predominance. Warning signs that might be documented are chest pain or discomfort, which may involve pressure, tightness or fullness, pain or discomfort in one or both arms, the jaw, neck, back or stomach, Shortness of breath, feeling dizzy or lightheaded, sweating or generalised nausea.

The Door to needle time (DTNT), referred to the period of time- when the patient first reports to the emergency of a hospital to the time when he reaches the Cath Lab for evaluation & Intervention, is often 30 minutes for a thrombolysis with r–TPA agents & 90 mins for a percutaneous coronary intervention (PCI). In some cases, as I have dealt with, it would be a CABG (Coronary artery bypass grafting) surgery, the same to be done with or without a sternotomy, as these days Minimally Invasive Cardiac Surgeries (MICS) is much in demand.

I have always emphasized on Preventive Cardiology which supposedly is the cornerstone in the western countries & therefore, identification of the High Risk Population supplemented with a meticulous individual & Familial history taking, together with a series of a blood workup & radio diagnostics, would certainly aid to screen & prevent such catastrophes.

To conclude, "the heart attack" as mentioned in colloquials, is not a death statement, but rather it is a wake up call for all the beautiful people around.

INDIAN MEDICAL ASSOCIATION (HQs.)

(Registered under the Societies Act XXI of 1860)
Mutually Affiliated with the British & Nepal Medical Associations
I.M.A. House, Indraprastha Marg, New Delhi-110 002
Telephones: +91-11-2337 0009 (10 lines), 23378680 / +91-9999116375, 9999116376, Fax: +91-11-23379470
Website: www.ima-india.org ; Email: hsg@ima-india.org, np@ima-india.org

National President	Immediate Past National President	Honorary Secretary General	Honorary Finance Secretary
Dr. Sharad Kr. Agarwal	**Dr. Sahajanand Pd. Singh**	**Dr. Anilkumar J. Nayak**	**Dr. Shitij Bali**
+91-9717111942	+91-9334118698	+91-9825051333	+91-9910755660
shareshmadr8@gmail.com	sahajsurgery.phulwarisharif@gmail.com	draniljnayak@yahoo.co.in	shitij.bali@yahoo.com

Message for the Annual Annals on *"Acute Coronary Syndrome - IMA AMSCON 2023"*

Dear Colleagues,

I am honored to extend my warmest greetings to the esteemed members of the Indian Medical Association Academy of Medical Specialties (IMA AMS) on the occasion of the publication of the prestigious annual Annals on **Acute Coronary Syndrome** for the year 2023.

As the National President of the Indian Medical Association (IMA), I am immensely proud of the significant contributions made by our dedicated healthcare professionals, researchers, and experts in the field of cardiology. Acute Coronary Syndrome is a critical area of medical practice that requires constant research, innovation, and collaboration to enhance patient care and outcomes.

IMA AMS Headquarters has been steadfast in its commitment to advancing medical knowledge and promoting excellence in healthcare. The annual Annals serve as a testament to the unwavering dedication of our medical community to keep pushing the boundaries of medical science.

I congratulate the editorial team, authors, and everyone involved in the creation of this invaluable resource. Your efforts in compiling the latest research and clinical insights into Acute Coronary Syndrome will undoubtedly benefit healthcare professionals and patients alike.

The release of the Annals during the IMA AMSCON 2023 in Kozhikode, Kerala, adds an extra layer of significance to this publication. I encourage all attendees of the conference to take advantage of this opportunity to enrich their knowledge and engage in fruitful discussions on this critical topic.

I would like to express my gratitude to IMA Kozhikode Branch for hosting this important event and to IMA AMS Headquarters for their continued dedication to advancing medical education.

May the Annals on Acute Coronary Syndrome for the year 2023 inspire further research, foster collaboration, and ultimately lead to improved patient care. I look forward to witnessing the positive impact of this publication on our medical community.

Wishing you all a successful IMA AMSCON 2023 and a future filled with achievements in the field of medicine.

With warm regards,

Dr. Sharad Kumar Agarwal
National President, IMA

INDIAN MEDICAL ASSOCIATION (HQs.)

(Registered under the Societies Act XXI of 1860)
Mutually Affiliated with the British & Nepal Medical Associations
I.M.A. House, Indraprastha Marg, New Delhi-110 002
Telephones: +91-11-2337 0009 (10 lines), 23378680 / +91-9999116375, 9999116376, Fax: +91-11-23379470
Website: www.ima-india.org ; Email: hsg@ima-india.org

National President	Immediate Past National President	Honorary Secretary General	Honorary Finance Secretary
Dr. Sharad Kr. Agarwal	**Dr. Sahajanand Pd. Singh**	**Dr. Anilkumar J. Nayak**	**Dr. Shitij Bali**
+91-9717111942	+91-9334118698	+91-9825051333	+91-9910755660
np@ima-india.org	sahajsurgery.phulwarisharif@gmail.com	draniljnayak@yahoo.co.in	shitij.bali@yahoo.com

IMA/HSG/2023 13.10.2023

MESSAGE

Greetings from Indian Medical Association (HQs.)!

I am delighted to know that IMA Kozhikode Branch under the auspices of IMA AMS HQs. is organising IMA AMSCON 2023, the Annual National Conference of Indian Medical Association Academy of Medical Specialties on 27th & 28th October 2023 at Kozhikode. Kerala.

I am also delighted to know that IMA AMS HQs. is publishing the prestigious annual Annals on Acute Coronary Syndrome for the year 2023. Acute Coronary Syndrome often causes severe chest pain or discomfort. It is a medical emergency that needs a diagnosis and care right away.

By publishing Annals, IMA AMS is doing a great job, and I hope it will give its members access to information they can use. This will undoubtedly increase the members' expertise and knowledge of the most recent developments in medicine and medical technology.

This type of conference gives the members a chance to interact in a democratic, healthy, and meaningful manner about matters relating to the medical field and the nation's citizens' health-related issues.

As you all know that IMA Aao Gaon Chalen Project was relaunched on 25th June, 2023, all over the country by our Chief Patron Dr. Ketan Desai Sir. In this regard, I request all of you to adopt at least one village and conduct various activities on a regular basis under this project. You are also requested to send village adoption activity report alongwith photographs to IMA HQs. so that a compiled document can be created. The Awards for this noble cause will be given by IMA HQs. either after the completion of one year on 24th June 2024 or on the occasion of Doctors Day next year.

Though, IMA had conducted Organ Donation Awareness Camp in the month of August, 2023, to continue it further I request all of you to create awareness about the Organ Donation and motivate the donors to donate their organs after their death to save more lives.

I convey my best wishes to the Advisory Board of Annals and wish the Annual Conference a tremendous success.

Long Live IMA!!

Dr. Anilkumar J. Nayak
Hony. Secretary General, IMA

Aao Gaon Chalen
Let's give health to every Indian

"One for All – All for One".... a cohesive, collective, enhance, communicative approachto breakall sectorial walls and bring all clinicians at one platform to help in building a Healthy Nation

Dr R V ASOKAN
National President Elect
Indian Medical Association

Message

Thank you for asking me to give a message for the Annals of IMA AMS Hqs. It is a matter of great satisfaction that IMA AMS has been able to produce their exemplary document every year. I understand considerable efforts go into producing the Annals. It has been a prestigious publication for IMA. I congratulate Dr. Shipa Basu Roy and Dr. Rajeev Ranjan Prasad for venturing into producing this quality update eagerly awaited by the members.

I also note with great satisfaction that Dr. Pankaj Mutneja and Dr. Srirang Abkari have given exemplary leadership to IMA AMS this year. Their synchronised work in AMS has furthered the cause of continuing medical education and the relevance of IMA AMS.

I wish the publication all the best.

Dr R V ASOKAN
National President Elect IMA

14.09.2023
Punalur

Dr. Shitij Bali
Hony. Finance Secretary,
IMA

Message

It gives me immense pleasure to note that Kozhikode Branch of IMA is organising its Annual National Conference - AMSCON 2023 on 27th & 28th October, 2023 at Kozhikode and an Annals are being released to commemorate this great occasion.

Such a Conference affords an opportunity to meet and greet old friends and make new ones. It further provides a platform where all of us can deliberate about the challenges being faced by our profession, and devise ways and means to confront them in a suitable manner. I am sure, the interaction amongst the honored members will go a long way in updating the fast-growing advances and studies in the world of medicine and such exquisite experience can be utilized for the service of humanity. I feel that this conference will enable all specialists to come together in one platform.

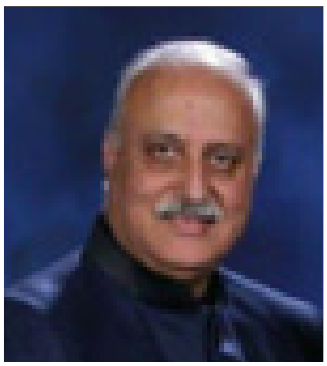
As we all know that Annals are important because it keeps the record in which events are arranged chronologically, year by year.

I am happy that IMA AMS is publishing the prestigious annual Annals on Acute Coronary Syndrome which will be a ready reckoner for the future generations.

I extend my warm greetings and felicitations to the organizers and the participants and wish the "AMSCON-2023" a grand success.

Long Live IMA!!

Dr. Shitij Bali
Hony. Finance Secretary, IMA



Dr. Pankaj Mutnej
National Chairman,
IMA AMS

Message

I am delighted to pen this message for the Annals of IMA AMS which will be released at AMSCON 2023 (27th & 28th October) at Calicut. Annals stand out as one of the most acclaimed publications of IMA. The stupendous effort which goes into it from conceptualizing the theme to making it a reality for the reader to go through is praise worthy. I congratulate the entire editorial team for the same.

At IMA AMS we have been working tirelessly to improve membership, open new State and Branch chapters, reactivate dormant chapters, create new course modules for IMA AMS courses and start new centers for the courses. We have visited many states, regularized Zonal conferences after the hiatus due to the covid-19 pandemic and started a newsletter showcasing the nationwide activities.

We are grateful to our Chief Patron Dr. Ketan Desai, for his guidance and blessings in all our activities. We thank Dr. Sharad Kumar Agarwal, National President IMA, Dr. Anil Kumar J Nayak, Hony. Secretary General, Dr. Shitij Bali, Hony. Finance Secretary for their support, encouragement and help at all times.

I must place on record the sincerity and dedication displayed by our dynamic Secretary Dr. Srirang Abkari in making IMA AMS a vibrant academic wing. He ensures coordination between all the team members, has innovative ideas and it has been truly a pleasure to be working with him.""I must congratulate the Kerala IMA AMS in general and IMA Kozhikode in particular for accepting to host the AMSCON at a short notice, patiently tiding over the delay due to the Nipah outbreak and making excellent preparations for a successful AMSCON.

My sincere thanks to all the National IMA AMS office bearers for their wholehearted support and cooperation, the State IMA AMS Office bearers for their excellent academic programs, Past National Chairmen and Secretaries of IMA AMS for laying a solid foundation for us to build upon and all the members of IMA AMS for being our pillars of strength.

I congratulate all the awardees for the honor conferred upon them for their sincere efforts and the Fellows who will receive fellowship of IMA AMS during the convocation.

Let us all take IMA AMS to new heights and create an academic body of international repute.

Long Live IMA!

Dr. Pankaj Mutneja
National Chairman,
IMA AMS

Dr. Nomeeta Shiv Gupta
Chairman Elect,
IMA AMS Hqrs

Message

Respected All,

I would like to congratulate IMA Kozhikode Branch for organizing IMA AMSCON-2023 at Calicut.

I am sure that it is going to be a huge success and also impart very good academics and all delegates will return home with new and academically revised messages.

I would also like to congratulate Dr Pankaj Mutneja and his team for putting in lots of efforts and releasing ANNALS of ACUTE CORONARY SYNDROME.

I wish the conference a great success.

Dr. Nomeeta Shiv Gupta
Chairman Elect, IMA AMS Hqrs

Dr. Srirang Abkari
Hony. Secretary
IMA AMS HQs.

Message

I am delighted to witness yet another issue of Annals of IMA AMS being published. It has been a remarkable journey right from the birth of an idea for such an important topic to finally ensure that it has seen the light of the day. "Acute coronary syndrome is a life-threatening medical condition which has myriad presentations, is often misdiagnosed and appropriate treatment is denied. Time is precious and any delay may mean danger of complications and even death. While our understanding of the subject, newer modalities of diagnosis and treatment have evolved, it will be meaningful only if the patient benefits from them in a timely fashion. The challenges are greater in rural areas where access to healthcare still has many limitations. "It is our endeavour at IMA AMS to spread the awareness of such clinically important medical conditions so that we save lives. This year we have tried to have eminent authors from all across the country and our efforts have paid off. The knowledge and vast experience of these distinguised clinicians will surely be of immense benefit for the reader. I thank each author for thier time and effort in enriching this issue of Annals.

We are fortunate to have such a visionary leader and I sincerely express my gratitude to our Chief Patron Dr. Ketan Desai for his blessings and guidance.

I would like to thank our dynamic National President Dr. Sharad Kumar Agarwal for his unstinted support and constant encouragement, our dedicated Hony. Secretary General Dr. Anil J Nayak for his invaluable advice and suggestions and our astute Hony. Finance Secretary Dr. Shitij Bali for all the help in financial matters.

Our beloved National Chairman Dr. Pankaj Mutneja leads our team from the front and his patience, hardwork and dedication are truly inspiring. I profusely thank all the National and State office bearers of IMA AMS for their best wishes, cooperation and sincere work for our academic wing. A special thanks to our Editors for their support and enthusiasm. In conclusion, I would like to quote Albert Einstein who said "Wisdom is not a product of schooling but of the lifelong attempt to acquire it." Let us therefore make learning a continual and integral part of our life and ensure that we can help humanity with our knowledge and skill.

Long Live IMA!

Dr. Srirang Abkari
Hony. Secretary
IMA AMS HQs.

NATIONAL OFFICE BEARERS OF IMA AMS

Chief Patron

Dr. Desai Ketan Dhirajlal
Past National President IMA Hqrs

Dr. Sharad Kumar Agarwal
National President
IMA Hqrs

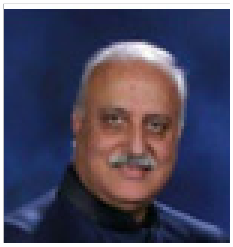
Dr. Sahajanand Prasad Singh
Imm. Past National President
IMA Hqrs

Dr. R. V. Asokan
National President Elect
IMA Hqrs, 2023-2024

Dr. Anilkumar J Nayak
Hony. Secretary General
IMA Hqrs

Dr. Shitij Bali
Hony. Finance Secretary
IMA Hqrs

NATIONAL IMA AMS HQRS



Dr. Pankaj Mutneja
National Chairman

Dr. Nomeeta Shiv Gupta
Chairman Elect

Dr. Nibedita Pani
Vice Chairman

Dr. Srirang Abkari
Hony. National Secretary

Dr. D. Shekhar Reddy
Joint Secretary, IMA AMS Hqrs

Dr. Hiren S Kothari
Joint Secretary, IMA AMS Hqrs

Dr. Rajeev Goel
Joint Secretary, IMA AMS Hqrs

Dr. Shilpa Basu Roy
Editor (Annals), IMA AMS Hqrs

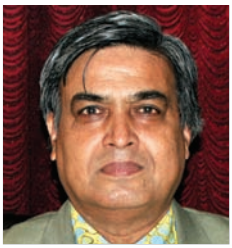
Dr. Rajiv Ranjan Prasad
Executive Editor (Annals), IMA AMS Hqrs

NATIONAL CHAIRPERSONS

Dr. M. Bhaskaran
Kerala 2008-2009

Dr. O.P. Tewari
Uttar Pradesh 2009-2010

Dr. A. Zameer Pasha
Tamil Nadu 2010-2011



Dr. Surendra Daga
West Bengal 2011-2012

Dr Ravi Wankhedkar
Maharashtra 2012-2013

Dr.Satish Kumar Raj
Uttar Pradesh 2013-2014

Dr. Ajoy Kumar Singh
Jharkhand 2014-2015

Dr. Kiranshankar Wasudeo Deoras
Chhattisgarh 2015-2016

Dr. Joseph Mani
Kerala 2016-2017

Dr. Madhuchanda Kar
West Bengal 2017-2018

Dr. Natwar Sharda
Madhya Pradesh 2018-2019

Dr. M. S. Ashraf
Tamil Nadu 2019-2020

Dr. D. Sreehari Rao
Andhra Pradesh 2020-2021

Dr. G.N. Prabhakara
Karnataka 2021-2022

NATIONAL SECRETARIES

Dr. G. Suresh
(2008)

Dr. B. N. Reddy
(2009-2010)

Dr. M.S. Haribabu
(2011-2012)

Dr. E. Prabhavathi
(2013-2014)

Dr. P. Pulla Rao
(2015-2016)

Dr. V. S. Rao
(2017-2018)

Dr. Mohan Gupta
(2019-2020)

Dr. Sanjeev Singh Yadav
(2021-2022)

State Chairmen & Secretaries of IMA AMS

Dr. P.A. Ramani
Chairman IMA AMS
AP State

Dr. G.T. V. Ramesh
Secretary IMA AMS
AP State

Dr. Sarbeswar Borah
Chairman IMA AMS
Assam State

Dr. Pradip Kumar Sarma
Hony. Secretary IMA AMS
Assam State

Dr. D. P. Singh
Chairman IMA AMS
Bihar State

Dr. Rajiva Ranjan
Hony. Secretary IMA AMS
Bihar State

Dr. Rabin Chakraborty
Chairman IMA AMS
Bengal State

Dr. Sekhar Chakraborty
Hony. Secretary IMA AMS
Bengal State

Dr. Har Vinod Jindal
Chairman IMA AMS
Chandigarh State

Dr. Aditya Jindal
Hony. Secretary IMA AMS
Chandigarh State

Dr. Rajesh Kumar Sinha
Chairman IMA AMS
Chhattisgarh State

Dr. Sangeeta Sinha
Secretary IMA AMS
Chhattisgarh State

Dr. R.K. Sinha
Chairman IMA AMS
Delhi State

Dr. Sanjiv Kumar
Hony. Secretary IMA AMS
Delhi State

Dr. Vidyut J. Desai
Chairman IMA AMS
Gujarat State

Dr. Dilip B. Gadhvi
Vice Chairman IMA AMS
Gujarat State

Dr. Ajay Arora
Chairman IMA AMS
Haryana State

Dr. Vandana Narula
Secretary IMA AMS
Haryana State

Dr. Abir Kumar Chakraverty
Chariman IMA AMS
Jharkhand State

Dr. V. K. Pandey
Secretary IMA AMS
Jharkhand State

State Chairmen & Secretaries of IMA AMS

Dr. Geeta J. Doppa
Chairman IMA AMS
Karnataka State

Dr. Suresh M. Kagalkar
Hon. Secretary, IMA AMS
Karnataka State

Dr. R. C. Sreekumar
Chairman, IMA AMS
Kerala State

Dr. Jose Kuruvilla
Hon. Secretary IMA AMS
Kerala State

Dr. Santosh Khadatare
Chairman, IMA AMS
Maharashtra State

Dr. Hemant Sonanis
Hony. Secretary IMA AMS
Maharashtra State

Dr. Amit Ganguli
Chairman IMA AMS
MP State

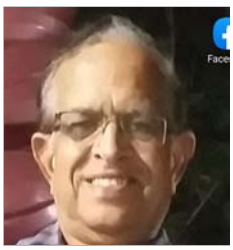
Dr. Amarendra Pandey
Secretary, IMA AMS
MP State

Dr. Bharat Panigrahy
Chairman IMA AMS
Orissa State

Dr. Ritanjali Mishra
Hon. Secretary IMA AMS
Orissa State

Dr. Ashok Uppal
Chairman of IMA AMS
Punjab State

Dr. Harvinder Singh Heer
Secretary IMA AMS
Punjab State



Dr. N.D. Misra
Chairman IMA AMS
Rajasthan

Dr. Kannan
Chairman IMA AMS
Tamil Nadu State

Dr. V. Rajesh Babu
Hon. Secretary IMA AMS
Tamil Nadu State

Dr. K. Vasantha Kumari
Chairman IMA AMS
Telangana State

Dr. V. Janaki
Secretary IMA AMS
Telangana State

Prof. Dr. Shiva Kant Misra
Chairman IMA AMS
UP State

Dr. Mandeep Singh
Secretary IMA AMS
UP State

Dr. S. P. Gupta
Chairman, IMA AMS
UA Chapter

Dr. Nakshatra Agarwal
Hony. Secretary IMA AMS
UA State

Organizing Committee - IMA AMSCON 2023

CHIEF PATRON:

DR.DESAI, KETAN DHIRAJLAL, PAST NATIONAL PRESIDENT IMA HQRS

NATIONAL IMA TEAM

DR. SHARAD KUMAR AGARWAL, NATIONAL PRESIDENT IMA HQRS
DR. R. V. ASOKAN, NATIONAL PRESIDENT ELECT IMA HQRS, 2023-2024
DR. SAHAJANAND PD. SINGH, IMM. PAST NATIONAL PRESIDENT IMA HQRS
DR. ANILKUMAR J. NAYAK, HONY. SECRETARY GENERAL IMA HQRS
DR. SHITIJ BALI, FINANCE SECRETARY IMA HQRS
DR. JAYESH M. LELE, NATIONAL VICE PRESIDENT 2022-23
DR. SACHCHIDANAND KUMAR, NATIONAL VICE PRESIDENT 2022-23
DR. SHAILESH H. SHAH, NATIONAL VICE PRESIDENT 2022-23
DR. DAGGUMATI SREE HARI RAO, NATIONAL VICE PRESIDENT 2022-23
DR. R. GUNASEKARAN, NATIONAL VICE PRESIDENT 2023-24
DR. SURESH GUTTA, NATIONAL VICE PRESIDENT 2023-24
DR. ASHOK SHARDA, NATIONAL VICE PRESIDENT 2023-24
DR. SHIVKUMAR UTTURE, NATIONAL VICE PRESIDENT 2023-24
DR. PRABHAKAR MUNISH, HONY.JT.SECRETARY
DR. PRAKASH LALCHANDANI, HONY.JT.SECRETARY
DR. M. VENKATCHALAPATHY, HONY.JT.SECRETARY
DR. PRADEEP KUMAR NEMANI, HONY.JT.SECRETARY, CALCUTTA
DR. MAHENDRA NATH THAREJA, HONY.JT.FIN.SECRETARY
DR. SARBARI DUTTA, HONY. JT. FINANCE SECRETARY STATIONED AT CALCUTTA , IMA
DR. THAKUR PADMANABHAN, HONY.ASST.SECRETARY
DR. PARAMJIT SINGH MAAN, HONY. ASST. SECRETARY

NATIONAL ADVISORS:

DR.ARULRHAJ, S.,PAST NATIONAL PRESIDENT
DR.ROY, SUDIPTO,PAST NATIONAL PRESIDENT
DR.MALIK, SANJIV, PAST NATIONAL PRESIDENT
DR.KUMAR, AJAY, PAST NATIONAL PRESIDENT
DR.ADHAO, ASHOK, PAST NATIONAL PRESIDENT
DR. SAMARAM, GOPARAJU, PAST NATIONAL PRESIDENT
DR. VINAY AGGARWAL, PAST NATIONAL PRESIDENT
DR. G. K. RAMACHANDRAPPA, PAST NATIONAL PRESIDENT
DR. K. VIJAY KUMAR, PAST NATIONAL PRESIDENT
DR. PATEL, JITENDRA B., PAST NATIONAL PRESIDENT
DR. A. MARTHANDA PILLAI, PAST NATIONAL PRESIDENT
DR. S. S. AGARWAL, PAST NATIONAL PRESIDENT
DR. WANKHEDKAR, RAVINDRA SITARAM, PAST NATIONAL PRESIDENT
DR. SANTANU SEN, PAST NATIONAL PRESIDENT
DR. RAJAN SHARMA, PAST NATIONAL PRESIDENT
DR. J.A. JAYALAL, PAST NATIONAL PRESIDENT

NATIONAL IMA AMS TEAM:

DR. PANKAJ MUTNEJA, CHAIRMAN, 2022-23
DR. NOMEETA SHIV GUPTA, CHAIRMAN, 2023-24
DR. NIBEDITA PANI, VICE-CHAIRMAN
DR. SRIRANG ABKARI, HONY.SECRETARY
DR. D. SHEKHAR REDDY, HONY. JOINT SECRETARY,-2022-24
DR. HIREN S. KOTHARI, HONY. JOINT SECRETARY,-2022-24
DR. RAJEEV GOEL, HONY. JOINT SECRETARY,-2022-24
DR. SHILPA BASU ROY, HONY. EDITOR (ANNALS),-2022-24
DR. RAJIV RANJAN PRASAD, EXECUTIVE EDITOR (ANNALS), 2022-2024

TEAM OF AMSCON-2023

STATE IMA

DR. SULPHI NOOHU, PRESIDENT IMA KERALA
DR. SAMUEL KOSHY, IMM. PAST PRESIDENT IMA KERALA
DR. JOSEPH BENEVAN, HONY. SECRETARY IMA KERALA

STATE IMA AMS

DR. SREEKUMAR R.C., CHAIRMAN IMA AMS KERALA
DR. JOSE KURUVILLA KOKKAT, SECRETARY IMA AMS KERALA

IMA KOZHIKODE

DR. VENUGOPALAN. B, BRANCH PRESIDENT
DR. K. SANDHYA KURUP, BRANCH SECRETARY
DR. ASHRAF T.P., TREASURER
DR. PRADEEP KUMAR V. G., ORGANISING CHAIRMAN
DR. SANKAR MAHADEVAN, ORGANISING SECRETARY
DR. AJIT BHASKAR, CO-CHAIRMEN
DR. ANNEN N KUTTY, CO-CHAIRMEN
DR. CHANDRASEKHARAN S, JOINT ORG. SECRETARY
DR. LILABI M. P., AMS CHAIRPERSON
DR. ANAND SUBRAMANYAN, AMS SECRETARY

From Secretary's Desk

Dr. Srirang Abkari
National Secretary IMA AMS

I am really honored as Secretary IMA AMS to communicate with you through these Annals. IMA Academy of Medical Specialities was established in the year 1979 with the following objectives:

- To provide a forum to Specialists and Super-specialties of all branches of Medicine to discuss multi-disciplinary matters of academic interest
- To promote and encourage unity among the members of IMA
- To enhance image of IMA
- To increase Life Membership and of Fellowship of IMA AMS
- To update all the members of IMA of the recent advances in the field of Medicine and allied subjects
- To conduct C.M.Es all over India
- To conduct various Specialty and sub-specialty courses

The theme for this issue of Annals is "Acute Coronary Syndrome." Being a very common and important medical problem I am sure it will immensely benefit all the members and help in saving patient's lives. I sincerely thank all the eminent authors for contributing to this issue.

MEMBERSHIP

As of 15th October following are the details of membership, chapters and fellows:

- 20 State Chapters
- 198 Branch Chapters
- 17,485 Life Members
- 2582 Fellows as on date

The State wise details of Life members and Fellowships are as follows…

TOTAL as on 15-10-2023			
S. No	State Name	Life Members & Associate LM	Fellows of IMA AMS
1	ANDHRA PRAEDESH	489	57
2	ASSAM	267	41
3	BENGAL	832	235
4	BIHAR	565	259
5	CHANDIGARH	139	19
6	CHATTISGARH	196	25
7	DELHI	711	239
8	GUJARAT	367	51
9	GOA	3	3
10	HARYANA	1402	225
11	HIMACHAL PRADESH	2	1
12	JAMMU & KASHMIR	12	3
13	JHARKHAND	151	54
14	KARNATAKA	1033	161
15	KERALA	3021	142
16	MADHYA PRADESH	182	46
17	MANIPUR	10	5
18	MAHARASHTRA	2618	105
19	ORISSA	298	46
20	OVERSEAS	59	54
21	PUNJAB	246	69

22	PONDICHERRY	4	3
23	RAJASTHAN	103	28
24	TAMILNADU	1324	326
25	TELAGANA	1229	160
26	TRIPURA	4	4
27	UTTAR PRADESH	1837	216
28	UTTARANCHAL	381	5
	Total	**17485**	**2582**

Life Memberships & Fellowships received from 1st Jan 2023 to till date

Life Memberships - 1057
Fellowships (for 2023) - 29

New State Chapters of IMA AMS:

1. Chandigarh State Chapter was opened on 9th April 2023.

New Wing of IMA AMS

New Branches of IMA A MS:

1. Madhya Pradesh State Chapter has opened "**Chhindwara"** New Local Branch Chapter. Branch Chapter is inaugurated on 8th January 2023.
2. Kerala State Chapter has opened **"Thodupuzha"** New Local Branch Chapter. Branch Chapter is inaugurated on 12th January 2023.
3. IMA AMS Wing of IMA Hyderabad City Branch was inaugurated on 29th March 2023, by Dr. Sharad Kumar Agarwal, National President IMA Hqrs
4. Maharashtra State Chapter has formed 8 New Branch Chapters: **1. Satara 2. Karad 3. Warananagar 4. Pandharpur 5. Bhandara 6. Tumsar 7. Atpadi 8. Nashik Road**
5. IMA AMS WING **Nandyal,** Andhra Pradesh

IMA AMS Accounts:

All accounts of IMA AMS Hqrs are maintained in centralized Tally, accounts updated monthly and submitted to IMA Hqrs. Bank Statements of IMA AMS Accounts and Audited Balance Sheet for the year 1st April 2022 to 31st March 2023 and Budget for the year -2023 submitted to IMA Hqrs.

The Academy shall have the following categories of membership:

1. **Life Members:** All Members of IMA possessing (i) Postgraduate qualifications recognized by the Medical Council of India or (ii) any post-graduate qualification awarded by National Medical Commission or (ii) any IMA Member possessing FCGP by passing the Examination.

2. **Overseas Members:** Overseas members shall be those members who are living outside India and fulfill the eligibility clause for either Life Membership or Associate Life Membership.

3. **Honorary Members:** Honorary Members shall be those on whom membership is conferred by the Academy Honoris Causa. The number of such members shall not exceed 10 at any given time.

The Academy shall have the following categories of Fellows:

1. Founder Fellows: whose total number shall be 75 only from all specialities and/or shall not exceed 10% of Life Membership of the Academy, elected from amongst Life Members as on 30th September, 1982.

2. Fellows: whose total number shall not exceed 1/3rd of the total membership of the Academy at any time and they should be Life Member of the Academy. New Life member is eligible to become a fellow in the same year of convocation conducted by IMA AMS H.Qrs once in a year. , Certificates can be issued after convocation only along with absent fee.

3. Honorary Fellows: Such Fellowship may be bestowed on eminent persons who have excelled themselves in Medical and Allied Sciences, to recognise their exceptional merit without any payment of Fellowship fee but their number should not be more than two persons per year.

IMA AMS Fees details and Mode of Payment details are given below:

1. Life Membership Fee : Rs 250/- + 45 (18% GST) Total Rs. 295/-
2. Overseas members (effective from 1-10-1988): U.S. Dollars 250 (No Share)
3. Fellowship Fee : Rs. 7500/- + 1350 (18% GST) Total Rs. 8830/-
4. Fellowship fee of Overseas Members U.S. Dollars 400 (No Share)

Mode of Payment: DD/Cheque in favour **of "IMA AMS"** payable at Hyderabad.

Required Documents: 1. IMA Life Membership Certificate 2. MBBS and PG Degree/Diploma Certificates 3**.** MCI Registration Certificate 4. Passport size colour photo.

Eligibility Criteria for IMA AMS Fellowship:

Nomination for Fellowship of the Academy shall be of Life Members who comply with the following minimum requirements:

- Life Membership of IMA
- Life Membership of the Academy Medical Specialities (IMA AMS)
- Practice in the Specialty of at least 10 years.

- Academic achievement, professional distinction, publication of Scientific Papers, research and teaching experience etc.
- Uninterrupted continuance of Membership/Life Membership of IMA after election/selection as Fellow, failing which, the Fellowship shall be liable to be withdrawn.
- All other requirements which may be prescribed by the Governing Council from time to time for the guidance of the Credential Committee.

Professorship:

Hon Professorships are being given to eligible candidates, on application for professorship. The Associate Life members are not eligible for Professorship and so also those who did not complete 25 years of postgraduation. IMA Professorships are now awarded only on approval by IMA Accreditation Council, New Delhi. Interested members are requested to send filled application form along with required documents to Hon Secretary General, IMA Hqrs, New Delhi address and one copy to Hon Secretary, IMA AMS Hqrs, Hyderabad on or before 31st July every year. The professorships are given on Teacher's Day, 5th September every year.

Updated Guidelines for Honorary Professorship of IMA AMS:

The applicant shall possess:

i. Registered MD / DM, MS / DCH or equivalent qualifications conferred by National Board of Examinations.
ii. Minimum 15 years of teaching experience of which 5 years should be as a recognized Postgraduate Teacher Doctoral Degree Supervisor or 15 years of Professional Experience in the concerned specialty after acquiring Postgraduate Degree / Diploma qualification as the case may be.
iii. Minimum 3 scientific publications in Indexed / Peer Reviewed National / International Journals of repute preferably Scopus, PubMed, Medler, Web of Science etc.
iv. Must be a member of IMA AMS for 10 years
v. Contributions for the advancement of Medical Education and active participation in IMA AMS, and have delivered Orations, accredited lectures or served as faculty in IMA AMS events.
vi. Willing to serve in the dissemination of knowledge and skills through IMA AMS platform.

IMA AMS Courses

IMA AMS conducts courses in medical specialties with sole intention of improving knowledge and skills of medical professionals in their respective fields. The duration of course in general is one year. These courses, however, are not recognized by MCI and Doctors undertaking these courses are not permitted to claim themselves as specialist or to display these certificates as additional qualification.

While conducting the courses the following pattern of revenue sharing has been adopted.

1. 30% share to IMA AMS Headquarters
2. 40% share to Academic centre (Institute/Hospital)conducting the course
3. 30% share IMA AMS State for its maintenance

Following is the provisional list of courses being offered by IMA Academy of Medical Specialities

1. Infertility
2. Fluorescein Angiography
3. Laser Photocoagulation in Retinal problems
4. Excimer, Laser & Lasik Surgery
5. Phacoemulsification
6. Training in Noninvasive Cardiology, Echocardiography and TMT
7. Critical Care in Cardiology
8. Advanced Micro-Surgery of Ear
9. Functional Sinus Endoscopy
10. Laser in ENT
11. Rhinoplasty
12. Joint Replacement
13. Arthroscopy
14. Spine Surgery
15. Upper GI Endoscopy - a. Basic b. Advanced
16. Laparoscopy - a. Basic b. Advanced
17. Rheumatology
18. Preventive Cardiology
19. Breast Oncology Surgery
20. G.I. Oncology Surgery
21. Head & Neck Oncology Surgery
22. Gynae Oncology Surgery
23. Oncology Pathology
24. Oncology Anaesthesiology
25. Medical Oncology
26. Uro-Oncology Surgery
27. Pediatric Hemato-Oncology
28. Bone Marrow Transplantation
29. Oncology Radiology
30. Cancer Re-Constructive Surgery
31. Interventional Pulmonology and Thoracic
32. Oncology
33. Onclology Orthopedics
34. Interventional Radiology
35. Pathology
36. Neuro Critical Care
37. Molecular Diagnostics

IMA Shall develop Courses Accredited by IMA Accreditation & Academic Council

In the first phase following subjects shall be included,

1. Primary Cardiology
2. Diabetology
3. Hypertension
4. Coronary Heart Disease
5. Emergency Practice
6. BCLS
7. ACLS
8. Blindness Control
9. Infectious Diseases
10. Vaccination
11. Occupational health
12. Asthma and COPD
13. Cancer
14. Emergency Medicine
15. Child Sexual Abuse
16. Vector Borne Diseases
17. Antenatal Care
18. AMR
19. Infection Control Strategy
20. Basic Surgical skills etc

As of now the following States are conducting Fellowship Courses

Andhra Pradesh, Karnataka, Delhi & Telangana. This year new centers have been approved for IMA AMS courses.

How to conduct Fellowship Courses in Respective States

All Long term fellowships Courses duration: 1 year

All Short term Fellowships Courses duration: 4 Months

Eligibility criteria:

Must be IMA Life Member and IMA AMS Life Member**,** Post-Graduation completed in their respective field.

Course Fee: Fee structure depends on respective State, Course fee Share as 30% towards Headquarters share, 40% towards Hospitals or training Centre's share and 30% IMA AMS Respective State Share.

- About 20 students can be admitted as per the facilities and infra-structure available in the Centre conducting the course. (More students may be permitted, subject to the facilities and infra-structure available).
- IMA AMS State Branch shall assess the facilities and infra-structure available in the Centre.
- Two Theory & two Practical Classes have to be conducted every month i.e. one class a week by the respective Centre. Due importance shall be given for clinical sessions.
- A minimum of 80% attendance shall be maintained by students.
- Monthly attendance and updates about classes shall be sent to IMA AMS of respective State.
- One assignment quarterly i.e. one every 3 months may be arranged for students.
- **"Theory examination"** shall be conducted by IMA AMS of respective State on day One. Theory paper will be corrected by the concerned faculty, who had conducted the courses.
- **"Practical examination"** i.e. Clinicals, log book discussions and general viva shall be conducted by respective Centre on day Two.
- Examination results shall be announced within one week of the exam and shall be informed to the Hqrs.
- A convocation fee has to be collected from the students by IMA AMS Chapter of respective State.
- State shall conduct graduation ceremony and invite AMS National Chairman & National Secretary for this function. IMA AMS Hqrs will be responsible for arranging the certificates for distribution to the students.

The pattern of question paper will be as follows:

THEORY EXAMINATION (TOTAL 100 Marks) consisting of

- Two long Questions each carrying 20 MARKS.
- Six short Questions each carrying 5 Marks
- Thirty MCQ's each carrying 1 Mark (30 MCQ'S)

PRACTICAL EXAMINATION (TOTAL 250) consisting of

One long case carrying 5O MARKS

- Two short cases each case carrying 25 Marks
- 10 Spotters each Spotter Carrying 5 marks
- Log Book, 10 different Cases, each case carrying 5 Marks
- General Viva carrying 50 marks

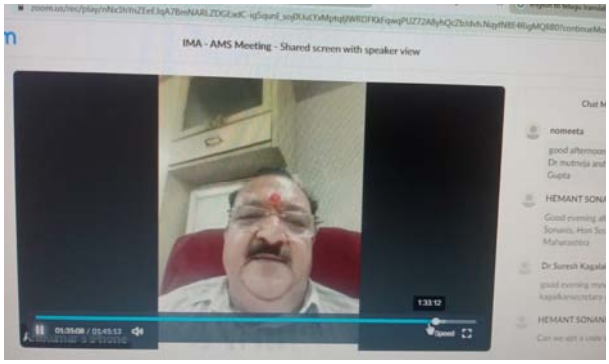
If any State is willing to conduct Fellowship Courses, kindly provide the following details:

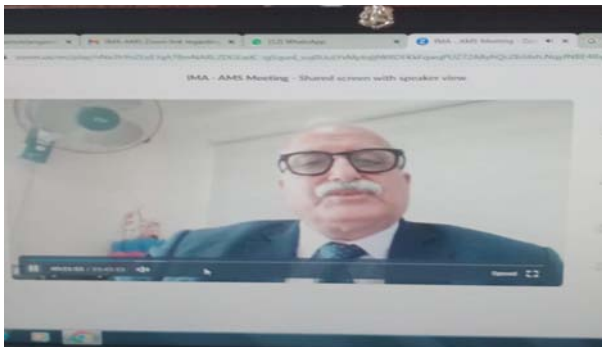
1. Modules of the Training
2. The time of the training period
3. The Name of Hospital/Center and Hospital History
4. Faculty Details

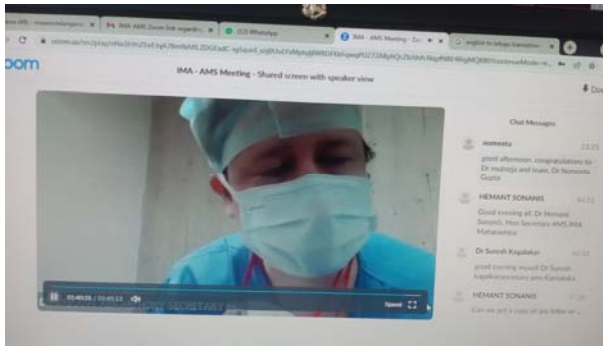
Kindly send your consent letter & above details to IMA AMS Hqrs. After the provision of the above information, a team will inspect the facilities to grant permission as per the Constitutional Guidelines of IMA AMS Hqrs.

The main Activities of IMA AMS during this year are as under.

1. **On 12th Jan 2023:** State Chairman & Secretaries Meeting of IMA AMS Hqrs was held on 12th Jan 2023 in a Virtual Way, from 4:00 PM to 5:30 PM, organized by IMA AMS Hqrs, Hyderabad. Total 25 Members have attended from various States across the country. The meeting was presided over by Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, and welcome address by Dr. Srirang Abkari, Hony. Secretary, IMA AAMS Hqrs, Message by Dr. Sharad Kumar Agarwal, National President IMA Hqrs, Dr. Anilkumar J Nayak, Hony. Secretary General, IMA Hqrs, Dr. Nomeeta Shiv Gupta, Chairman Elect 2023-2024, IMA AMS Hqrs. The Main agenda of this meeting was increasing Membership, Formation of District Branches and State wise Monthly Activities of IMA AMS.







2. **On 18th Jan 2023:** National President IMA Hqrs, Dr. Sharad Kumar Agarwal gave a prime talk on Facebook live on 18th Jan 2023. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.
3.

4. **On 25th Jan 2023:** IMA AMS National Chairman, Dr. Pankaj Mutneja visited IMA AMS Head Hqrs Hyderabad. He was warmly received and welcomed into the IMA AMS Hq office.




There were discussions regarding:

- **Fee Structure of IMA AMS Life Membership:** Now IMA AMS Fee of Rs.250/-+18% GST Total Rs. 295/- & Fellowship Fee of Rs. 7500/-+18% GST Total Rs. 8850/-
- Governing Council Meeting
- 4 – National Zonal Conference's (East, West, North & South)
- National AMSCON-2023
- Monthly CMEs all over India (In Association with State Chapters)
- Conducting Various Speciality Courses of IMA AMS
- Union Territories and small State Branches to start an AMS State Chapter and formation of District Branches.
- Budget for the year 2023

5. **On 27th & 28th Jan 2023:** Dr. Pankaj Mutneja, National Chairman and Dr. Srirang Abkari, Hony. Secretary of AMS participated in the IMA President and Secretary of States & Office Bearers meet on 27th & 28th January 2023, Delhi. Dr. Srirang Abkari, Secretary Presented IMA AMS Hqrs Activity Report.


6. **On 18th & 19th Feb 2023:** Dr. Pankaj Mutneja, National Chairman participated in **GLOBALCON-2023** at Jabalpur, MP State. Dr. Pankaj Mutneja was the Chief Guest at the Inauguration Ceremony. Dr. Pankaj Mutneja, in his Inaugural address stressed on the changing scenario of the medical profession and the challenges we are facing and likely to face in coming times notably violence against doctors. The IMA Headquarters is fully aware of these challenges and is regularly in touch with the concerned authorities at the center to pursue these issues.


7. IMA AMS Hqrs for the first time launched a NEWSLETTER and the 1st Edition of **IMA AMS E-Newsletter** of January was released. Subsequently monthly newsletters released and posted on the AMS website: https://ima-ams.org
It showcases the activities of the IMA AMS Hqs, various State and Branch chapters, has updates on memberships, recognizes states with best membership for the month, has image challenge quiz for readers. It has been very well received by the readers.

8. **From14th to 16th March 2023:** IMA HQRS Audit team led by Dr. Anand Prakash, National Joint Secretary IMA visited AMS HQRS from14th to 16th March 2023. We had a very good interaction and received valuable suggestions. We thank the entire team for their visit.

9. **27th March 2023:** Protest Day was observed by IMA AMS Hqrs in support of Rajasthan IMA against Rajasthan Government Draconian Right on 27th March 2023.

10. **29th March 2023:** Dr. Sharad Kumar Agarwal, National President visited the IMA AMS HQs office at Hyderabad. He was warmly welcomed. The 2nd IMA AMS Newsletter was released. He interacted with us and gave his valuable advice. Dignitaries from IMA TS were present. TEAM IMA AMS thanks you for the visit and your guidance. We are grateful to our National President for his support and encouragement.





11. Dr. Sharad Kumar Agarwal, National President IMA visited the IMA HYDERABAD CITY and inaugurated **"IMA AMS Wing"** on 29th March 2023. Thank you Sir for your presence and encouragement.


12. **On 6th April 2023:** Dr. Srirang Abkari, Hony. Secretary IMA AMS Hqrs attended Finance standing Committee meeting held on 6th April 2023 at Delhi. Bank Statements of IMA AMS Accounts and Provisional Balance Sheet for the month of 1st Oct 2022 to 31st March 2023 submitted to IMA Hqrs for FSC Meeting.
13. **On 7th April 2023:** IMA SAMARPAN DIVAS- WALKATHON FROM MAULANA AZAD MEDICAL COLLEGE TO IMA HOUSE NEW DELHI "For the Health of People of India" National Leaders participated on "**WORLD HEALTH DAY"- SAMARPAN DIVAS"** on 7th April 2023.



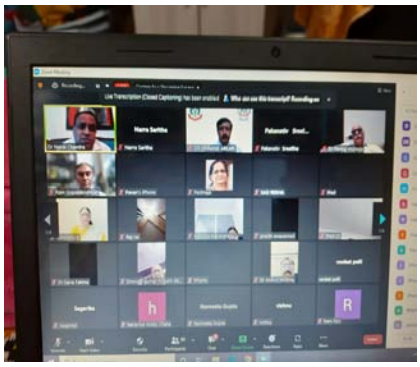
14. **On 9th April 2023:** National **IMA AMS North Zonal Conference** was held on 9th April 2023 at Chandigarh. Inauguration by Dr. Pankaj Mutneja, Chairman AMS Hqrs. Dr. Rajan Sharma, Past National President IMA Hqrs, Dr. Nomeeta Shiv Gupta, Chairman Elect, AMS Hqrs, Dr. Srirang Abkari, Secretary AMS Hqrs, Dr. Ramneek Sharma, President IMA Chandigarh, Dr. Vivek Malhotra, Secretary IMA Chandigarh, Dr.

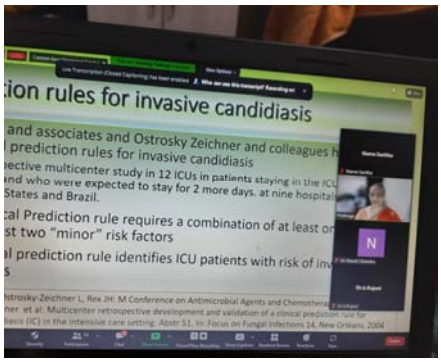
Rajeev Goel, Joint Secretary AMS Hqrs, Dr. Rajiv Ranjan Prasad, Executive Editor (Annals) AMS Hqrs, Dr. Ramneek Singh Bedi, and Dr. Har Vinod Jindal, New Chairman AMS Chandigarh State were present. This programme was conducted by IMA & IMA AMS Chandigarh Branch. Scientific programme started from 9:30 to 12:30 PM. National and State Leaders participated in this program. The **inaugural function** was conducted from 12:30 pm to 2:00 pm.

15. **On 9th April 2023:** 38th Governing Council Meeting of IMA AMS was held on 9th April 2023, at Chandigarh State, Dr. Sharad Kumar Agarwal, National President, IMA Hqrs, Dr. R. V. Asokan, National President Elect, IMA Hqrs, Dr. Shitij Bali, Hony. Finance Secretary IMA Hqrs attended on virtually. The meeting was presided over by Dr. Pankaj Mutneja National Chairman IMA AMS. Dr. Nomeeta Shiv Gupta, Chairman Elect IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs, Dr. Rajeev Goel, Joint Secretary, IMA AMS Hqrs, Dr. Rajiv Ranjan Prasad, Executive Editor, (Annals) IMA AMS Hqrs are attended this meeting. The main agenda meeting included discussion on AMSCON-2023, Zonal Conferences, IMA AMS Courses, Life Membership fee and Fellowship fee structure, Membership drive, State IMA AMS Activities, Advertisements for Newsletter and Annals, Opening of State and Local Branches of IMA AMS, Annals of IMA AMS, New Software and computer for IMA AMS Hqs office and Proposal for 4 Vice Chairman (1 from each zone) and Treasurer.

16. IMA Chandigarh State Chapter has opened **"IMA AMS Chandigarh State Branch"** inaugurated on **9th April 2023** with 108 Life Members of IMA AMS Chandigarh, Inaugurated by Dr. Pankaj Mutneja, Chairman AMS Hqrs, Dr. Rajan Sharma, Past National President IMA Hqrs, Dr. Nomeeta Shiv Gupta, Chairman Elect, AMS Hqrs, Dr. Srirang Abkari, Secretary AMS Hqrs, Dr. Ramneek Sharma, President IMA Chandigarh, Dr. Vivek Malhotra, Secretary IMA Chandigarh, Dr. Rajeev Goel, Joint Secretary AMS Hqrs, Dr. Rajiv Ranjan Prasad, Executive Editor (Annals) AMS Hqrs, Dr. Ramneek Singh Bedi, and Dr. Har Vinod Jindal, New Chairman AMS Chandigarh State and Dr. Parmjit Singh, New Secretary of IMA AMS Chandigarh State were present.

17. **On 15th & 16th April 2023:** Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs & Dr. Srirang Abkari, Hony. Secretary IMA AMS Hqrs attended Central Working Committee meeting held at Ahmedabad, Gujarat. Activity Report of IMA AMS Hqrs and resolutions passed in governing council were submitted to IMA Hqrs for CWC Meeting and gave Power Point presentation.
18. **On 5th May 2023:** IMA AMS Hqrs conducted a live webinar on "FUNGAL INFECTION UPDATES #1" from 7:30 pm to 9:30 PM. **Session 1:** Invasive Candidiasis and its Changing Epidemiology by Dr. Ram Gopalakrishnan, Infectious disease specialist Apollo Hospitals, Chennai. **Session 2:** Laboratory diagnosis of invasive Candidiasis by Dr. P. Umabala, Prof. & Head Dept. of Microbiology & in-charge, AMDRC, NIMS, Hyderabad. **Session 3:** Clinical Scores for the prediction of invasive candidiasis in the critically III and Initiation of empiric therapy by Dr. D. Padmaja, Prof. Dept of Anaesthesiology and intensive care, NIMS, Hyderabad. **Session 4:** Management of invasive Candidiasis in adults by Dr. P. Vishnu Rao, Infectious disease specialist Apollo Hospital, Hyderabad. **Session 5:** Prevention of Health care associated Invasive Candidiasis by Dr. Srirang Abkari, Consultant physician, Udai Omni Hospital, Hyderabad & Hony. Secretary IMA AMS Hqrs. Moderators:Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs & Dr. Naval Chandra, Chairman API Hyderabad.





19. **On 12th May 2023:** IMA AMS Hqrs conducted a live webinar on "OSTEOARTHRITIS-KNEE JOINTS" 8:00 pm, by Dr. Udai Prakash, Director & Chief of joint Replacement Surgery & Sports injuries Unit, Udai Omni Hospital, Hyderabad.

20. **14th May 2023:** Dr. Pankaj Mutneja, National Chairman, IMA AMS attended CME of IMA AMS Uttarakhand State Branch at Kashipur, Uttarakhand as the Chief Guest. There was a membership drive and close to 140 new AMS members were made.

21. **On 26th May 2023:** Virtual meeting of the SASSM along with IMA Officials including Chairman and members of IMA Academic and Accreditation Board at 11:30 am on 26th May, 2023 to discuss the viability and suitability of the courses. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs & Dr. Srirang Abkari Secretary IMA AMS Hqrs attended.

22. **On 28th May 2023:** Dr Pankaj Mutneja National Chairman of IMA AMS Annual Conference of IMA AMS Bihar State on 28th May 2023. He was warmly welcomed by Imm National IMA past President Dr Sahjanand PD Singh Ex Election commission Member Hq. Dr Brajnandan Kumar and organised by Dr D.P. Singh Chairman, IMA AMS & Secretary Dr Rajiva Ranjan at Bhagalpur.



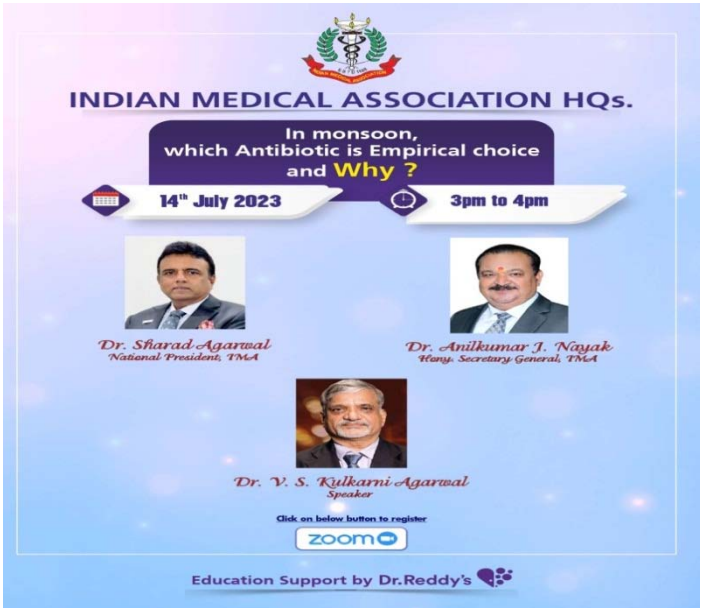

23. **On 7th June 2023:** National President IMA Hqrs, Dr. Sharad Kumar Agarwal gave a prime talk on Facebook live on 7th June 2023. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

24. **On 25th June 2023:** Inauguration of Aao Gaon Chale project by IMA HYDERABAD CITY BRANCH on 25th June 2023. Slum adopted and Medical Camp started. Dr. Srirang Abkari, Hony. Secretary IMA AMS Hqrs and other office bearers participated.

25. **On 26th June 2023:** IMA AMS Hqrs conducted **Office Bearers Meeting** on 26th June 2023 at 8 PM on virtual way, discussed on IMA AMS software upgrade. Mr. Mintu Nath, Director SaaScraft Studio (India) Pvt. Ltd explained about the new software in PPT format.
26. **On 27th June 2023:** IMA AMS Hqrs conducted a live webinar on "**Bronchial Asthma**" at 8:00 pm. **Session 1:** Bronchial Asthma in Adults by Dr. Pradyut Waghray, MD(Chest), FRCP LONDON (UK), FCCP (USA), FAMS (India), Chairman and managing director of the Kunal Institute of Medical Specialities Pvt Ltd Hyderabad, Prof and HOD of Pulmonary medicine SVS medical College, Sr. Consultant Pulmonologist Apollo hospitals jubilee hills Hyderabad. Chairpersons are Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs & Dr. Nibedita Pani, Vice Chairman IMA AMS Hqrs. **Session 2:** Bronchial Asthma- A Paediatric perspective by Dr. Pritesh Nagar, Paediatrician, Hyderabad. Chairpersons were Dr. E. Ravindra Reddy, Past National Vice President IMA & Dr. Nomeetha Shiv Gupta, Chairman Elect IMA AMS.
27. **On 13th July 2023:** Indian Medical Association Hqrs conducted a meeting on **"Nations Voice on NEXT"** by IMA Standing Committee for Action and IMA Medical Students Network (MSN) 8.00 pm. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

28. **On 14th July 2023:** Indian Medical Association Hqrs conducted CME on 14th July 2023 at 3 PM to 4 PM. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

29. **On 21st July 2023: :** Indian Medical Association Hqrs conducted CME on 21st July 2023 at 3 PM to 4 PM. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

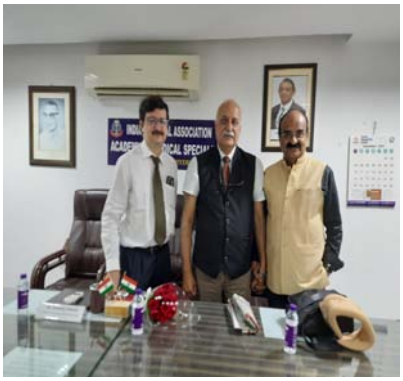


30. **On 9th September 2023:** Indian Medical Association Hqrs conducted CME on 9th September 2023 at 5 pm to 6 pm. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

31. **On 8th and 9th September:** IMA AMS Karnataka State conference was organised by IMA Tumkuru in association with IMA KSB. Dr Daggumati Seehari Rao Vice President IMA HQ , Dr Pankaj Mutneja Chairperson IMA AMS HQ and Dr Srirang Abkari Hon Secretary IMA AMS HQ , Dr Shivakumar Lakkol President IMA KSB were guests of honour. Dr Geeta Doppa Chairman IMA AMS Karnataka State Chapter and Dr Suresh Kagalkar Sec IMA AMS Karnataka State Chapter were guests of honor. The conference was attended by Past Presidents of IMA KSB, Past Chairpersons of IMA AMS Karnataka State Chapter . Under the guidance of Dr GN Prabhakar Director AKN Sinha Institute, organising chairperson Dr Shantakumar , organising secretary Dr Veerabhadraiah and office bearers of IMA Tumkuru and members of IMA Tumkuru organised the AMSCON 23 in an excellent manner. Active participation of woman doctors was there in organising the conference. Around 600 delegates registered, 38 scientific papers, 35 posters were presented by various post graduates throughout Karnataka. Dr B M Alur oration was given by Dr Rangegowda renowned urologist from Tumkur. There were excellent scientific sessions by experienced faculty. This conference was a great success.

32. **On 17th September 2023:** Honored to receive Dr. Pankaj Mutneja, National Chairman IMA AMS at Hyderabad. He visited AMS office and was the Chief Guest for the Convocation Ceremony of IMA AMS Telangana State to award certificates of fellowship for Infertility and Laproscopy Courses. Dr. BN Rao, President IMA TS, Dr. Vasantha Kumari Chairman IMA AMS and the office bearers and other dignitaries graced the occasion.






33. **On 7th & 8th October 2023:** National **IMA AMS Eastern Zonal Conference was** held on 7th & 8th October 2023 organized by IMA Siliguri Branch under the aegis of Indian Medical Association Bengal State Branch at Montana Vista, Siliguri. Branch Leaders from different local branches and Leaders of junior doctors participated enmasse. Overwhelming participation in the conference by more than 650 registered delegates made this conference a historic one. Dr. Pankaj Mutneja, Chairman AMS Hqrs and Dr. Srirang Abkari, Secretary AMS Hqrs attended this event.


34. **On 12th October 2023:** Indian Medical Association Hqrs conducted CME on **"Arthritis Uniting for a Pain-Free World"** on12th October 2023. Dr. Pankaj Mutneja, Chairman IMA AMS Hqrs, Dr. Srirang Abkari, Secretary IMA AMS Hqrs have participated in live programme.

IMA AMS Andhra Pradesh, Assam, Bihar, Bengal, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Orissa, Uttar Pradesh, Uttaranchal, Tamil Nadu & Telangana States have conducted a total of **193** Academic Programmes (CMEs, Video Clippings, Workshops, journal Clubs, State Conferences) of Various Specialties under the IMA AMS Hqrs. Dr. Pankaj Mutneja, Chairman and Dr. Srirang Abkari, Hony. Secretary IMA AMS Hqrs and various State Chairman & Secretaries and IMA senior leaders have participated in these.

Suggestions & Appeal:

1. Request to form a new IMA AMS State Chapter to the following States: **ARUNACHAL PRADESH**, **RAJASTHAN, GOA, HIMACHAL PRADESH, MANIPUR, MEGHALAYA, MIZORAM, NAGALAND, SIKKIM, JAMMU & KASHMIR, PONDICHERRY and TRIPURA**.
2. For Union Territories and small State Branches to start an AMS State Chapter the minimum membership strength of the AMS Body has been reduced to 50 only.
3. For Local Branch within a state, only 20 members are needed to start the Branch.
4. Request the State Presidents and Hon State Secretaries and the Chairmen and State Secretaries of IMA AMS to increase membership and fellowships of IMA AMS and start IMA AMS courses.
5. State Chapters/Branch Chapters to conduct at least one activity in every month either CME or Webinar on behalf of IMA AMS in your respective State Chapters and their Branch Chapters involving basics Speciality. **IMA AMS HQrs will provide free Zoom Link to conduct State/Branch webinars.** AMS State Chapter and National Chapter must be included in that programme. The IMA AMS Hqrs will monitor all the activities and recognition of your efforts will be done and you will be eligible for AMS National Awards in the National Conference (AMSCON) of IMA AMS.
6. We request all the office bearers to enroll at least 3 Members & Fellows of IMA AMS to strengthen our AMS which is working towards reaching new goals and academic heights in the coming years.

We expect all your kind cooperation in the membership drive, please feel free to express any of your doubts, thoughts and advice.

IMA AMS ANNALS:

Annals are published every year on the occasion of AMSCON - IMA AMS National Conference. IMA AMS has brought out Annals on **COVID-19, EPILEPSY, MEDICAL EMERGENCIES** and **SURGICAL EMERGENCIES** in the recent past**.** This issue on "**Acute Coronary Syndrome"** is ready for National Conference and it will be released in AMSCON-2023, at Kozhikode, Kerala. All E-Annals are posted on the AMS website: https://ima-ams.org

IMA AMS NEWSLETTER:

IMA AMS Hqrs have released 6 Editions of **IMA AMS E-Newsletters and** posted on the AMS website: https://ima-ams.org

IMA AMS OFFICE:

We strive to be responsive, prompt and efficient in our work and communications. Sincere thanks to our office staff Mrs. Saritha and Mr. Rakesh for their active involvement and hardwork. We have improved our office infrastructure and await new software which will revolutionize the functioning and make it easy for the members, State and Branch Chapters of IMA AMS.

IMA AMS COURSES: We have inspected and approved new (six) centers for IMA AMS Courses in many states this year and hope to accomplish more by the year end. An important impediment was the course modules for new courses and we have created new course modules and submitted to accreditation committee and followed their suggestions. We will roll them out soon.

My sincere thanks to our Chief Patron Dr. Ketan Desai, Dr. Sharad Kumar Agarwal, National President -2022-2023, Dr. R.V. Asokan, National President Elect-2023-2024, Dr. Anilkumar J Nayak, Hony. Secretary General 2022-2024, IMA Hqrs, Dr. Shitij Bali, Finance Secretary 2022-2024, IMA Hqrs, Dr. Sahajanand Prasad Singh, Imm. Past National President IMA Hqrs, Dr. Pankaj Mutneja, National Chairman IMA AMS Hqrs, Dr. Nomeeta Shiv Gupta, National Chairman Elect-2023-2024, IMA AMS Hqrs, Dr. Nibedita Pani, Vice Chairman, IMA AMS Hqrs, Dr. D. Shekhar Reddy, Joint Secretary, IMA AMS Hqrs, Dr. Hiren S. Kothari, Joint Secretary IMA AMS Hqrs, Dr. Rajeev Goel, Hony. Joint Secretary IMA AMS Hqrs, Dr. Shilpa Basu Roy, Hony. Editor (Annals), IMA AMS Hqrs, Dr. Rajiv Ranjan Prasad, Executive Editor (Annals), IMA AMS Hqrs, Dr. G. N. Prabhakara, Imm. Past Chairman IMA AMS Hqrs and Dr. Sanjeev Singh Yadav, Imm. Past Secretary IMA AMS Hqrs for their valuable guidance and suggestions. We acknowledge the support and encouragement of all the National IMA office bearers, Past Presidents and Secretaries of IMA and IMA AMS, State Chairman, Secretaries and office bearers of IMA AMS.

Long Live IMA & IMA AMS

Dr. Srirang Abkari
Hony. Secretary, IMA AMS Hqrs

Few Photos of Assam State:

Few Photos of Bihar State:

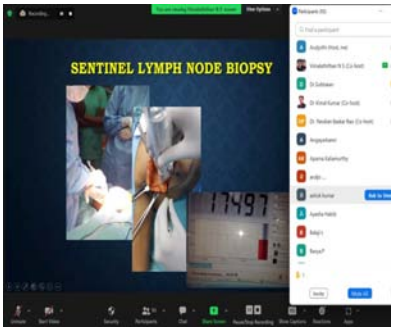
Few Photos of Bengal State:

Few Photos of Chandigarh State:

Few Photos of Chattisgarh State:

Few Photos of Haryana State:

Few Photos of Tamil Nadu State:



Few Photos of Telangana State:

Few Photos of Karnataka State:

Few Photos of Kerala State:

Few photos from MP State:

Few Photos of Maharashtra State:

LOKMAT TIMES

Community News

Dr. Trilok Patil, Dr. Aditya Parihar, Dr. Sachin Gathe, Dr. Saurabh Mukewar, Dr. Vaibhav Banait, Dr. Anjali Bhandarkar, Dr. Kamalakar Pawar, Dr. Prashant Bhandarkar, Dr. Vandana Kate, Dr. Pradeep Rajderkar, Dr. Archana Kothari, Dr. Yogesh Bang, Dr. Y.S.Deshpande, Dr. Piyush Kherde and Dr. Kanhaiya Chandak.

IMA Nagpur conducts CME on Gastrointestinal disorders

Indian Medical Association Nagpur branch conducts Continuing Medical Education (CME) on Gastrointestinal disorders at Dr. Dinkar Hardas Hall. Dr. Vandana Kate, president IMA Nagpur briefed the audience about CME. Dr. Prashant Bhandarkar consultant gastroenterologist, hepatologist and endoscopist delivered the first lecture on "GERD". Dr. Saurabh Mukewar gastroenterologist, hepatologist and endoscopist delivered the second lecture on " Peptic Ulcer and G.I. Bleed ".

The third and fourth lecture was delivered by Dr. Yogesh Bang DNB surgical gastroenterology and Dr. Amit Agarwal MD (Medicine) and DM (gastroenterology) on the topics " Surgical management of Cholecystitis and Gallstones" and " Constipation and IBS". The last lecture on " Viral hepatitis" was delivered by Dr. Vaibhav Banait, MD DM Gastroenterology.

Dr. Pradip Rajderkar physician and past president IMA was the chief guest for the program. Present on the occasion were Dr. Kush Jhunjhunwala vice president IMA MS, Dr. Archana Kothari co-chairman IMA MS AMS, Dr. Ashish Diswal Hon Jt secretary IMA MS , Dr. Rajesh Sawarbandhe finance director IMA MS PPS and Dr. Anjali Bhandarkar chairman IMA Nagpur branch. Dr. Kamalakar Pawar, Hon.Secretary proposed a vote of thanks. A total of 42 delegates attended the programme.

Nagpur First
Page No. 5 Jul 16, 2023
Powered by: enelego.com

Few Photos of Orissa State:

Few Photos of Uttar Pradesh State:

Few Photos of Uttarakhand State:

SHIMIST
SAXENA HOSPITAL INSTITUTE OF MINIMALLY INVASIVE SURGERY TRAINING

Indian Medical Association
ACADEMY OF MEDICAL SPECIALITIES

SAXENA HOSPITAL INSTITUTE OF MINIMALLY INVASIVE SURGERY TRAINING

15 YEARS OF TRUST

4500+ TRAINED SUCCESSFULLY

We provide Education & Training Programs in **Minimally Invasive Surgeries**

1 Year Fellowships Recognised by

IMA-AMS

- GENERAL SURGERIES
- GYNAECOLOGY
- UROGYNAECOLOGY
- UROLOGY

Courses by SHIMIST

LONG TERM COURSES

- 3 Month Courses
- 6 Month Courses
- 1Year Courses

SHORT TERM COURSES

- 3 Days Courses
- 7 Days Courses
- 1 Month Courses
- 2 Month Courses

For further queries please contact :
+919416051211, +917404546475

Visit us at :
www.shimist.in

shimist.sonepat@gmail.com | Website : www.shimist.in
/@shimistbydr.akhilsaxena4442

HEGDE FERTILITY

Conception. A Miracle. A Science

Touching Hearts of Millions Since 1977

Top 1 Fertility Hospital in South India

Top 1 Fertility Hospital in Hyderabad

An OMS - Times of India Initiative

Top 3 Fertility Hospital in India

Hegde Fertility Launches One Year

FELLOWSHIP CERTIFICATE COURSE IN INFERTILITY

In Collaboration with and approved by

INDIAN MEDICAL ASSOCIATION (IMA – AMS)

*Certificates will be issued by IMA-AMS

For more details Contact:

+91 9100345266

art.training@hegdehospital.com

HITEC CITY | MALAKPET | MIYAPUR | SUCHITRA | ATTAPUR

8880 747474 | www.hegdefertility.com | Follow us:

Contents...

		Page #
1.	Introduction to Acute Coronary Syndromes – Dr. Srirang Abkari	01
2.	Pathophysiology Of Acute Coronary Syndrome – Dr. Raj Shekhar Pande	04
3.	Acute Coronary Syndrome (ACS) – Dr. S Balaji	19
4.	Introduction to Acute Coronary Syndromes – Dr. Priya Karthik Prabhu	21
5.	Cardiac Biomarkers In Acute Coronary Syndrome Dr. Varsha Koul & Dr. Puneet Singla	31
6.	Role of Echocardiography in Acute Coronary Syndrome – Dr. Gopinath	41
7.	Role of Intracoronary Imaging and Physiology in Acute Coronary Syndrome Dr. Jayesh Prajapati, Dr. Poojan Prajapati & Iva Patel	53
8.	Management of Acute Coronary Syndrome Dr. Lekha Adik Pathak & Dr. Ronak V Ruparelia	69
9.	Antiplatelet agents – Dr. P.V. Nishanth	77
10.	Fibrinolytic Strategy for ST-Segment– Elevation Myocardial Infarction Dr. Omer Mustafa Hassan	89
11.	Role of Anticoagulants and GpIIb/IIIa in Acute Coronary Syndrome Prof Dr Satyanarayan Routray & Dr Sradhananda Rout	100
12.	Role of Coronary Angiogram in Acute Coronary Syndrome Dr. Ravi Shankar Sharma	107
13.	Role of CT Coronary Angiography and Cardiac MRI in Coronary Artery Disease Dr. Deepak Bulla	122
14.	Percutaneous Coronary Interventions in ACS Dr Rajeev Menon & Dr. Chenna Keshava	128
15.	Surgical Management of Ischemic Heart Disease Patient Prof (Dr) Santanu Dutta	141
16.	Acute Coronary Syndrome (ACS): Understanding a Critical Cardiac Condition Dr. Shubham Agarwal	151
17.	Recent Advances In Acute Coronary Syndrome – Dr. T. Govindan Unni	158
18.	Acute Coronary Syndrome in Young Adults – Dr. Dilip Ratnani	167
19.	Differential Diagnosis Of The Acute Coronary Syndrome – A Doctor ' S Dilemma Dr . Birupaksha Biswas	175
20.	Targeting residual CV risk in Statin Era: Cholesterol or Inflammation Dr. Rajiv Agarwal	179
21.	Perioperative Management of Ischemic Heart Disease Dr Soumi Das	183

Introduction to Acute Coronary Syndromes

Dr. Srirang Abkari
Consultant Physician
Udai Omni Hospital
Hyderabad

Acute coronary syndromes (ACS) are characterized by a sudden reduction in blood supply to the heart and comprise ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina. Every year, more than 7 million people in the world are estimated to be diagnosed with ACS. It is responsible for one-third of total deaths in people above the age of 35 years. The American Heart Association (AHA) estimates that one individual has a heart attack every 41 seconds.

The commonly associated risk factors for the disease are smoking, hypertension, diabetes mellitus, hyperlipidemia, male sex, physical inactivity, family obesity, and poor nutritional practices. Cocaine drug abuse can also lead to vasospasm. A family history of early myocardial infarction (less than 55 years of age) is also a high-risk factor.

The typical symptom of ACS is sub-sternal chest pain, often described as crushing or pressure-like feeling, radiating to the jaw and/or left arm. This classic presentation is not seen always, and the presenting complaint could be very vague and subtle with main complaints often being difficulty in breathing, lightheadedness, isolated jaw or left arm pain, nausea, epigastric pain, sweating, and weakness. Female gender, patients with diabetes, and older age are all associated with ACS presenting with vague or atypical symptoms. Therefore, a high degree of suspicion is warranted in such presentations.

On physical examination, general distress and diaphoresis are often noticed. Heart sounds are frequently normal. At times, gallop and murmur can be heard. Lung exam is normal, although at times creptiations may be heard indicating associated congestive heart failure (CHF). Bilateral pedal edema may be present indicating CHF. The rest of the systems are typically within normal limits unless associated pathologies are present. The presence of tenderness on abdominal palpation should make the physician consider other pathologies like pancreatitis and gastritis. The presence of unequal pulses should immediately raise the suspicion for aortic dissection. The presence of unilateral leg swelling should prompt a work-up for pulmonary embolism. Hence a thorough physical exam is very important to rule out other life-threatening differential diagnoses.

AHA guidelines maintain that any person who has complaints suspicious of ACS should get an electrocardiogram (ECG) within 10 minutes of arrival.

STEMI is caused by complete occlusion of the coronary artery and accounts for approximately 30% of ACS. ACS without significant ST-segment elevation on ECG, termed NSTE-ACS, account for approximately 70% of ACS, are caused by partial or intermittent occlusion of the artery and are associated with ST-segment depressions (approximately 31%), T-wave inversions (approximately 12%), ST-segment depressions combined with T-wave inversions (16%), or neither (approximately 41%). For patients with STEMI, coronary catheterization and percutaneous coronary intervention (PCI) within 2 hours of presentation significantly reduces mortality, with fibrinolytic therapy reserved for patients without

access to immediate PCI. For high-risk patients with NSTE-ACS without contraindications, prompt invasive coronary angiography followed by percutaneous or surgical revascularization is associated with lower rates of death.

It is important that healthcare providers all over the world maintain a high degree of suspicion and vigilance while assessing patients with possible ACS. Along with this, public education and prompt recognition of symptoms are crucial. Another significant aspect of controlling this disease is educating the public about lifestyle modification and healthier life choices. A critical aspect of timely treatment for STEMI and ACS depends on availability of adequate emergency medical services and training. Only through this multi-pronged approach can practitioners control this high mortality disease.

Electrocardiography was introduced by Willem Einthoven at the dawn of the 20th century. Well into the 21st century, we still triage patients with acute myocardial infarction on the basis of this venerable technology: ST segments up or not. Although this approach remains the appropriate evidence-based strategy today, we need to ponder if we apply a more pathophysiologically based categorization of the acute coronary syndromes aiming towards the future goal of more individualized therapy. For decades, plaque rupture has dominated our thinking about the pathophysiology of ACS. However, current evidence suggests that a sole focus on plaque rupture vastly oversimplifies this complex collection of diseases and obscures other mechanisms that may mandate different management strategies. There have been proposals made segmenting coronary artery thrombosis caused by plaque rupture into cases with or without signs of concomitant inflammation. This distinction may have important therapeutic implications as direct anti-inflammatory interventions for atherosclerosis emerge. Pathology and in vivo imaging studies have identified superficial plaque erosion as a frequent and important mechanism underlying ACS. In contrast with plaque rupture, the pathophysiological mechanisms leading to plaque erosion remain poorly understood. There is a need to develop and validate soluble and imaging biomarkers that truly reflect the underlying mechanism that yields acute ischemia. Point-of-care assessment of such biomarkers would be of immense help in rendering their use clinically practical in the triage of patients who present with ACS, with the goal of sparing some the need for urgent invasive diagnostic or therapeutic measures.

The recently released guidelines by the European Society of Cardiology suggest that if ACS is suspected, think ***'A.C.S.'*** for the initial triage and assessment. This involves performing an electrocardiogram (ECG) to assess for **A**bnormalities or evidence of ischaemia, taking a targeted clinical history to assess the clinical **C**ontext of the presentation, and carrying out a targeted clinical examination to assess for clinical and haemodynamic **S**tability. Patients with ST-elevation myocardial infarction (STEMI) require primary percutaneous coronary intervention (PPCI) (or fibrinolysis if PPCI within 120 min is not feasible); patients with non-ST-elevation ACS (NSTE-ACS) with very high-risk features require immediate angiography ± PCI if indicated; patients with NSTE-ACS and high-risk features should undergo inpatient angiography (angiography within 24 h should be considered). A combination of antiplatelet and anticoagulant therapy is indicated acutely for patients with ACS. The majority of patients with ACS will eventually undergo revascularization, most commonly with PCI. Once the final diagnosis of ACS has been established, it is important to implement measures to prevent recurrent events and to optimize cardiovascular risk. This consists of medical therapy, lifestyle changes and cardiac rehabilitation, as well as consideration of psychosocial factors.

References:

1. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and Treatment of Acute Coronary Syndromes: A Review. JAMA. 2022;327(7):662–675. doi:10.1001/jama.2022.0358

2. Singh A, Museedi AS, Grossman SA. Acute Coronary Syndrome. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459157/

3. Crea F, Libby P. Acute Coronary Syndromes: The Way Forward From Mechanisms to Precision Treatment. Circulation. 2017 Sep 19;136(12):1155-1166. doi: 10.1161/CIRCULATIONAHA.117.029870. PMID: 28923905; PMCID: PMC5679086.

4. Ramon A Partida, Peter Libby, Filippo Crea, Ik-Kyung Jang, Plaque erosion: a new in vivo diagnosis and a potential major shift in the management of patients with acute coronary syndromes, European Heart Journal, Volume 39, Issue 22, 07 June 2018, Pages 2070–2076, https://doi.org/10.1093/eurheartj/ehx786

5. Robert A Byrne, Xavier Rossello, J J Coughlan, Emanuele Barbato, Colin Berry, Alaide Chieffo, Marc J Claeys, Gheorghe-Andrei Dan, Marc R Dweck, Mary Galbraith, Martine Gilard, Lynne Hinterbuchner, Ewa A Jankowska, Peter Jüni, Takeshi Kimura, Vijay Kunadian, Margret Leosdottir, Roberto Lorusso, Roberto F E Pedretti, Angelos G Rigopoulos, Maria Rubini Gimenez, Holger Thiele, Pascal Vranckx, Sven Wassmann, Nanette Kass Wenger, Borja Ibanez, ESC Scientific Document Group , 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC), European Heart Journal, 2023;, ehad191, https://doi.org/10.1093/eurheartj/ehad191

Pathophysiology Of Acute Coronary Syndrome

Dr. Raj Shekhar Pande
Ex-Medical Specialist, Al-Horreya Hospital Tobruk, Libya
Presently, Honorary Secretary, IMA M.P. State Branch
Visiting Consultant, Suvidha Hospital & Research Centre, Jabalpur
E-mail ID: rspande56@gmail.com

Abstract

In recent years, acute coronary syndrome (ACS) has received a lot of medical research and clinical trials which have contributed immensely to understanding the pathophysiological mechanisms involved improving the patient's outcome. The pathophysiological mechanisms involved are complex, not fully understood but of great significance in diagnosing and treating ACS patients.

ACS is usually caused by an atheromatous thrombus, the mechanisms being plaque rupture with or without systemic inflammation, plaque erosion and calcified nodules. Of late, non-atherosclerotic causes too have started to gain momentum. These are coronary vasospasm, spontaneous coronary artery dissection (SCAD), myocardial bridging (MB), stress induced cardiomyopathy (Takotsubo Syndrome) and coronary embolism due to thrombus causing obstruction.

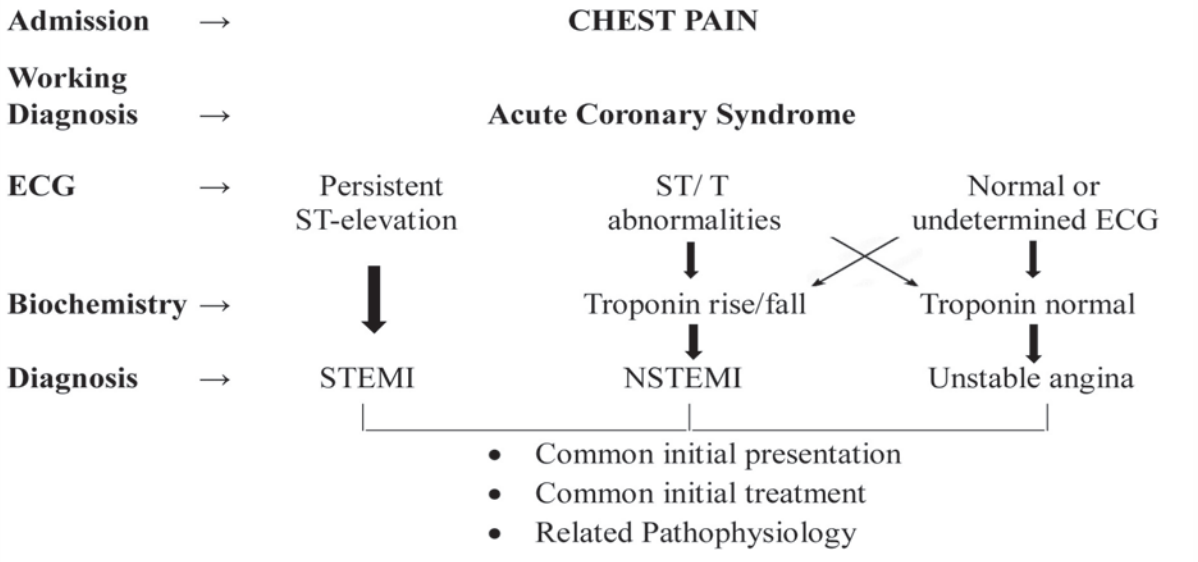
Advances in genetics have greatly improved our understanding of ACS with mechanisms that are complex, may overlap or even coexist by providing impressive data from a large field of investigations have opened new vistas that are being understood.

The present review is aimed at providing the clinician newer insights into the pathophysiological mechanisms involved with an aim to improve the diagnosis and management of such cases.

Introduction

Cardiovascular diseases are a leading cause of mortality worldwide with ischemic heart disease (IHD) accounting for majority of deaths and acute coronary syndrome being most critical (1,2).

The clinical spectrum of ACS includes unstable angina, non-ST segment elevation myocardial infarction (NSTEMI) and ST- segment elevation myocardial infarction (STEMI). These clinical entities graduate according to the severity and rapidity of the action is required for their management.



Unstable angina suggests acute myocardial injury with no biochemical evidence. NSTEMI and STEMI are associated with an increase/decrease in troponin levels coupled with clinical evidence of ischemia.

The pathophysiology of ACS has centred along atherosclerotic and non-atherosclerotic causes. The atherosclerotic causes are plaque rupture of lipid rich thin fibrous caps, plaque erosion with thrombus formation occurs mainly in the area of endothelial desquamation without fibrous cap destruction covering the plaque (3). Calcified nodules are defined by the presence of fracture in the calcified sheet with fibrin and a disrupted fibrous cap overlying the thrombus (4).

Non atherosclerotic causes in the absence of thrombosis can also lead to myocardial ischemia include coronary vasospasm, spontaneous coronary artery dissection (SCAD), myocardial bridging (MB), stress induced cardiomyopathy (Takotsubo Syndrome), and coronary artery embolism (5) from elsewhere in the body.

At times multiple pathophysiological mechanisms may coexist and/ or overlap in ACS necessitating different treatment options.

Finally, impressive advances in genetics have opened the wide field for research in the pathophysiological mechanisms, diagnosis and its therapeutic implications.

PATHOPHYSIOLOGY OF ACS: MECHANISMS

The pathophysiological mechanisms which cause ACS are: -

ATHEROSCLEROTIC

- Plaque rupture with or without systemic inflammation.
- Plaque erosion
- Calcified nodules

NON - ATHEROSCLEROTIC

- Coronary vasospasm
- Spontaneous coronary artery dissection (SCAD)
- Myocardial bridging (MB)
- Stress- induced cardiomyopathy
- Coronary artery embolism

ATHEROSCLEROTIC

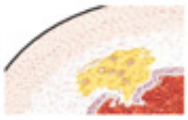
Plaque Rupture

Plaque rupture is seen when the fibrous cap in the lumen ruptures or breaks (6) triggering thrombosis (7) which is characterized by a large lipid core filled with macrophage foam cells, debris and a thin fibrous cap (< 65 mm) that includes extra cellular matrix components (EMC) covering the lipid necrotic area of the plaque (8). Thin capped fibroatheromata (TCFA) or vulnerable plaques, as they are often referred to have been dominantly studied and found in majority fatal myocardial infarcts. Interstitial collagen produced by vascular smooth muscle cells (VMCs) provide strength and its decreased synthesis or increased breakdown is related to TCFA rupture and an impaired ability to repair the fibrous cap that protects the plaque (9, 10). Coronary thrombosis, caused by plaque rupture can be classified as with or without systemic inflammation.

Plaque Rupture with Systemic Inflammation

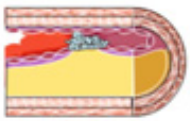
In plaque rupture associated with systemic inflammation, increased C- reactive protein (CRP) is seen in ACS (11). Inflammation activates macrophages to produce matrix metalloproteinases (MMPs) and cathepsin (12), which degrade the extra cellular matrix of the plaque accentuated by reduced levels of their corresponding inhibitors. Inflammation is important in both the beginning and development of plaque rupture and adaptive immunity in coronary instability. The number of pro inflammatory CD34+ T cells is increased in ACS, while the number of T helper cell 17 (Th17) and CD4+, CD25 regulatory T cells (Tregs) decreased (13). Activated Th17 promotes formation of a thick collagen increasing plaque stability, while plaques are rendered unstable when Th17 is reduced. Tregs maintain immune homeostasis by releasing anti-inflammatory

Atherosclerotic plaque thrombosis



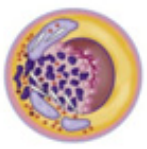
Plaque rupture

- Thin fibrous cap breaks or fissures
- Large lipid core is exposed to blood
- Red thrombosis
- With or without systemic inflammation
- The concept of "vulnerable plaque " may be gradually replaced by "vulnerable patient"



Plaque erosion

- Intact fibrous cap
  Rich in hyaluronic acid
  Abundant VSMCs
  Lack of macrophages
- Specific innate immune activation:MMP-2,14 degrade collagen IV; Massive expression of MPO;TLR2 upregulation
- ECs death and desquamation; basement membrane is exposed
- NETs formation and platelet recruitment; White thrombosis
- Plaque erosion is of increasing importance in the era of intensive risk factor control



Calcific nodule

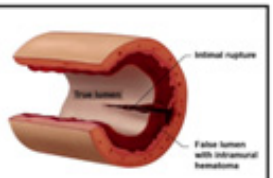
- Necrotic core and collagen calcification
- Calcification is susceptible to mechanical stress
- Nodular calcification leading to disruption of the fibrous cap and covering the lumen thrombus

Non-atherosclerotic causes

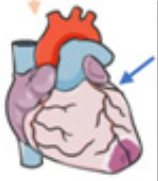
- Endothelial NO release is insufficient
- Oxidative stress and inflammation
- Genetic mutations, sympathovagal imbalance
- Drug induction

Coronary vasospasm

- False lumen formation
- Hematoma compression results in occlusion blood flow
- Inside-out or outside-in

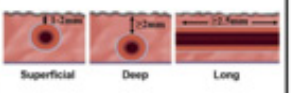


Spontaneous coronary artery dissection



ACS

- Congenital malformation
- Coronary artery penetrates the heart muscle



Myocardial bridging

- sympathetic stimulation
- catecholamine elevation: vascular spasm or cause myocardial toxicity directly
- psychological stress (depression, anxiety), coronary artery or microvascular spasm, metabolic and energy changes, and inflammation

Stress-induced cardiomyopathy (Takotsubo syndrome)

- Direct: material in the left cardiac structure
- Paradoxical: caused by a thrombus such as deep vein thrombosis
- Iatrogenic

Coronary artery embolism

factors such as interleukin (IL)-10 and transforming growth factor ß1 (TGF - ß1). Insufficient suppression and severe inflammatory reactions are seen in reducing amounts of circulating Tregs point to the possible benefits of colchicine and methotrexate in ACS patients (14). Humanised anti-interleukin 1 ß monoclonal antibody (15) canakinumab in patients with previous myocardial infarction and CRP levels more than 2 mg/L showed a 15% reduction in primary endpoint of MI and 17% fall in secondary endpoint that included urgent revascularization. Revascularization procedures reduced 30% in the group that received canakinumab 150 mg subcutaneously every three months substantiating inflammation to atherosclerotic events (16,17,18).

Plaque Rupture without Systemic Inflammation

Plaque rupture without systemic inflammation is caused by extreme emotional disturbances, physical exertion and mechanical stress on the vessel walls predispose to plaque instability due to sympathetic nervous system activation which result in a surge of catacholamines associated with tachycardia, hyper-coagulability, rise in blood pressure and intense microvascular constriction favouring platelet activation and platelet rupture (19). Beta 3 adrenergic stimulation can release proinflammatory monocytes which can amplify local inflammation (20). Local changes in the equilibrium between esterified and free cholesterol may also promote plaque rupture (21). Emotional or physical stress can also trigger instability in the already predisposed plaque provoking events.

Plasma LDL cholesterol, on entering the arterial wall, accumulates in mononuclear phagocytes via scavenger receptors. Death of these lipid laden macrophage foam cells cause accumulation of extracellular esters and cholesterol monohydrate in the lipid rich necrotic core of the plaque. Apoptotic bodies and microparticles that contain procoagulant tissue factor are released by dying macrophages. The diagnosis of plaque rupture in clinical practice remains difficult, but imaging techniques such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have provided excellent insights for assessment of vulnerable atherosclerotic plaques that are prone to rupture. OCT can better characterize tissue types and the presence of thin capped fibroatheromas while IVUS has greater penetration depth and can provide adequate assessment of plaque burden and vessel remodelling - an important feature of culprit lesions in ACS which are also characterized by a large plaque burden (22). OCT studies have co-localised cholesterol crystals (23) in coronaries with thin capped plaques contributing to stability and resisting plaque rupture by increasing the stiffness of the lipid pool (24). Endovascular imaging has given us added information on the newer role of TCFA in ACS. The results of the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study showed that less than 5% TCFA resulted in clinical events (25). Another recently concluded study of 5869 cases of sudden cardiac death found less than 24% had evidence of acute plaque rupture suggesting the role of other factors like myocardial hypertrophy, fibrosis, acute ischemia etc. than plaque rupture alone (26). In recent times, the occurrence of plaque rupture in asymptomatic ACS has shifted the focus on "vulnerable patients" i.e., patients who are more susceptible to ACS or sudden cardiac death. These cases possess vulnerable plaques, vulnerable blood and vulnerable myocardium (27). Vulnerable plaques are thin capped fibroatheroma, vulnerable blood present in a hypercoagulable state is prone to thrombosis and caused by an imbalance between coagulation, anti-coagulation and fibrinolysis in the body, and the vulnerable myocardium is prone to fatal arrhythmias due to electrical instability in the cardiomyocytes.

The fact that ACS is a systemic disease and plaque rupture, a crucial step in its progression should necessitate a combination of lipid lowering strategies, anti-platelet therapy, anticoagulants and revascularization procedures such as percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG). Additional secondary prevention measures include life-style modifications such as controlled diet, cessation of smoking, control of diabetes and blood pressure together with cardiac rehabilitation are

crucial in reducing the risk of recurrence. Intensive lipid lowering reduces the size of the lesion and lipid core resulting in accumulation of lipids in the plaque besides promoting healing and plaque regression (28). A proportionate increase in fibrous tissue such as ECM in plaques enhances fibrous cap stability. The fact that ACS events occur despite effective control of LDL particles suggest the possibility of other mechanisms in triggering ACS.

Plaque Erosion

Plaque erosion is represented by superficial lesions of the atherosclerotic plaque as the cause of ACS is seen in 20-40% cases (29,30,31). It presents as an eroded plaque with intact fibrous caps and a high concentration of ECM molecules like proteoglycans, glycosaminoglycans and high hyaluronic acid content (32), with corresponding cell surface CD 44. Vascular smooth muscle cells (VMCs) are abundant, macrophages are less aggregated, and lipids lacking (33). These platelets rich in thrombus are christened "white thrombus". Table-1 shows differences in thrombosis due to plaque rupture and plaque erosion.

The EROSION study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular OCT - Based Management in Plaque Erosion) suggested effective platelet therapy without stents avoiding stent related complications (34). In recent years, the clinical presentation of ACS has shifted from being STEMI to a pro NSTEMI in most patients with plaque erosion. Plaque erosion is common in women, younger patients, those displaying lower prevalence of diabetes mellitus, hypertension, LDL cholesterol and C-reactive protein and a higher concentration of haemoglobin (35,36) can cause increased blood viscosity resulting in high endothelial shear stress, activation of platelets and the coagulation systems (37). Plaque erosion usually presents as a non-occlusive thrombus that embolizes distally because of less disruption of the arterial integrity and a larger lumen (38). Plaque erosion affects the left anterior descending artery more often (39) and human studies have shown thrombus in zones of high endothelial shear stress. The fluid dynamic impact causes degradation of the basement membrane, endothelial cell desquamation and death (40). Inflammation and minimally oxidised LDL promote expression of matrix metalloproteinases (MMP) -14 and MMP-2, which degrade type 4 collagen which is the main component of the basement membrane (41,42).

Enhanced activation of toll- like receptor (TLR) -2 favours recruitment of granulocytes (43) - mostly neutrophils to form neutrophil extracellular traps (NETs), which can entrap circulating platelets promoting atherosclerosis (44). Finally, impaired endothelium homeostasis (implied in endothelial to mesenchymal transition) contributes to plaque erosion and loss of integrity together with expression of MMP-2, transforming growth factor ß2 (TGF ß2) and vascular growth factor (VEGF) (45,

Table 1. Differences in thrombosis due to plaque rupture and erosion.

	Erosion	**Rupture**
Fibrous cap	Thick and intact	Thin, fissured
Thrombus	"White"Rich in platelets	"Red"Rich in fibrin
Mechanism of activation	Collagen	Tissue factor
Prevailing cells	Smooth muscle cells	Macrophages
Remodelling	Lower degree, outward remodelling	Marked positive remodelling
NET presence	++	+/±
Common clinical outcome	Non-STEMI	STEMI

46). OCT can provide optical biopsy and other invasive techniques such as index of micro circulation resistance (IMR) and coronary flow reserve (CFR) can be used for studying coronary microcirculation which comprise of vessels d" 500 millimicrons in diameter and when Coronary microvascular dysfunction (CMD) occurs, it can play an important role in ACS after reperfusion therapy which besides affecting IMR and CFR is of great significance for the diagnosis, prognosis and treatment of ACS.

Calcified Nodules

Calcified plaque are divided into superficial calcific sheets (most common), eruptive calcific nodules and calcified protrusions (47). Calcified nodules range from 4-7% as the cause for ACS (48). These heavily calcified lesions are more frequently seen in the elderly, genetically predisposed and in those with chronic kidney disease (49,50). Calcified nodules are defined as crater like prominent nodular calcifications with a luminal surface attached thrombus. Calcified nodules usually occur in the proximal to mid-section of the highly curved right coronary artery. External mechanical stress and surrounding rigid collagen calcification breaks the calcification in the necrotic core into fragments which damage capillaries causing intra plaque haemorrhage which soon protrudes into the lumen destroying the fibrous cap and endothelium and forming calcified nodules (51).

IVUS identified five types of calcified nodules. They are: -

Type 1: eccentric calcific nodule without calcification at the opposite side of the calcified nodule.

Type 2: an eccentric calcified nodule with broad (e" 180° arc) superficial calcification at the opposite side of the calcified nodule.

Type 3: an eccentric calcified nodule with narrow (< 180° arc) superficial calcification pattern at the opposite side of the calcified nodule.

Type 4: multiple calcified nodules within the lumen.

Type 5: calcified nodule with visible lumina thrombus (52)

The outcome of patients with calcified nodules is target lesion failure. One study showed 82.4% of target lesions after stent implantation were caused by calcified nodules (53) and recurrent ACS after percutaneous coronary intervention (PCI) due to increased risk of coronary calcification related cardiac events. Proper plaque modification is the key to the treatment of calcified nodules and plaque modification techniques include coronary rotational atherectomy (CRA), excimer laser coronary angioplasty (ELCA) and coronary intravascular lithotripsy (IVL).

NON-ATHEROSCLEROTIC

The non-atherosclerotic causes of ACS leading to myocardial ischemia are coronary vasospasm, spontaneous coronary artery dissection (SCAD), myocardial bridging (MB), stress-induced cardiomyopathy (Takotsubo Syndrome) and coronary artery embolism causing obstruction.

Coronary Vasospasm without plaque rupture is a poorly understood cause of ACS. It is defined as a transient epicardial constriction of the coronary artery leading to vascular occlusion resulting in myocardial ischemia. Coronary vasospasm is more common in men between 40-70 years of age and in post- menopausal women (54). The exact pathophysiological mechanism of coronary vasospasm is unclear with a number of factors contributing to better understanding of the complex process. These include ANS disorders, endothelial dysfunction, inflammation, oxidative stress, VMCs hyper-responsiveness, and genetics (55,56,57). Coronary vasospasm and the ANS are related, as coronary vasospasms are predominantly seen early morning with circadian changes and acetylcholine release. Some authors suggest routine use of acetylcholine to unhide coronary vasospasm in ACS patients with coronary angiography negative for clear culprit lesions. Vascular dysfunction plays an important role in the pathogenesis of coronary vasospasm with decreased nitric oxide (NO) release due to endothelial dysfunction leading to increased

smooth muscle reactivity which predisposes to coronary vasospasm. Drugs like cocaine, amphetamine, marijuana and alcohol (58) can induce coronary vasospasm. The Ergonovine test to provoke coronary vasospasm - most reliable during coronary angiography shows a reduction in coronary artery diameter accompanied by chest pain or ischemic ECG changes. Cardiac magnetic resonance (CMR) - gold standard for the diagnosis of MINOCA (Myocardial Infarction with Non-Obstructive Coronaries) can locate the area of myocardial injury, but its use is controversial. Nitrates, calcium channel blockers and smoking cessation are some of the effective ways to relieve and treat coronary vasospasm.

Spontaneous Coronary Artery Dissection (SCAD) is rare, seen in women and young patients without risk factors for atherosclerosis. SCAD is secondary to the formation of a false lumen in the coronary intima-media leading to formation of intra mural haematoma which compresses the vascular lumen resulting in coronary blood flow obstruction and ACS (59). It is still unclear whether endothelial dysfunction and coronary vasospasm are associated with SCAD. Coronary angiography or PCI treatment provide inconclusive diagnosis and treatment. Most patients are cured by medical management which is preferred over immediate revascularization as PCI is associated with an elevated rate of technical failure due to wiring of the false lumen or extension of the dissection. However revascularization should be considered if high risk features are present.

Myocardial Bridging shows a segment of the coronary artery that would otherwise travel on the epicardium penetrates the muscle layer (60). This segment of the coronary artery is called the mural coronary artery and the cardiac muscle covering it is called myocardial bridging. It commonly involves the left anterior descending artery and is a congenital anomaly - mostly asymptomatic and their hemodynamic effects are associated with thickness and length of the bridge. MB is divided into superficial type running in the ventricular groove and a deep type that runs close to the right ventricular septum. Coronary CT angiography diagnoses MB by showing the vascular segment running in the myocardium. MB generally has a favourable prognosis and symptomatic cases are given beta blockers and calcium channel blockers. When drug treatment is ineffective, surgical treatment can be considered.

Stress Induced Cardiomyopathy is transient, reversible and occurs after a stressful event is characterized by transient abnormalities of left ventricular wall motion and clinical manifestations akin ACS especially seen in post-menopausal women (61) with STEMI on ECG. It is also called Takotsubo Syndrome (TTS). The exact pathophysiological mechanisms are unclear, but sympathetic stimulation leading to increased circulating and local catacholamines can induce vascular spasm or cause direct myocardial toxicity (62) Other pathophysiological mechanisms are psychological stress, coronary artery microvascular spasms, inflammation and metabolic/energy changes. The treatment is removal of the predisposing factors to alleviate stress and treating the primary disease, besides symptomatic and supportive measures.

Coronary Embolism is seen when emboli from the heart, proximal artery wall or other parts of the body enter the coronary artery obstructing the blood flow leading to myocardial ischemia, injury or even necrosis. Infective endocarditis and valve replacement are most common causes of coronary embolism. It is seen in 3-5% cases and is divided into three types - direct, paradoxical and iatrogenic (63). Direct coronary embolism refers to embolism caused from the left cardiac structures and result in severe obstruction of the coronary artery. Atrial fibrillation (AF) alone and rheumatic valvular disease (RVD) with AF can cause direct coronary artery embolism. Paradoxical coronary embolism is caused by detachment of a thrombus that forms outside the coronary artery e.g., deep vein thrombosis and travel in the blood into the coronary arteries to cause ACS (64). Iatrogenic coronary embolism occurs during interventions. Air embolism, the commonest iatrogenic coronary embolism involves the right coronary artery and the diagnosis is based on

history, coronary angiography and other imaging studies. The treatment options include thrombus aspiration, stent implantation, balloon angioplasty, drug anti-coagulation and anti-infective therapy.

GENETICS IN ACS

The role of non-coding RNAs in the identification of plaque rupture and plaque erosion is being extensively studied. Non- coding RNAs are MicroRNAs (miRNAs), Long non-coding RNAs (lncRNAs) and Circular RNAs (circRNAs).

MicroRNAs (miRNAs) have improved our understanding of the development of CAD with different miRNA expression in acute and chronic coronary syndrome (65). miRNAs were found to be related to altering several key actors of atherosclerosis. miR-34a, miR-217 and miR-146 have been associated with regulatory mechanisms in endothelial senescence (66), miR-126 control inflammation and reduce leukocyte infiltration in the plaque and vessel walls (67), miR-143 and miR-145 promote differentiation of SMCs, which are reduced in atherosclerotic vessels (68). Cardiac muscle specific miR-208b and miR-499 were proposed as biomarkers of AMI (69,70) and were significantly effective in predicting MI when compared to controls even if no adjunctive impact to troponin diagnostic accuracy was shown (71). Cardiac miR-1, miR-499 and other non-cardiac miR-21 increased the diagnostic value when added to troponin irrespective of comorbidities and cardiovascular risk factors in the patient. Inflammation related mi-RNAs like miR-181c and miR-362 levels were higher in ACS patients (72) suggesting the role of these inflammatory miRNAs to be more on plaque vulnerability than myocardial injury (73). In the absence of standardization, selecting miRNAs and interpretation of the findings must be done with caution.

Long non-coding RNAs (lncRNAs), important for the normal development and progression of diseases (74) are associated with cellular functions in both - within the nucleus and cytoplasm. Two hypoxia - sensitive human endothelial lncRNAs were found to have an important role in angiogenesis (75). The potential value of of lncRNAs as diagnostic markers is being investigated in patients with MI. Urothelial carcinoma associated infarction - another lncRNA, which displayed significant reduction in the early phase of MI, but subsequently increased on day 3 has an important role to play in glucose metabolism (76), cell proliferation and apoptosis inhibition with most cardioprotective actions derived from their interaction with miR-1. An additive value to troponin and other myocardial injury markers has been proposed for UCAI (77).

Circular RNAs (circRNAs) are a significant class of non-coding RNA molecules. An additive value to circular RNAs (circRNAs) have been identified which are present in large numbers in the human body. They are expressed in a tissue specific or disease specific manner (78,79,80). Their biological functions are unknown but certain circRNAs serve as miRNAs sponges (81,82) which interact with RNA - binding proteins to regulate transcription or translate into proteins (83,84). The key mechanism of the impact of circRNAs on MI involved oxidation stress- induced cardiomyocyte apoptosis CiRS-7, also named Cdr-1 showed increased expression of CiRS-7 and cardiac infarct size and cell apoptosis which was counter balanced by miR-7 expression in infarcted cardiomyocytes. Despite promising findings from preclinical studies, poor understanding of the biology of circRNAs hamper its complete translation into the clinical field.

Gene Therapy with drugs like Olpasiran and Inclisiran are being studied for their beneficial effects. Olpasiran significantly reduces Lipoprotein (a) by more than 95% compared to placebo (85). It is given subcutaneously at 12 weekly intervals in atherosclerotic cardiovascular diseases (86), but larger trials are necessary to demonstrate the clinical benefits of Lipoprotein (a) lowering in such cases (87,88).

Inclisiran can be used as an adjunct to diet and maximally tolerated statin therapy for the management of cases of heterozygous familial hypercholesterolemia or CAD requiring additional lipid lowering (89). Inclisiran converts subtilisin / kexin type 9 synthesis and is given subcutaneously

in two doses at three months interval, then every six months thereafter.

The results of the ORION-10 and ORION -11 trials showed that Inclisiran significantly reduced LDL levels by approximately 50% in high risk patients (90).

Conclusion

ACS has been on the forefront of scientific research and its pathophysiology more diverse than thought previously. It mainly involves atherosclerotic causes like plaque rupture, plaque and calcified nodules characterised by specific histologic features and clinical outcomes. Non-atherosclerotic causes also result in myocardial ischemia and ACS.

With evolution of newer vascular imaging techniques, our understanding of the diagnosis of ACS has greatly improved and largely contributed to better management strategies. Ruptured plaques necessitate urgent reperfusion, plaque erosions suggest conservative management and calcified nodules remain unexplored regarding their optimal management strategy.

With advancement, future studies should establish the importance of detecting the underlying mechanisms of ACS and open newer avenues for better diagnosing and personalised treatment decisions.

References

1. GBD 2019 Diseases and Injuries Collaborators Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019. Lancet 2020, 396, 1204–1222. [Cross Ref]

2. GBD 2017 Causes of Death Collaborators Global, Regional, and National Age-Sex-Specific Mortality for 282 Causes of Death in 195 Countries and Territories, 1980–2017: A Systematic Analysis for the Global Burden of Disease Study 2017. Lancet 2018, 392, 1736–1788. [Cross Ref]

3. De Luca, G.; Navarese, E.P.; Suryapranata, H. A Meta-Analytic Overview of Thrombectomy during Primary Angioplasty. Int. J. Cardiol. 2013, 166, 606–612. [Cross Ref]

4. Virmani, R.; Burke, A.P.; Farb, A.; Kolodgie, F.D. Pathology of the Vulnerable Plaque. J. Am. Coll. Cardiol. 2006, 47, C13–C18. [Cross Ref]

5. De Luca, G.; Schaffer, A.; Wirianta, J.; Suryapranata, H. Comprehensive Meta-Analysis of Radial vs Femoral Approach in Primary Angioplasty for STEMI. Int. J. Cardiol. 2013, 168, 2070–2081. [Cross Ref]

6. Marchini JF, Manica A, Crestani P, Dutzmann J, Folco EJ, Weber H, et al. Oxidized Low-Density Lipoprotein Induces Macrophage Production of Prothrombotic Microparticles. Journal of the American Heart Association. 2020~ 9: e015878.

7. Marx C, Novotny J, Salbeck D, Zellner KR, Nicolai L, Pekayvaz K, et al. Eosinophil-platelet interactions promote atherosclerosis and stabilize thrombosis with eosinophil extracellular traps. Blood. 2019~ 134: 1859–1872

8. Wirka RC, Wagh D, Paik DT, Pjanic M, Nguyen T, Miller CL, et al. Atheroprotective roles of smooth muscle cell phenotypic modulation and the TCF21 disease gene as revealed by singlecell analysis. Nature Medicine. 2019~ 25: 1280–1289.

9. Lu W, Park S, Meng Z, Wang F, Zhou C. Deficiency of Adipocyte IKKâ Affects Atherosclerotic Plaque Vulnerability in Obese LDLR Deficient Mice. Journal of the American Heart Association. 2019~ 8: e012009.

10. Seneviratne AN, Edsfeldt A, Cole JE, Kassiteridi C, Swart M, Park I, et al. Interferon Regulatory Factor 5 Controls Necrotic Core Formation in Atherosclerotic Lesions by Impairing Efferocytosis. Circulation. 2017~ 136: 1140–1154.

11. Denegri A, Boriani G. High Sensitivity C-reactive Protein (hsCRP) and its Implications in Cardiovascular Outcomes. Current Pharmaceutical Design. 2021~ 27: 263–275.

12. Gough PJ, Gomez IG, Wille PT, Raines EW. Macrophage expression of active MMP-9 induces acute plaque disruption in apoE-deficient mice. The Journal of Clinical Investigation. 2006~ 116: 59–69.

13. Crea F, Libby P. Acute Coronary Syndromes. Circulation. 2017~ 136: 1155–1166.

14. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, et al. Colchicine in Patients with Chronic Coronary Disease. The New England Journal of Medicine. 2020~ 383: 1838–1847.

15. Pepe M, Napoli G, Biondi-Zoccai G, Giordano A. Anti-Inflammatory Therapy for Acute Coronary Syndromes: is it Time for a Shift in the Treatment Paradigm? Journal of Cardiovascular Pharmacology. 2022~ 80: 633–635.

16. Shaw LJ, Min JK, Nasir K, Xie JX, Berman DS, Miedema MD, et al. Sex differences in calcified plaque and long-term cardiovascular mortality: observations from the CAC Consortium. European Heart Journal. 2018~ 39: 3727–3735.

17. Sato Y, Kawakami R, Sakamoto A, Cornelissen A, Mori M, Kawai K, et al. Sex Differences in Coronary Atherosclerosis. Current Atherosclerosis Reports. 2022~ 24: 23–32.

18. Hu S, Zhu Y, Zhang Y, Dai J, Li L, Dauerman H, et al. Management and Outcome of Patients With Acute Coronary Syndrome Caused by Plaque Rupture Versus Plaque Erosion: An Intravascular Optical Coherence Tomography Study. Journal of the American Heart Association. 2017~ 6: e004730.

19. Henriet P, Emonard H. Matrix metalloproteinase-2: not (just) a "hero" of the past. Biochimie. 2019~ 166: 223–232.

20. Vissers MC, Pullar JM, Hampton MB. Hypochlorous acid causes caspase activation and apoptosis or growth arrest in human endothelial cells. Biochemical Journal. 1999~ 344: 443–449.

21. Mathew AV, Li L, Byun J, Guo Y, Michailidis G, Jaiswal M, et al. Therapeutic Lifestyle Changes Improve HDL Function by Inhibiting Myeloperoxidase-Mediated Oxidation in Patients with Metabolic Syndrome. Diabetes Care. 2018~ 41: 2431–2437.

22. Homorodean C., Leucuta D.C., Ober M., Homorodean R., Spinu M., Olinic M., Tataru D., Olinic D.M. Intravascular ultrasound insights into the unstable features of the coronary atherosclerotic plaques: A systematic review and meta-analysis. Eur. J. Clin. Investig. 2022; 52: e13671. doi: 10.1111/eci.13671. - DOI - PubMed

23. Quillard T, Franck G, Mawson T, Folco E, Libby P. Mechanisms of erosion of atherosclerotic plaques. Current Opinion in Lipidology. 2017~ 28: 434–441.

24. Sawa Y, Tsuruga E, Iwasawa K, Ishikawa H, Yoshida S. Leukocyte adhesion molecule and chemokine production through lipoteichoic acid recognition by toll-like receptor 2 in cultured human lymphatic endothelium. Cell and Tissue Research. 2008~ 333: 237–252.

25. Xu Y, Mintz GS, Tam A, McPherson JA, Iñiguez A, Fajadet J, et al. Prevalence, Distribution, Predictors, and Outcomes of Patients with Calcified Nodules in Native Coronary Arteries. Circulation. 2012~ 126: 537–545.

26. Holmström L, Juntunen S, Vähätalo J, Pakanen L, Kaikkonen K, Haukilahti A, et al. Plaque histology and myocardial disease in sudden coronary death: the Fingesture study. European Heart Journal. 2022~ 43: 4923–4930.

27. Nissen SE. Vulnerable Plaque and Einstein's

Definition of Insanity. Journal of the American College of Cardiology. 2020~ 75: 1383–1385.

28. Vergallo R, Crea F. Atherosclerotic Plaque Healing. New England Journal of Medicine. 2020~ 383: 846–857.

29. Kwon, J.E.; Lee, W.S.; Mintz, G.S.; Hong, Y.J.; Lee, S.Y.; Kim, K.S.; Hahn, J.-Y.; Kumar, K.S.; Won, H.; Hyeon, S.H.; et al. Multimodality Intravascular Imaging Assessment of Plaque Erosion versus Plaque Rupture in Patients with Acute Coronary Syndrome. Korean Circ. J. 2016, 46, 499–506. [Cross Ref] [PubMed]

30. Arbustini, E.; Dal Bello, B.; Morbini, P.; Burke, A.P.; Bocciarelli, M.; Specchia, G.; Virmani, R. Plaque Erosion Is a Major Substrate for Coronary Thrombosis in Acute Myocardial Infarction. Heart 1999, 82, 269–272. [Cross Ref] [PubMed]

31. Sato, Y.; Hatakeyama, K.; Yamashita, A.; Marutsuka, K.; Sumiyoshi, A.; Asada, Y. Proportion of Fibrin and Platelets Differs in Thrombi on Ruptured and Eroded Coronary Atherosclerotic Plaques in Humans. Heart 2005, 91, 526–530. [Cross Ref]

32. Kolte D, Libby P, Jang I. New Insights into Plaque Erosion as a Mechanism of Acute Coronary Syndromes. JAMA. 2021~ 325:1043.

33. Alkhalil M, Kuzemczak M, Bell A, Stern S, Welsford M, Cantor WJ, et al. A practical approach to prescribing antiplatelet therapy in patients with acute coronary syndromes. Canadian Medical Association Journal. 2022~ 194: E205–E215.

34. Jia H, Dai J, Hou J, Xing L, Ma L, Liu H, et al. Effective antithrombotic therapy without stenting: intravascular optical coherence tomography-based management in plaque erosion (the EROSION study). European Heart Journal. 2017~ 38: 792–800.

35. Shaw LJ, Min JK, Nasir K, Xie JX, Berman DS, Miedema MD, et al. Sex differences in calcified plaque and long-term cardiovascular mortality: observations from the CAC Consortium. European Heart Journal. 2018~ 39: 3727–3735.

36. Sato Y, Kawakami R, Sakamoto A, Cornelissen A, Mori M, Kawai K, et al. Sex Differences in Coronary Atherosclerosis. Current Atherosclerosis Reports. 2022~ 24: 23–32.

37. Yamamoto E, Yonetsu T, Kakuta T, Soeda T, Saito Y, Yan BP, et al. Clinical and Laboratory Predictors for Plaque Erosion in Patients With Acute Coronary Syndromes. Journal of the American Heart Association. 2019~ 8: e012322.

38. Hu S, Zhu Y, Zhang Y, Dai J, Li L, Dauerman H, et al. Management and Outcome of Patients With Acute Coronary Syndrome Caused by Plaque Rupture Versus Plaque Erosion: An Intravascular Optical Coherence Tomography Study. Journal of the American Heart Association. 2017~ 6: e004730.

39. Yamamoto, E.; Thondapu, V.; Poon, E.; Sugiyama, T.; Fracassi, F.; Dijkstra, J.; Lee, H.; Ooi, A.; Barlis, P.; Jang, I.-K. Endothelial Shear Stress and Plaque Erosion: A Computational Fluid Dynamics and Optical Coherence Tomography Study. JACC Cardiovasc. Imaging 2019, 12, 374–375. [Cross Ref]

40. Vergallo, R.; Papafaklis, M.I.; Yonetsu, T.; Bourantas, C.V.; Andreou, I.;Wang, Z.; Fujimoto, J.G.; McNulty, I.; Lee, H.; Biasucci, L.M.; et al. Endothelial Shear Stress and Coronary Plaque Characteristics in Humans: Combined Frequency-Domain Optical Coherence Tomography and Computational Fluid Dynamics Study. Circ. Cardiovasc. Imaging 2014, 7, 905–911. [Cross Ref]

41. Libby, P.; Pasterkamp, G.; Crea, F.; Jang, I.-K. Reassessing the Mechanisms of Acute Coronary Syndromes. Circ. Res. 2019, 124, 150–160. [Cross Ref] [PubMed]

42. Rajavashisth, T.B.; Liao, J.K.; Galis, Z.S.; Tripathi,

S.; Laufs, U.; Tripathi, J.; Chai, N.N.; Xu, X.P.; Jovinge, S.; Shah, P.K.; et al. Inflammatory Cytokines and Oxidized Low Density Lipoproteins Increase Endothelial Cell Expression of Membrane Type1-Matrix Metalloproteinase. J. Biol. Chem. 1999, 274, 11924–11929. [Cross Ref] [PubMed]

43. Quillard, T.; Araújo, H.A.; Franck, G.; Shvartz, E.; Sukhova, G.; Libby, P. TLR2 and Neutrophils Potentiate Endothelial Stress, Apoptosis and Detachment: Implications for Superficial Erosion. Eur. Heart J. 2015, 36, 1394–1404. [Cross Ref] [PubMed]

44. Folco, E.J.; Mawson, T.L.; Vromman, A.; Bernardes-Souza, B.; Franck, G.; Persson, O.; Nakamura, M.; Newton, G.; Luscinskas, F.W.; Libby, P. Neutrophil Extracellular Traps Induce Endothelial Cell Activation and Tissue Factor Production Through Interleukin-1_and Cathepsin G. Arterioscler. Thromb. Vasc. Biol. 2018, 38, 1901–1912. [Cross Ref]

45. Cooley, B.C.; Nevado, J.; Mellad, J.; Yang, D.; St Hilaire, C.; Negro, A.; Fang, F.; Chen, G.; San, H.; Walts, A.D.; et al. TGF-_Signaling Mediates Endothelial-to-Mesenchymal Transition (EndMT) during Vein Graft Remodeling. Sci. Transl. Med. 2014, 6, 227ra34. [Cross Ref]

46. Evrard, S.M.; Lecce, L.; Michelis, K.C.; Nomura-Kitabayashi, A.; Pandey, G.; Purushothaman, K.-R.; D'Escamard, V.; Li, J.R.; Hadri, L.; Fujitani, K.; et al. Endothelial to Mesenchymal Transition Is Common in Atherosclerotic Lesions and Is Associated with Plaque Instability. Nat. Commun. 2016, 7, 11853. [Cross Ref]

47. Sugiyama T, Yamamoto E, Fracassi F, Lee H, Yonetsu T, Kakuta T, et al. Calcified Plaques in Patients with Acute Coronary Syndromes. JACC: Cardiovascular Interventions. 2019~ 12: 531– 540.

48. Virmani, R.; Kolodgie, F.D.; Burke, A.P.; Farb, A.; Schwartz, S.M. Lessons from Sudden Coronary Death: A Comprehensive Morphological Classification Scheme for Atherosclerotic Lesions. Arterioscler. Thromb. Vasc. Biol. 2000, 20, 1262–1275. [Cross Ref]

49. Xu, Y.; Mintz, G.S.; Tam, A.; McPherson, J.A.; Iñiguez, A.; Fajadet, J.; Fahy, M.; Weisz, G.; De Bruyne, B.; Serruys, P.W.; et al. Prevalence, Distribution, Predictors, and Outcomes of Patients with Calcified Nodules in Native Coronary Arteries: A 3-Vessel Intravascular Ultrasound Analysis from Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPE. Circulation 2012, 126, 537–545. [Cross Ref]

50. Budoff, M.J.; Rader, D.J.; Reilly, M.P.; Mohler, E.R.; Lash, J.; Yang, W.; Rosen, L.; Glenn, M.; Teal, V.; Feldman, H.I.; et al. Relationship of Estimated GFR and Coronary Artery Calcification in the CRIC (Chronic Renal Insufficiency Cohort) Study. Am. J. Kidney Dis. 2011, 58, 519–526. [Cross Ref]

51. Torii S, Sato Y, Otsuka F, Kolodgie FD, Jinnouchi H, Sakamoto A, et al. Eruptive Calcified Nodules as a Potential Mechanism of Acute Coronary Thrombosis and Sudden Death. Journal of the American College of Cardiology. 2021~ 77: 1599–1611.

52. Pengchata, P.; Pongakasira, R.; Wongsawangkit, N.; Phichaphop, A.; Wongpraparut, N. Characteristics and Pattern of Calcified Nodule and/or Nodular Calcification Detected by Intravascular Ultrasound on the Device-Oriented Composite Endpoint (DoCE) in Patients with Heavily Calcified Lesions Who Underwent Rotational Atherectomy-Assisted Percutaneous Coronary Intervention. J. Interv. Cardiol. 2023, 2023, 6456695. [Google Scholar] [Cross Ref] [PubMed]

53. Sato Y, Finn AV, Virmani R. Calcified nodule: a rare but important cause of acute coronary syndrome with worse clinical outcomes. Atherosclerosis. 2021~ 318: 40–42.

54. Hung, M.-J.; Hu, P.; Hung, M.-Y. Coronary

Artery Spasm: Review and Update. Int. J. Med. Sci. 2014, 11, 1161–1171. [Cross Ref]

55. Yasue H, Mizuno Y, Harada E. Coronary artery spasm – Clinical features, pathogenesis and treatment. Proceedings of the Japan Academy, Series B. 2019~ 95: 53–66.

56. Mehta PK, Thobani A, Vaccarino V. Coronary Artery Spasm, Coronary Reactivity, and their Psychological Context. Psychosomatic Medicine. 2019~ 81: 233–236.

57. Conklin DJ, Bhatnagar A, Cowley HR, Johnson GH, Wiechmann RJ, Sayre LM, et al. Acrolein generation stimulates hypercontraction in isolated human blood vessels. Toxicology and Applied Pharmacology. 2006~ 217: 277–288.

58. De Luca, G.; Schaffer, A.; Wirianta, J.; Suryapranata, H. Comprehensive Meta-Analysis of Radial vs Femoral Approach in Primary Angioplasty for STEMI. Int. J. Cardiol. 2013, 168, 2070–2081. [Cross Ref]

59. Chen, S.; Markman, J.L.; Shimada, K.; Crother, T.R.; Lane, M.; Abolhesn, A.; Shah, P.K.; Arditi, M. Sex-Specific Effects of the Nlrp3 Inflammasome on Atherogenesis in LDL Receptor-Deficient Mice. JACC Basic Transl. Sci. 2020, 5, 582–598. [Cross Ref] [PubMed]

60. Fournier, B.M.; Parkos, C.A. The Role of Neutrophils during Intestinal Inflammation. Mucosal Immunol. 2012, 5, 354–366. [Cross Ref] [PubMed]

61. Couch LS, Channon K, Thum T. Molecular Mechanisms of Takotsubo Syndrome. International Journal of Molecular Sciences. 2022~ 23: 12262.

62. Ridker, P.M.; Everett, B.M.; Thuren, T.; MacFadyen, J.G.; Chang,W.H.; Ballantyne, C.; Fonseca, F.; Nicolau, J.; Koenig,W.; Anker, S.D.; et al. Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease. N. Engl. J. Med. 2017, 377, 1119–1131. [Cross Ref]

63. De Luca, G.; Schaffer, A.; Wirianta, J.; Suryapranata, H. Comprehensive Meta-Analysis of Radial vs Femoral Approach in Primary Angioplasty for STEMI. Int. J. Cardiol. 2013, 168, 2070–2081. [Cross Ref]

64. Morton, A.C.; Rothman, A.M.K.; Greenwood, J.P.; Gunn, J.; Chase, A.; Clarke, B.; Hall, A.S.; Fox, K.; Foley, C.; Banya,W.; et al. The Effect of Interleukin-1 Receptor Antagonist Therapy on Markers of Inflammation in Non-ST Elevation Acute Coronary Syndromes: The MRC-ILA Heart Study. Eur. Heart J. 2015, 36, 377–384. [Cross Ref]

65. Ahlin, F.; Arfvidsson, J.; Vargas, K.G.; Stojkovic, S.; Huber, K.; Wojta, J. MicroRNAs as Circulating Biomarkers in Acute Coronary Syndromes: A Review. Vascul. Pharmacol. 2016, 81, 15–21. [Cross Ref] [PubMed]

66. Deng, S.; Wang, H.; Jia, C.; Zhu, S.; Chu, X.; Ma, Q.; Wei, J.; Chen, E.; Zhu, W.; Macon, C.J.; et al. MicroRNA-146a Induces Lineage-Negative Bone Marrow Cell Apoptosis and Senescence by Targeting Polo-Like Kinase 2 Expression. Arterioscler. Thromb. Vasc. Biol. 2017, 37, 280–290. [Cross Ref]

67. Kumar, S.; Kim, C.W.; Simmons, R.D.; Jo, H. Role of Flow-Sensitive MicroRNAs in Endothelial Dysfunction and Atherosclerosis. Arterioscler. Thromb. Vasc. Biol. 2014, 34, 2206–2216. [Cross Ref]

68. Holmberg, J.; Bhattachariya, A.; Alajbegovic, A.; Rippe, C.; Ekman, M.; Dahan, D.; Hien, T.T.; Boettger, T.; Braun, T.; Swärd, K.; et al. Loss of Vascular Myogenic Tone in MiR-143/145 Knockout Mice Is AssociatedWith Hypertension-Induced Vascular Lesions in Small Mesenteric Arteries. Arterioscler. Thromb. Vasc. Biol. 2018, 38, 414–424. [CrossRef] [PubMed]

69. Dimmeler, S.; Zeiher, A.M. Circulating MicroRNAs: Novel Biomarkers for Cardiovascular Diseases? Eur. Heart J. 2010, 31, 2705–2707. [Cross Ref] [PubMed]

70. Wang, G.-K.; Zhu, J.-Q.; Zhang, J.-T.; Li, Q.; Li, Y.; He, J.; Qin, Y.-W.; Jing, Q. Circulating MicroRNA: A Novel Potential Biomarker for Early Diagnosis of Acute Myocardial Infarction in Humans. Eur. Heart J. 2010, 31, 659–666. [Cross Ref] [PubMed]

71. Devaux, Y.; Mueller, M.; Haaf, P.; Goretti, E.; Twerenbold, R.; Zangrando, J.; Vausort, M.; Reichlin, T.; Wildi, K.; Moehring, B.; et al. Diagnostic and Prognostic Value of Circulating MicroRNAs in Patients with Acute Chest Pain. J. Intern. Med. 2015, 277, 260–271. [Cross Ref] [PubMed]

72. Barraclough, J.Y.; Joglekar, M.V.; Januszewski, A.S.; Martínez, G.; Celermajer, D.S.; Keech, A.C.; Hardikar, A.A.; Patel, S. A MicroRNA Signature in Acute Coronary Syndrome Patients and Modulation by Colchicine. J. Cardiovasc. Pharmacol. Ther. 2020, 25, 444–455. [Cross Ref]

73. Fichtlscherer, S.; De Rosa, S.; Fox, H.; Schwietz, T.; Fischer, A.; Liebetrau, C.; Weber, M.; Hamm, C.W.; Röxe, T.; Müller-Ardogan, M.; et al. Circulating MicroRNAs in Patients With Coronary Artery Disease. Circ. Res. 2010, 107, 677–684. [Cross Ref]

74. Bär, C.; Chatterjee, S.; Thum, T. Long Noncoding RNAs in Cardiovascular Pathology, Diagnosis, and Therapy. Circulation 2016, 134, 1484–1499. [Cross Ref]

75. Fiedler, J.; Breckwoldt, K.; Remmele, C.W.; Hartmann, D.; Dittrich, M.; Pfanne, A.; Just, A.; Xiao, K.; Kunz, M.; Müller, T.; et al. Development of Long Noncoding RNA-Based Strategies to Modulate Tissue Vascularization. J. Am. Coll. Cardiol. 2015, 66, 2005–2015. [Cross Ref]

76. Li, Z.; Li, X.; Wu, S.; Xue, M.; Chen, W. Long Non-Coding RNA UCA1 Promotes Glycolysis by Upregulating Hexokinase 2 through the MTOR-STAT3/MicroRNA143 Pathway. Cancer Sci. 2014, 105, 951–955. [Cross Ref]

77. Yan, Y.; Zhang, B.; Liu, N.; Qi, C.; Xiao, Y.; Tian, X.; Li, T.; Liu, B. Circulating Long Noncoding RNA UCA1 as a Novel Biomarker of Acute Myocardial Infarction. BioMed Res. Int. 2016, 2016, 8079372. [Cross Ref] [PubMed]

78. Aufiero, S.; van den Hoogenhof, M.M.G.; Reckman, Y.J.; Beqqali, A.; van der Made, I.; Kluin, J.; Khan, M.A.F.; Pinto, Y.M.; Creemers, E.E. Cardiac CircRNAs Arise Mainly from Constitutive Exons Rather than Alternatively Spliced Exons. RNA 2018, 24, 815–827. [Cross Ref] [PubMed]

79. Rybak-Wolf, A.; Stottmeister, C.; Gla•ar, P.; Jens, M.; Pino, N.; Giusti, S.; Hanan, M.; Behm, M.; Bartok, O.; Ashwal-Fluss, R.; et al. Circular RNAs in the Mammalian Brain Are Highly Abundant, Conserved, and Dynamically Expressed. Mol. Cell 2015, 58, 870–885. [Cross Ref]

80. Jeck, W.R.; Sorrentino, J.A.; Wang, K.; Slevin, M.K.; Burd, C.E.; Liu, J.; Marzluff, W.F.; Sharpless, N.E. Circular RNAs Are Abundant, Conserved, and Associated with ALU Repeats. RNA 2013, 19, 141–157. [Cross Ref] [PubMed]

81. Hansen, T.B.; Jensen, T.I.; Clausen, B.H.; Bramsen, J.B.; Finsen, B.; Damgaard, C.K.; Kjems, J. Natural RNA Circles Function as Efficient MicroRNA Sponges. Nature 2013, 495, 384–388. [Cross Ref] [PubMed]

82. Hansen, T.B.; Wiklund, E.D.; Bramsen, J.B.; Villadsen, S.B.; Statham, A.L.; Clark, S.J.; Kjems, J. MiRNA-Dependent Gene Silencing Involving Ago2-Mediated Cleavage of a Circular Antisense RNA. EMBO J. 2011, 30, 4414–4422. [Cross Ref]

83. Zhang, Y.; Zhang, X.-O.; Chen, T.; Xiang, J.-F.; Yin, Q.-F.; Xing, Y.-H.; Zhu, S.; Yang, L.; Chen, L.-L. Circular Intronic Long Noncoding RNAs. Mol. Cell 2013, 51, 792–806. [Cross Ref]

84. Li, Z.; Huang, C.; Bao, C.; Chen, L.; Lin, M.; Wang, X.; Zhong, G.; Yu, B.; Hu, W.; Dai, L.; et al. Exon-Intron Circular RNAs Regulate

Transcription in the Nucleus. Nat. Struct. Mol. Biol. 2015, 22, 256–264. [Cross Ref]

85. O'Donoghue, M.L.; Rosenson, R.S.; Gencer, B.; López, J.A.G.; Lepor, N.E.; Baum, S.J.; Stout, E.; Gaudet, D.; Knusel, B.; Kuder, J.F.; et al. Small Interfering RNA to Reduce Lipoprotein(a) in Cardiovascular Disease. N. Engl. J. Med. 2022, 387, 1855–1864. [Cross Ref]

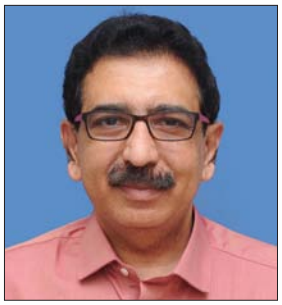
86. Reyes-Soffer, G.; Ginsberg, H.N.; Berglund, L.; Duell, P.B.; Heffron, S.P.; Kamstrup, P.R.; Lloyd-Jones, D.M.; Marcovina, S.M.; Yeang, C.; Koschinsky, M.L.; et al. Lipoprotein(a): A Genetically Determined, Causal, and Prevalent Risk Factor for Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association. Arterioscler. Thromb. Vasc. Biol. 2022, 42, e48–e60. [Cross Ref]

87. Bergmark, C.; Dewan, A.; Orsoni, A.; Merki, E.; Miller, E.R.; Shin, M.-J.; Binder, C.J.; Hörkkö, S.; Krauss, R.M.; Chapman, M.J.; et al. A Novel Function of Lipoprotein [a] as a Preferential Carrier of Oxidized Phospholipids in Human Plasma. J. Lipid Res. 2008, 49, 2230–2239. [Cross Ref]

88. Que, X.; Hung, M.-Y.; Yeang, C.; Gonen, A.; Prohaska, T.A.; Sun, X.; Diehl, C.; Määttä, A.; Gaddis, D.E.; Bowden, K.; et al. Oxidized Phospholipids Are Proinflammatory and Proatherogenic in Hypercholesterolaemic Mice. Nature 2018, 558, 301–306. [Cross Ref]

89. O'Donoghue, M.L.; Giugliano, R.P.; Wiviott, S.D.; Atar, D.; Keech, A.; Kuder, J.F.; Im, K.; Murphy, S.A.; Flores-Arredondo, J.H.; López, J.A.G.; et al. Long-Term Evolocumab in Patients With Established Atherosclerotic Cardiovascular Disease. Circulation 2022, 146, 1109–1119. [Cross Ref] [PubMed]

90. Wright, R.S.; Ray, K.K.; Raal, F.J.; Kallend, D.G.; Jaros, M.; Koenig, W.; Leiter, L.A.; Landmesser, U.; Schwartz, G.G.; Friedman, A.; et al. Pooled Patient-Level Analysis of Inclisiran Trials in Patients With Familial Hypercholesterolemia or Atherosclerosis. J. Am. Coll. Cardiol. 2021, 77, 1182–1193. [Cross Ref] [PubMed]



Acute Coronary Syndrome (ACS)

Dr. S Balaji
Interventional Cardiologist,
Sri Ramakrishna Hospitals, Tamil Nadu
docbalaji1@gmail.com

Acute Coronary Syndrome (ACS) is a critical and potentially life-threatening condition characterized by the sudden disruption of blood flow to the heart muscle due to coronary artery disease. It encompasses a spectrum of conditions including unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), and ST segment elevation myocardial infarction (STEMI). ACS represents a medical emergency that demands prompt recognition, diagnosis, and intervention to prevent irreversible damage to the heart muscle and subsequent complications.

Introduction:

ACS arises from atherosclerotic plaque rupture or erosion, resulting in the formation of a thrombus that partially or completely occludes a coronary artery. This disruption in blood flow leads to myocardial ischemia, which, if prolonged, results in irreversible cell death (myocardial infarction). The clinical presentation of ACS can vary widely depending on the severity of the underlying pathology, the extent of coronary artery involvement, and individual patient factors.

Pathophysiology:

The primary underlying mechanism of ACS is atherosclerosis, a chronic inflammatory process characterized by the accumulation of lipid-rich plaques in the coronary arteries. These plaques can become unstable due to factors such as inflammation, oxidative stress, and mechanical stress, leading to rupture or erosion. When this occurs, platelet activation and aggregation occur, resulting in the formation of a thrombus that can partially or completely obstruct blood flow in the affected artery.

Clinical Presentation:

The clinical presentation of ACS is diverse, but the hallmark symptom is chest pain or discomfort. However, not all patients experience typical chest pain, and atypical presentations are not uncommon, especially in certain patient populations. The clinical presentation of ACS can be categorized into typical and atypical symptoms.

Typical Symptoms:

- **Chest Pain or Discomfort:** The classic symptom is a pressing, squeezing, or crushing chest pain that is often described as substernal or retrosternal. It can radiate to the left arm, neck, jaw, back, or even the epigastric region. The pain is often severe and prolonged, lasting for more than 20 minutes and is not relieved by rest or nitroglycerin.
- **Associated Symptoms:** Patients may experience associated symptoms such as shortness of breath, diaphoresis (excessive sweating), nausea, and vomiting. These symptoms can further support the diagnosis of ACS.

Atypical Symptoms:

- **Elderly Patients:** Elderly individuals may present with confusion, dizziness, or syncope (fainting) without significant chest pain.
- **Diabetic Patients:** Diabetic patients might have neuropathy that blunts or alters the perception of pain. They might experience dyspnea (shortness of breath) without

prominent chest pain which would present as anginal equivalent

- **Women:** Women are more likely to experience atypical symptoms such as profound fatigue, nausea, back pain, or a vague discomfort rather than the classic chest pain.
- **Stable Angina to Unstable Angina:** Some patients with a history of stable angina may experience a change in the pattern of their symptoms, with an increase in frequency, duration, or severity of chest discomfort, leading to unstable angina.

Differentiating Between Types of ACS:

- **Unstable Angina (UA):** Patients with UA experience anginal symptoms that are new in onset, occur at rest, or have an increasing frequency, severity, or duration. Cardiac biomarkers (troponin) are not elevated in UA.
- **Non-ST Segment Elevation Myocardial Infarction (NSTEMI):** NSTEMI is characterized by elevated cardiac biomarkers (troponin) indicating myocardial necrosis. There is no persistent ST segment elevation on the electrocardiogram (ECG), but there may be ST segment depression or T wave inversion.
- **ST Segment Elevation Myocardial Infarction (STEMI):** STEMI is characterized by persistent ST segment elevation on the ECG in the setting of elevated cardiac biomarkers. It indicates complete coronary artery occlusion and requires urgent reperfusion therapy (angioplasty or thrombolytic therapy) to restore blood flow.

Management:

The management of ACS aims to restore blood flow to the affected myocardium, relieve symptoms, prevent complications, and minimize future cardiovascular events. The treatment strategy varies depending on the type of ACS, the patient's clinical status, and the presence of comorbidities.

Conclusion:

ACS represents an acutemedical condition that requires timely recognition, accurate diagnosis, and appropriate intervention. The clinical presentation can vary widely, and healthcare professionals must be vigilant in considering ACS even in atypical cases especially in elderly, diabetic patients and women. Early intervention not only improves outcomes but also reduces the risk of complications and mortality. As our understanding of ACS continues to evolve, advancements in diagnosis and treatment strategies are helping to enhance patient outcomes and quality of life.

ECG in Acute Coronary Syndrome

Dr. Priya Karthik Prabhu
Consultant Interventional Cardiologist
G.Kuppuswamy Naidu Memorial Hospital,
Coimbatore, Tamil Nadu

Introduction

STEMI

- Evolution of ECG changes
- Localisation of MI with culprit artery
- Complications
- Diagnosis of MI in the presence of BBB

NSTEMI/UA

Acute coronary syndrome (ACS) is caused by rupture of an atheromatous plaque, resulting in partial or total occlusion of the vessel lumen by a thrombus. ACS encompass a spectrum of conditions that include patients presenting with recent changes in clinical symptoms or signs, with or without changes on 12-lead electrocardiogram (ECG) and with or without acute elevations in cardiac troponin (cTn) concentrations.

The diagnosis of myocardial infarction (MI) is associated with cTn release and is made based on the fourth universal definition of MI. It can be categorised into ST elevation myocardial infarction (STEMI) or non ST elevation myocardial infarction (NSTEMI) based on ECG changes. Unstable angina is defined as myocardial ischaemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis.

ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

Pathophysiology

When a coronary artery is totally occluded with thrombus, the myocardium will undergo necrosis which starts as early as 15-20 minutes. The infarcted region consists of a central core of necrotic tissue, surrounded by a zone of injured tissue which is in turn surrounded by a zone of ischemic tissue. The ECG manifestations are as follows :

- Myocardial necrosis/infarction is represented by a QS complex
- Myocardial injury is represented by elevated and convex upward ST segment elevation
- Myocardial ischemia is reflected by an inverted symmetrical pointed T wave

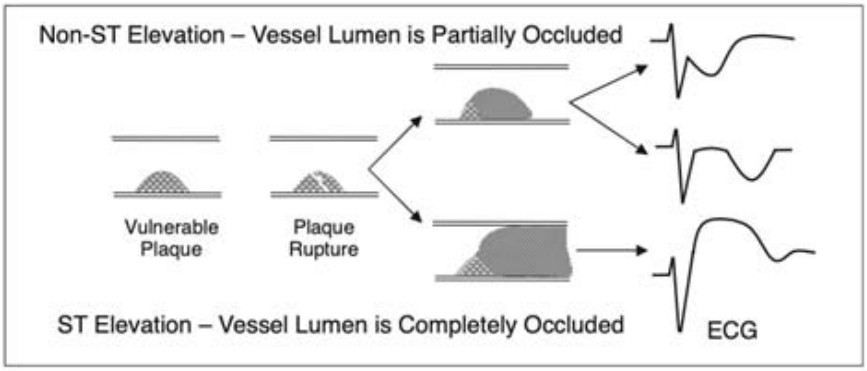


FIGURE : ECG Changes of Acute Coronary Syndrome (1)

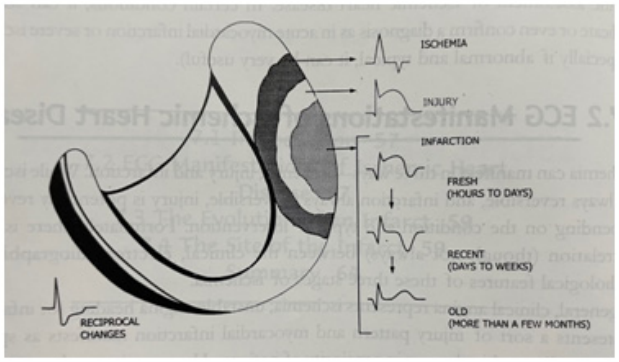


FIGURE:ECG manifestations of ischemia, injury & infarction (2)

The following sequence of ECG changes usually occurs unless the occluded artery is immediately reperfused by fibrinolysis or primary angioplasty:

- Peaked or hyperacute T waves
- Elevation of the ST segments
- Changes in the QRS complex with development of pathologic Q waves or decrease in the size or amplitude of the R waves

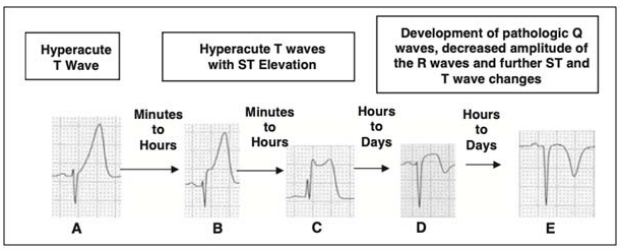


FIGURE : Sequence of ECG changes in STEMI (1)

The ST segment elevation pattern seen with acute MI is technically called a current of injury and indicates that damage involves the transmural & epicardial (outer) layer of the heart as a result of severe ischemia. It is seen in leads which are oriented towards the epicardial surface. The other leads reveal reciprocal ST depression.

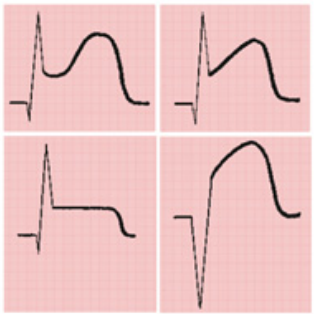


FIGURE : Variable shapes of ST segment elevations seen with STEMI (3)

Usually the ST segments are coved or convex upwards. But, the ST segment elevations seen with acute MI may have different morphologies.

ECG LOCALISATION OF INFARCTIONS

The orientation of the frontal & horizontal plane leads to the left ventricle and anatomical distribution of the coronary arteries is essential to understand the ECG manifestations.

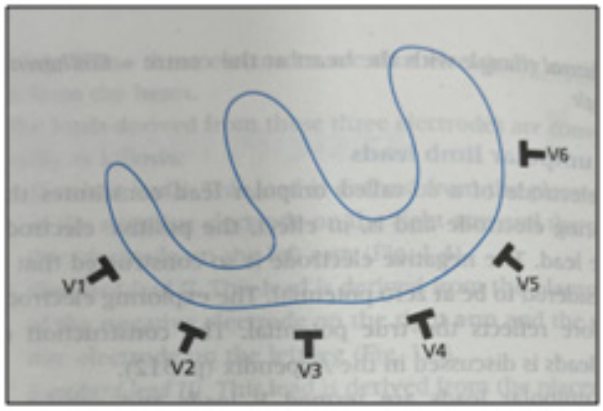


FIGURE : Orientation of precordial leads to ventricles (2)

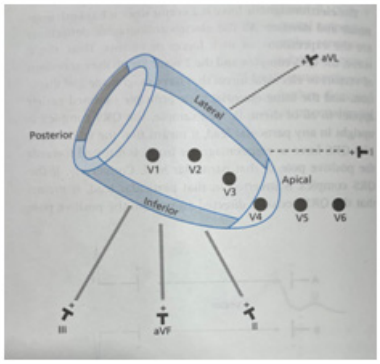


FIGURE :Orientation of various leads to LV cone (2)

The ECG features of MI are usually localised to particular regions of the left ventricle & occasionally involve right ventricular free wall.

The following groups of leads represent certain areas of the heart:

V1-2: ventricular septum.

V2-4: anterior wall of the LV. V2 overlaps the septum and anterior wall and is both a septal and anterior lead.

V1-V3: anteroseptal wall of the LV.

V4-V6, I, and aVL: anterolateral wall of the LV.

V4-V6: lateral wall of the LV. V4 overlaps the anterior and lateral walls of the LV and is both an anterior and lateral lead.

V7-V9: (special posterior precordial leads) posterior wall of the LV.

V3R to V6R: (special right-sided precordial leads) right ventricle.

I and aVL: basal anterolateral or high lateral wall of the LV.

II, III, and aVF: inferior or diaphragmatic wall of the LV.

ANTERIOR WALL MYOCARDIAL INFARCTION (AWMI)

AWMI occurs due to occlusion of left anterior descending coronary artery. It can be subdivided based on extent of involvement into :

- Extensive AWMI - lead I, aVL, V1-6
- Anteroseptal MI - V1-4
- Anterolateral MI - I,aVL,V5-6

The following ECGs (A-D) depict serial changes in the evolution of AWMI

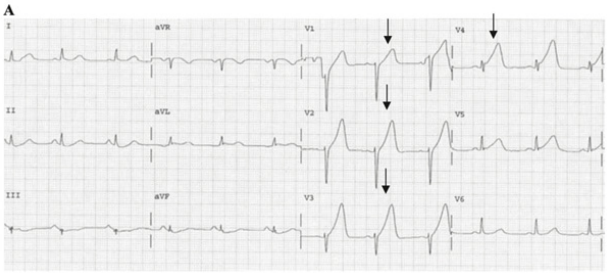


FIGURE : HYPERACUTE AWMI -Tall, hyperacute T waves (arrows) in V1 to V4 with elevation of the ST segments in V3-4

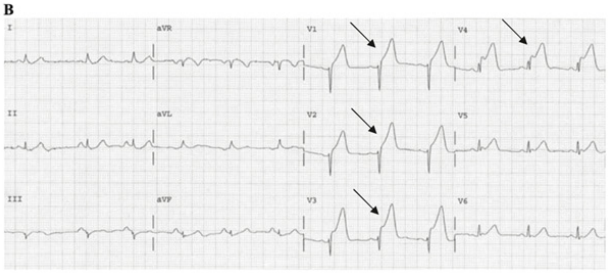


FIGURE : ECG after 15 minutes : Acute AWMI - ST elevation has developed in V1 to V4

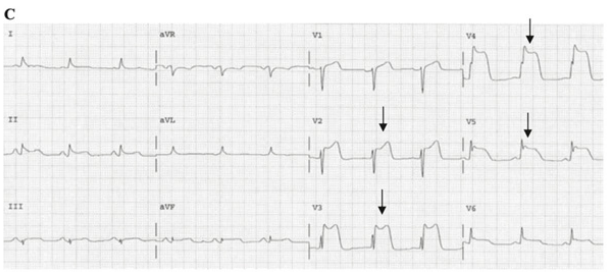


FIGURE : ECG after 1.5 hours - ST elevation has become more pronounced in V2 to V6. This appearance is called "Tombstoning" where the ST segment is around the same level as the height of the R wave and top of the T wave . The QRS complex, ST segment, and T wave therefore blends together to form a large monophasic complex similar to the shape of a transmembrane action potential. This pattern of ST elevation seen in V3-5 usually indicates a grave prognosis.

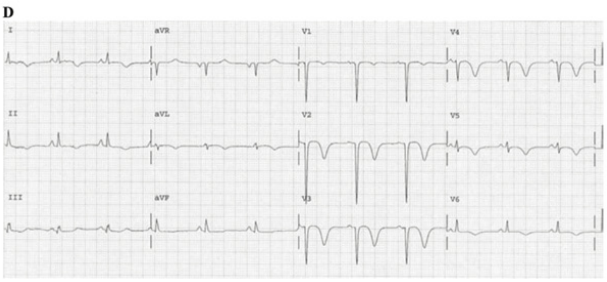


FIGURE : ECG after 2 weeks - Evolved AWMI : QS complexes are seen in V1 to V4. The ST segments are isoelectric and the T waves are inverted from V1-6 and leads I, II, and aVL.

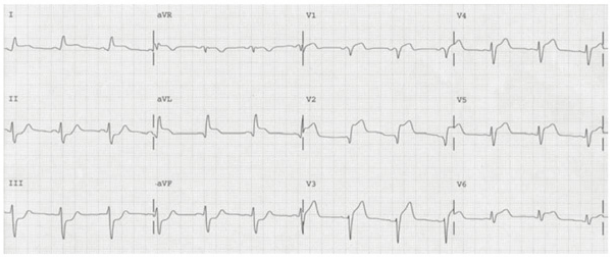


FIGURE : EXTENSIVE AWMI : ST elevation seen in V1-6,I,AVL with reciprocal ST depression in L II,III,aVF

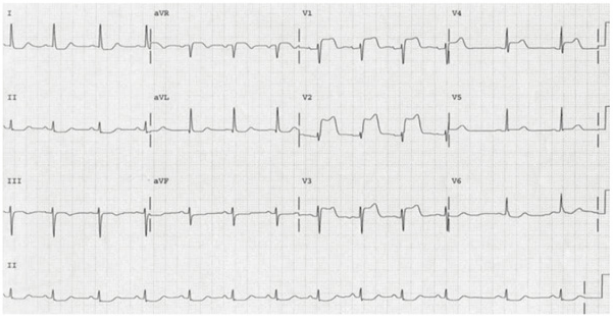


FIGURE : ACUTE ANTEROSEPTAL MI - ST elevation seen in V1-4

INFERIOR WALL MYOCARDIAL INFARCTION (IWMI)

In 85% to 90% of patients with acute inferior MI, the culprit vessel is the Right Coronary Artery (RCA) and in the remaining 10% to 15%, the Circumflex (LCX) coronary artery. ST elevation is seen in leads II,III,aVF

The culprit artery can be identified based on certain parameters :

RCA :

- ST elevation in Lead III > aVF > II
- S depression in lead I,aVL
- Associated RVMI (ST elevation in V1,V3R,V4R)

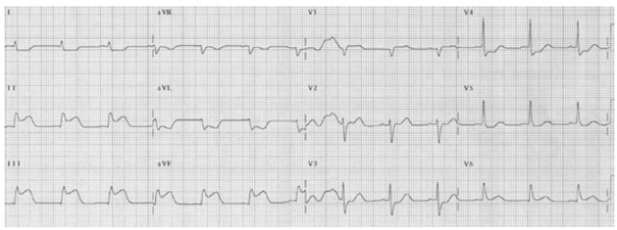


FIGURE : ST segment elevation is present in II, III, and aVF with reciprocal ST depression in I and aVL consistent with acute inferior MI due to occlusion of the right coronary artery.

LCX

- ST elevation in Lead II > aVF > III
- ST elevation in V5,6
- No ST depression or sometimes ST elevation in I,aVL

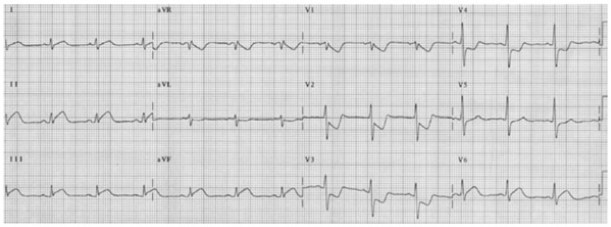


FIGURE : Acute IWMI due to circumflex artery occlusion. ST elevation in lead II is more prominent than lead III. Additionally, the ST segment is isoelectric in aVL and minimally elevated in lead I. ST depression is present in V1 to V3 with ST elevation in V6

RIGHT VENTRICULAR MI

Isolated RVMI is rare & is usually associated with IWMI. The ECG features are

- Elevated ST segments > 1 mm in right oriented precordial leads (V3R-V6R). V4R is the most sensitive.
- Reciprocal ST segment depression in V2 which is 50% or less than magnitude of ST elevation in lead aVF
- ST segment elevation in V1 with ST depression in V2 (discordant relationship)

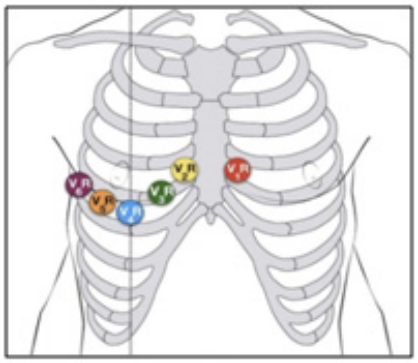


FIGURE : Placement of right sided precordial leads

V1R- left 4th ICS adjacent to sternum

V2R- right 4th ICS

V3R- between V2R & V4R

V4R- right 5th ICS in midclavicular line

V5R-same plane as V4R in anterior axillary line

V6R- same plane as V4R in mid axillary line

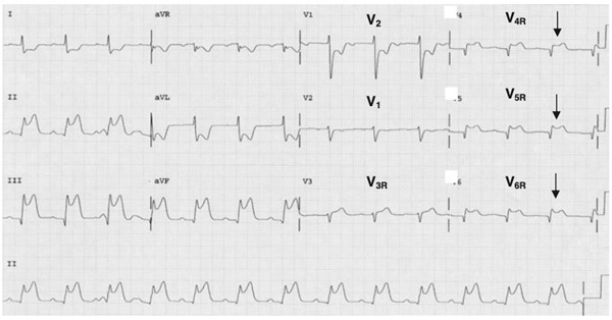


FIGURE : Acute IWMI with Right sided precordial leads showing ST elevation in V4R to V6R

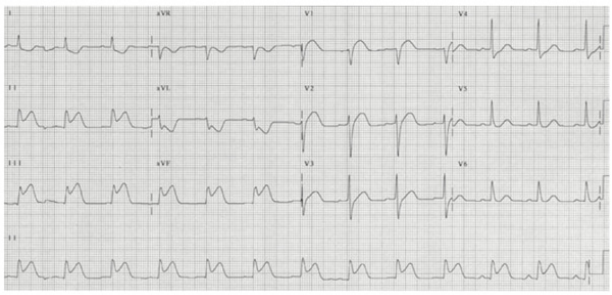


FIGURE: Acute IWMI with RVMI which is denoted by ST uptake in V1-V3. ST elevation in V1 > ST elevation in V3 indicates RVMI

POSTERIOR WALL MI

PWMI occurs commonly due to occlusion of circumflex artery. The electrodes oriented to the posterior wall of the heart (V7-9) show ST elevation. The precordial leads V1-3 are oriented to the anterior wall and reflect the inverse change/ mirror image of acute MI.

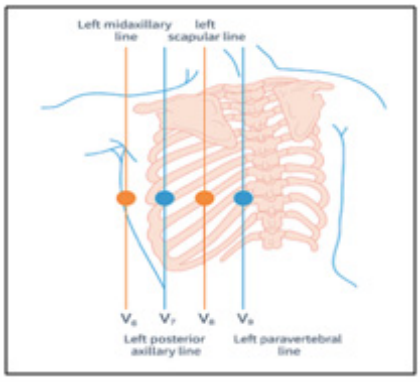


FIGURE : Placement of posterior leads

V7 Posterior axillary line at the same horizontal plane as for V4 to V6 electrodes

V8 Posterior scapular line at the same horizontal plane as V4 to V6 electrodes

V9 Left border of spine at the same horizontal plane as V4 to V6 electrodes

The ECG changes in V1-3 are :

- Tall slightly widened R wave in V1-3
- Depressed concave upwards ST segment in V1-3
- Upright, widened & tall T wave in V1-3

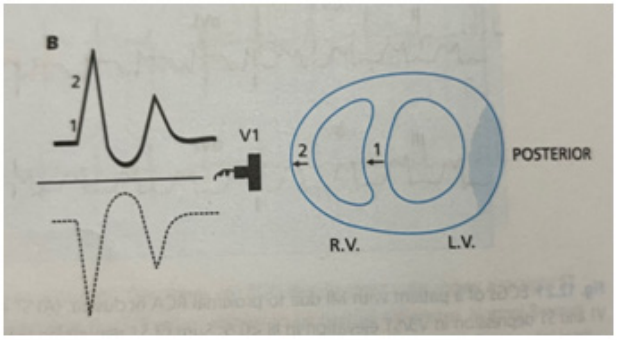


FIGURE :The leads V1-V3 reflect the changes mentioned above which is a mirror image of Q with ST elevation & T inversion seen in posterior leads (2)

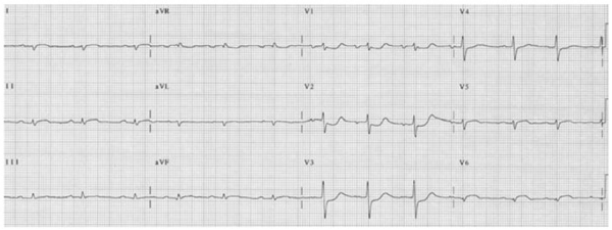


FIGURE : ECG of a 58- year-old male presenting with chest pain. There is ST elevation in leads I, V5, and V6, and ST depression in V1-3

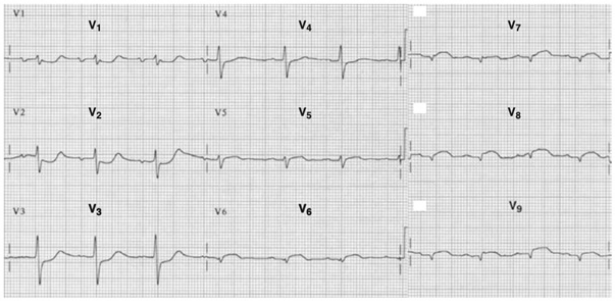


FIGURE : Recording of precordial leads together with V7 to V9. ST elevation is present in V6 as well as V7 to V9 consistent with acute posterolateral MI

There is an overlap between inferior, lateral, and posterior infarctions based on the arterial distribution and involvement. The terms are often used in combination depending on which leads are involved. For example,

- ILWMI
- IPWMI
- PLWMI
- IPLWMI
- IPL+RVMI

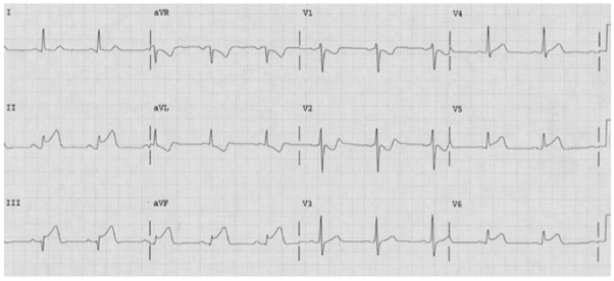


FIGURE : Acute ILWMI with ST elevation in leads II,IIIa,VF,V5,V6

HIGH LATERAL WALL MI

ST elevation in leads I & aVL only denotes high lateral wall MI which is usually caused by occlusion of diagonal or obtuse marginal

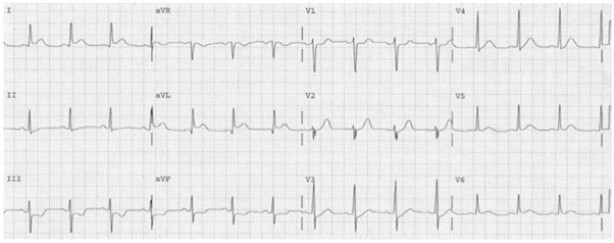


FIGURE : High Lateral wall MI- ST elevation in I, aVL

COMPLICATIONS OF ACUTE MI

Apart from diagnosing the location of MI with the culprit artery, ECG is also helpful for the diagnosis of possible complications like arrythmias or conduction blocks.

VENTRICULAR ARRYTHMIAS

Ventricular arrythmia is the most common cause of sudden cardiac arrest in a patient with acute MI. Electrical instability of the myocardium during MI & during reperfusion can result in :

- Frequent ventricular ectopics
- Idioventricular rhythm
- Monomorphic ventricular tachycardia (VT)
- Polymorphic VT
- Ventricular fibrillation (VF)

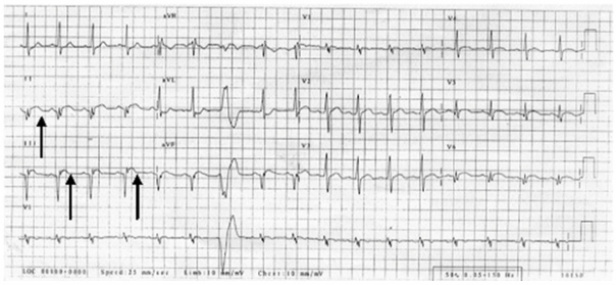


FIGURE : IWMI with ventricular ectopic (wide QRS with secondary ST-T changes); arrows point to Q with St elevation in inferior leads

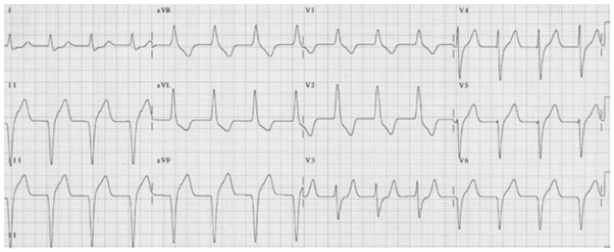


FIGURE : Accelerated idioventricular rhythm (wide QRS complexes with rate between 50-110 bpm) in a patient with acute IWMI. The rate of ventricular ectopic pacemaker is higher than the sinus rate and this rhythm usually indicates reperfusion.

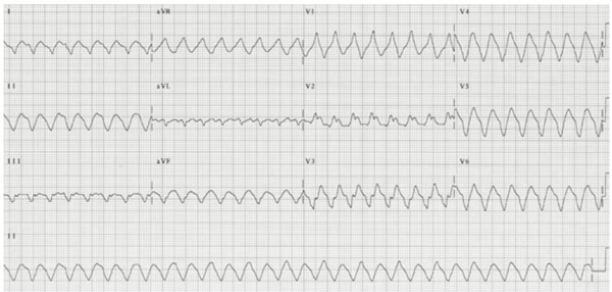


FIGURE : Monomorphic Ventricular tachycardia - regular wide QRS tachycardia with uniform QRS complexes in each lead

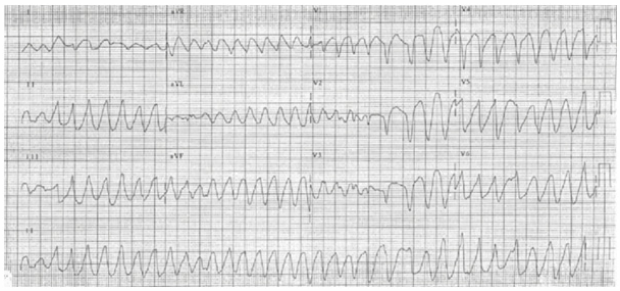


FIGURE : Polymorphic ventricular tachycardia - a form of ventricular tachycardia in which there are multiple ventricular foci with the resultant QRS complex varying in amplitude, axis, and duration.

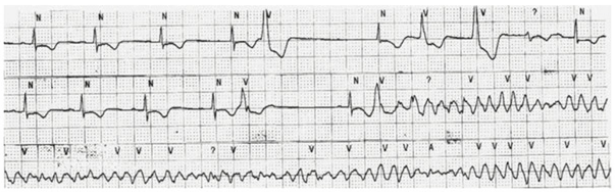


FIGURE : Rhythm strip showing ventricular fibrillation (bizarre complexes without any identifiable P,QRS or T waves in a patient with acute Lateral wall MI

ATRIAL ARRYTHMIAS

Atrial infarction, reflex autonomic balance, sudden hemodynamic stress on atria due to acute LV dysfunction / valve regurgitation are the common reasons for atrial arrythmias. The following arrythmias may be seen in acute MI :

- Atrial ectopics
- Atrial tachycardia
- Atrial fibrillation

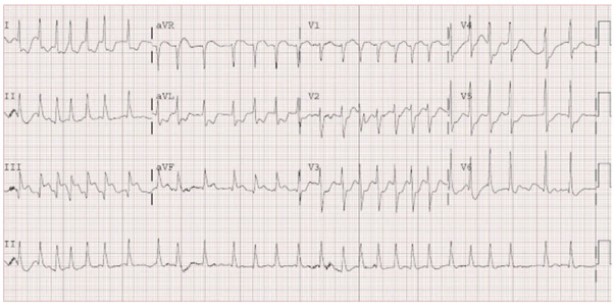


FIGURE : Acute Inferior + RVMI with atrial fibrillation with fast ventricular rate (irregular narrow QRS tachycardia) usually indicates underlying atrial infarction

SINUS BRADYCARDIA & TACHYCARDIA

Sinus tachycardia more common in AWMI due to LV dysfunction

Sinus bradycardia more common in IWMI due to increased vagal tone

CONDUCTION BLOCKS

- LBBB - new onset LBBB in AWMI is a diagnostic criteria for diagnosis of acute MI
- RBBB-appearance of qRBBB in an AWMI indicates proximal LAD occlusion & is due to infarction of the interventricular septum
- Hemiblocks - LAHB/LPHB can also be seen

ATRIOVENTRICULAR BLOCKS

Varying degree of AV nodal blocks are frequently seen in IWMI. It is due to reflex vagal activation / occlusion of AV nodal artery arising from PDA. The types of AV blocks seen are

- First degree AV block
- Second degree AV block
- Complete heart block (CHB)

The CHB in IWMI usually has narrow QRS, a stable escape rhythm with good rate and reverts within 2-3 days, maximum upto 1 week. The level of block is intranodal.

AV block in AWMI is due to extensive infarction of IVS with damage to His-Purkinje system (infra nodal). It is secondary to occlusion of septal branch of LAD. High degree AV block may precede CHB. CHB is usually sudden in onset, has a slow, unstable escape rhythm with wide QRS morphology. Asystole is common. Urgent temporary pacemaker is required. CHB persisting despite reversal of ischemia will require PPI.

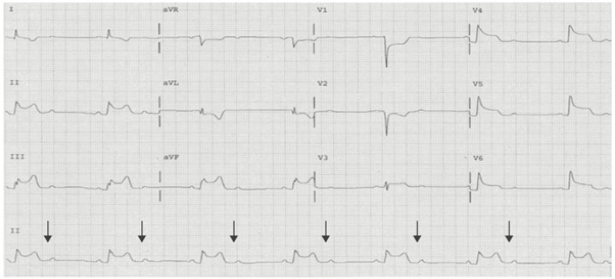


FIGURE : Acute inferolateral wall MI with 2:1 atrioventricular block (Every alternate P wave is not conducted-denoted by arrows)

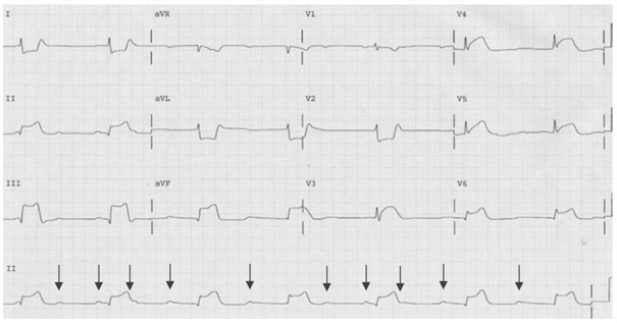
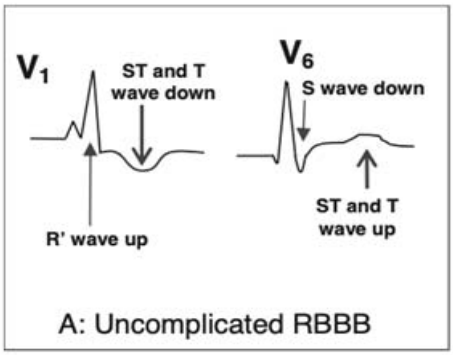


FIGURE : Acute IWMI with complete heart block. The P waves and QRS complexes are completely dissociated and many P waves are merged in the QRS complexes

DIAGNOSIS OF ACUTE MI IN THE PRESENCE OF UNDERLYING BBB

RIGHT BUNDLE BRANCH BLOCK

RBBB does not interfere with the diagnosis of acute STEMI. When ST elevation MI is complicated by RBBB, the ST segments become concordant (same direction) in relation to the terminal portion of the QRS complex. Thus, in anterior MI, the ST segments are elevated in V1 and often in V2 because terminal R' waves are normally present in these leads. Similar concordant changes may be noted in leads II, III, and aVF when there is inferior MI.



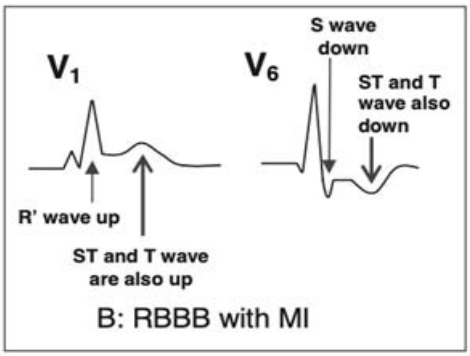


FIGURE : ST-T Changes in RBBB. (A) In uncomplicated RBBB, the ST segment and T wave are normally discordant (opposite in direction) to the terminal portion of the QRS complex. (B) When ST elevation myocardial infarction occurs, the ST segment (and T wave) becomes concordant (same direction) in relation to the terminal portion of the QRS complex. (1)

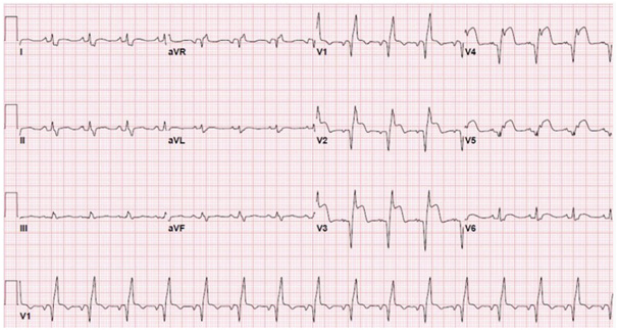


FIGURE : Acute AWMI with RBBB - ST elevation seen in leads V1-V5

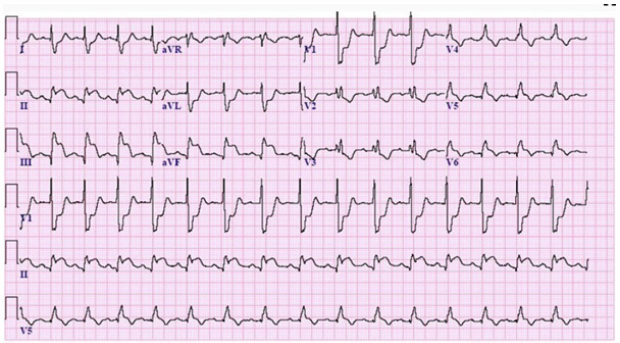


FIGURE : Acute IWMI with RBBB - ST elevation seen in leads II,III,aVF

LEFT BUNDLE BRANCH BLOCK

New onset LBBB with symptoms indicates acute anterior wall MI

In patients with documented LBBB earlier, it is difficult to diagnose AWMI due to masking effect of LBBB on QRS-ST-T changes. Modified Sgarbosa's criteria is used for diagnosing AWMI.

An acute IWMI can be diagnosed routinely since there is no masking effect in the inferior leads.

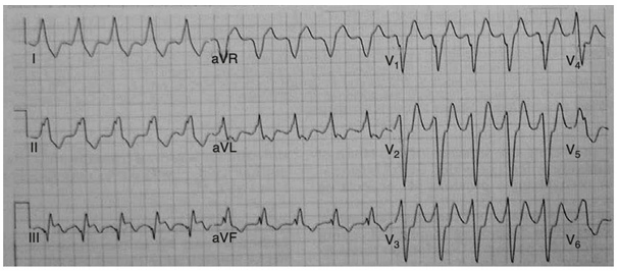


FIGURE : Acute IWMI in LBBB

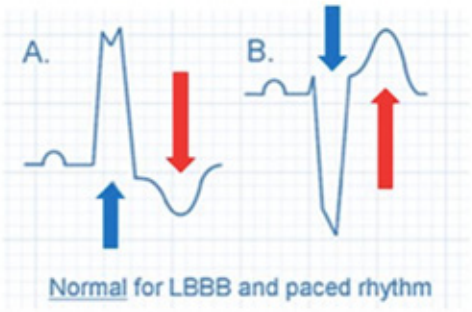
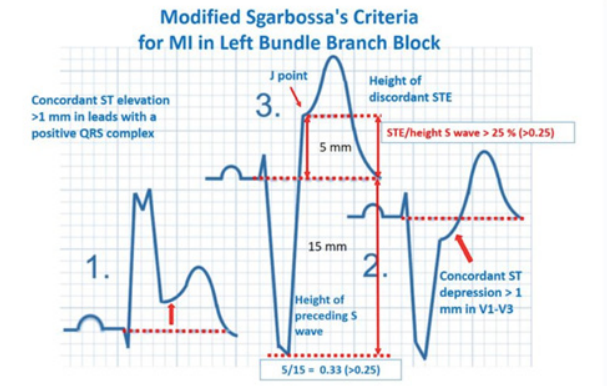


FIGURE : Discordant ST-T changes in LBBB (ST deviation is opposite to dominant QRS)

Smith-Modified Sgarbossa Criteria

- **Concordant ST elevation** ≥ 1 mm in ≥ 1 lead
- **Concordant ST depression** ≥ 1 mm in ≥ 1 lead of V1-V3
- ***Proportionally* excessive discordant STE** in ≥ 1 lead anywhere with ≥ 1 mm STE, as defined by ≥ 25% of the depth of the preceding S-wave



Any one criteria if positive is deemed 80% sensitive & 99% specific in diagnosing MI (5)

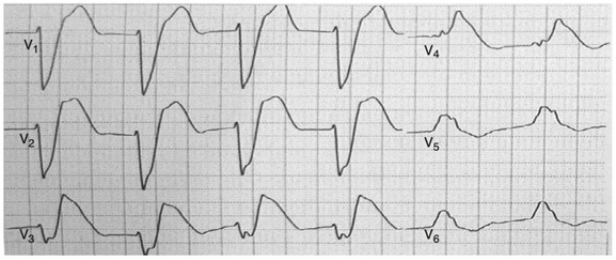


FIGURE : Anterior wall MI with LBBB-ST elevation in V1-V3 > 25% of preceding R wave

NON ST ELEVATION MI / UNSTABLE ANGINA

Patients with acute coronary syndrome due to subendocardial ischemia usually have ST depression, T-wave inversion, or less-specific ST and T wave abnormalities. Some patients may not show any changes in the ECG. These patients are diagnosed to have unstable angina with no evidence of myocardial necrosis or non-ST elevation myocardial infarction (NSTEMI) when evidence of myocardial necrosis is present (troponin positive).

The following ECG changes may be seen :

1. J point and ST segment depression of ? 1 mm below baseline.
2. Symmetrically inverted T waves measuring ? 2 mm.
3. The ST and T wave abnormalities may be less specific.

TABLE : LOCALISATION OF STEMI WITH INFARCT RELATED ARTERY (1)

Leads with ST Elevation	Location of the MI	Infarct-Related Artery
II, III, aVF	Inferior wall of the left ventricle	RCA in 85% to 90% LCx in 10% to 15%
I and aVL	High lateral	LCx or first diagonal branch of LAD
V1-V4	Anteroseptal	LAD
V1-6, I, aVL	Extensive anterior	LAD
V5-V6 + I, aVL	Lateral	LCx
ST depression in V1-V3 + tall R waves	Posterior	LCx

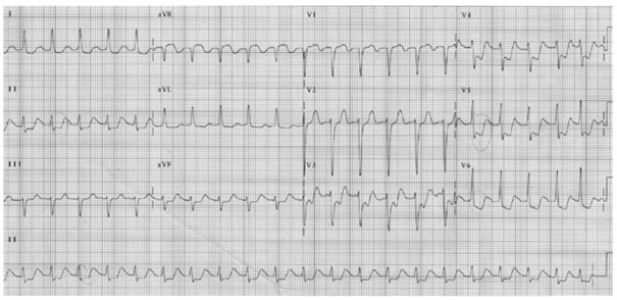


FIGURE : ECG showing ST depression in almost all the leads and ST elevation in lead aVR > V1 which indicates left main disease or severe triple vessel disease

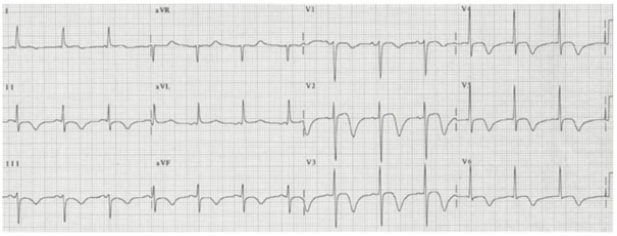


FIGURE : ECG showing deep, symmetrical T wave inversions in V1-6, II,III,aVF with troponin positive suggestive of NSTEMI

HIGH RISK SUBSETS IN ACUTE MI

The following subsets are at a higher risk of complications / adverse prognosis

- Large infarcts with ST elevation in many leads
- Multiple infarctions
- Global ST depression with aVR ST elevation (s/o left main disease)
- New bundle branch blocks
- Ventricular arrythmias - VT/VF
- CHB

CONCLUSION

ECG is the basic investigation to diagnose acute coronary syndromes in any patient presenting with chest pain. It is used to diagnose the type of MI, localize the culprit artery and identify complications which help in prompt management.

REFERENCES :

1. Basic and bedside electrocardiography - Romulo F.Baltazar
2. Leo Schamroth - An introduction to electrocardiography; 8th edition
3. Goldberger's clinical electrocardiography - A simplified approach; 9th edition
4. A primer of ECG - A simple and deductive approach - K.P.Misra
5. Smith SW, Dodd KW, Henry TD, Dvorak DM, Pearce LA. Diagnosis of ST elevation myocardial infarction in the presence of left bundle branch block with the ST elevation to S?wave ratio in a modified Sgarbossa rule. Ann Emerg Med. 2012; 60:766-776.
6. ECG pictures have been taken from various textbooks mentioned above and from journals.

Cardiac Biomarkers In Acute Coronary Syndrome

Dr. Varsha Koul
Consultant, Department of Cardiology, Batra Hospital and Medical Research Centre, New Delhi
Email Id - varshakoul@gmail.com
Dr. Puneet Singla
Senior Resident, Department of Cardiology, Batra Hospital and Medical Research

Acute Coronary Syndrome

Acute Coronary Syndrome (ACS) encompasses a range of conditions, including unstable angina, Non-ST Elevation Myocardial Infarction (NSTEMI), and ST Elevation Myocardial Infarction (STEMI). It is one of the leading causes of admission to the Emergency Room (ER) worldwide. The diagnosis of ACS involves the evaluation of clinical signs and symptoms, electrocardiographic assessment, and measurement of circulating cardiac biomarkers.[1]

Patients who arrive with suspected ACS are initially categorized based on their ECG results for the purpose of initial management. Following this initial assessment, patients can be further categorized depending on the elevation in cardiac troponin levels. These two factors, i.e., ECG changes and elevated cardiac troponin, play the most crucial role in the initial assessment and diagnosis of ACS patients, aiding in risk assessment as well as determining the initial treatment approach. However, after the phase of acute management and stabilization has concluded, the majority of elements within the subsequent treatment approach are applicable uniformly to all patients with ACS, regardless of their initial ECG results or whether cardiac troponin elevation was present or absent upon presentation. Therefore, these aspects can be collectively addressed within a standardized pathway.[2]

Acute myocardial infarction is characterized by cardiomyocyte necrosis occurring in the clinical context of acute myocardial ischemia. This encompasses MI resulting from atherothrombotic events (referred to as Type 1 MI) as well as other potential causes of myocardial ischemia and myocyte necrosis, categorized as Type 2 to Type 5 MI. It's worth noting that myocardial injury represents a distinct condition, denoting the release of troponin due to mechanisms unrelated to myocardial ischemia, which does not meet the criteria for a frank MI. Whether myocardial injury is acute or chronic depends on the presence of dynamic changes in elevated troponin levels observed during serial testing. Various factors can trigger myocardial injury, including myocarditis, sepsis, takotsubo cardiomyopathy, heart valve diseases, cardiac arrhythmias, and heart failure (HF).[2]

Throughout the management of patients presenting with ACS, healthcare providers must exercise careful consideration of alternative differential diagnoses during their clinical assessment which are driven by distinct underlying pathological processes, exhibit different prognostic implications, and often necessitate distinct treatment approaches.

Biomarkers

Biomarkers are quantifiable biological substances used to indicate a particular biological state relevant to a specific disease process. An ideal biomarker should possess qualities such as precision, quick measurability, assistance in early diagnosis, reproducibility, and aid in disease management. In recent years, there has been a drastic transformation in the utilization of laboratory markers. Early biomarker evaluation involved the measurement of total enzyme activity of aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine kinase (CK), but these markers were relatively non-specific.

However, the development of immunoassays, as well as technical advances in automation, allowed the measurements of the CK MB isoenzyme (CK-MB) in mass rather than in activity and myoglobin.[3] Currently, cardiac troponins (CTn) have the highest sensitivity and specificity for myocardial necrosis and represent the biochemical gold standard for diagnosing acute myocardial infarction (AMI).[2] Some recent biomarkers are mentioned in Table 1. However, most of these are currently available only as a research tool and are yet to find a place in diagnostic or therapeutic algorithms.

Table 1: Recent cardiac Biomarkers

BIOMARKER	DESCRIPTION
MARKERS PREDICTING DEATH AND/OR ISCHEMIC EVENTS	
Cardiac myosin-binding protein C	Structural myocardial protein with discriminatory power similar to hsTn to diagnosis MI; may be particularly useful in early presentation after symptom onset
Chemokine ligand-5, -18, and -21	Mediators of monocyte recruitment induced by ischemia
Cysteine-rich angiogenic inducer 61	Matricellular protein involved in angiogenesis, inflammation, and fibrotic tissue repair; serves as a ligand for activated platelets binding to integrin aIIbâ3
Fibrin clot properties (clot lysis time, maximum turbidity)	Functional measures of clot resistance to lysis
Fibroblast growth factor 23	Multiple pleotropic effects of cardiovascular structure and function
Growth differentiation factor-15	Member of the transforming growth factor-beta cytokine superfamily that is released from cardiomyocytes after ischemia and reperfusion injury
Heart-type fatty acid-binding protein	Cytoplasmic protein involved in intracellular uptake and buffering of free fatty acids in the myocardium
Interleukin-6	Stimulator of hepatic synthesis of C-reactive protein
Interleukin-17	Produced by CD4+ T cells, it plays a role in host immunity and development of an unstable plaque
Membrane attack complex	Ischemia leads to changes in myocardial cell surface molecule expression, rendering the cell membrane a target for the complement system, ultimately leading to cell lysis
Myeloperoxidase	Hemeprotein released during degranulation of neutrophils and some monocytes
Pentraxin-3	Inflammatory marker associated with thin-cap vulnerable plaques
Placental growth factor	Member of the vascular endothelial growth factor family that is strongly upregulated in atherosclerotic lesions and acts as a primary inflammatory instigator of atherosclerotic plaque instability

Pregnancy-associated plasma protein A	Zinc-binding metalloproteinase found in vulnerable plaques that cause destabilization of the fibrous plaque
Progenitor cells	Mononuclear cells mobilized from the bone marrow into the circulation in response to tissue injury and contribute to repair and regeneration
Secretory phospholipase A2	Hydrolyzes phospholipids to generate lysophospholipids and fatty acids, thereby enhancing susceptibility of the vessel atherosclerosis
Soluble suppression of tumorigenicity-2	Member of the interleukin-1 receptor family that is a biomarker of myocardial fibrosis and remodeling
Triggering receptor expressed on myeloid cells-1	Immune receptor and member of the immunoglobulin superfamily that amplifies innate immune response
Trimethyllysine	Nutrient precursor of the gut microbiota-derived metabolite trimethylamine N-oxide
MARKERS PREDICTING HEART FAILURE	
Copeptin	Peptide fragment of provasopressin
Galectin-3	A galactoside-binding lectin mainly secreted by activated macrophages
Midregional proadrenomedullin	Peptide fragment of the vasodilatory peptide adrenomedullin
Midregional proatrial natriuretic peptide	Peptide fragment of atrial natriuretic peptide
Neopterin	Marker of monocyte activation
Osteoprotegerin	Modulator of immune function and inflammation

Table 2- Time course of most commonly used cardiac biomarkers

Markers	Onset (in hours)	Peak (in hours)	Duration
Troponin	3-12	18-24	10 days
Creatine kinase (total and MB)	3-12	18-24	36-48 hours
Lactate dehydrogenase	6-12	24-48	6-8 days
Myoglobin	1-4	6-7	24 hours

High-sensitivity cardiac troponins

Following the exclusion of clinical and ECG signs indicative of STEMI or extremely high-risk NSTE-ACS, biomarkers play a complementary role in the assessment, risk determination, and care of individuals with suspected ACS.[4] It is advised to measure a biomarker associated with cardiomyocyte injury, preferably high-sensitivity cardiac troponin (hs-cTn), in all patients with suspected ACS.[5] If the clinical presentation aligns with myocardial ischemia, an increase and/or decrease in cTn levels above the 99th percentile

observed in healthy individuals indicates a diagnosis of MI in accordance with the criteria outlined in the fourth universal definition of MI. In patients with MI, cTn levels typically rise swiftly (usually within 1 hour when high-sensitivity assays are employed) after the onset of symptoms and remain elevated for a variable duration (usually several days).[6]

Technological progress has resulted in the enhancement of cardiac troponin (cTn) assays, increasing their precision in detecting and quantifying cardiomyocyte injury. Extensive multicentre studies consistently show that high-sensitivity cTn (hs-cTn) assays improve the accuracy of diagnosing myocardial infarction (MI) at the initial presentation compared to conventional assays, especially in patients presenting shortly after experiencing chest pain. This enables a quicker confirmation or exclusion of MI. In general, both hs-cTn T and hs-cTn I subunit assays seem to provide comparable diagnostic accuracy in the early diagnosis of MI.[7,8]

We should try and refrain from using the terms 'normal' and 'abnormal' to describe hs-cTn levels and instead adopt the terms 'non-elevated' and 'elevated' to denote hs-cTn levels below and above the 99th percentile, respectively.[2]

Additionally, it's crucial to recognize that apart from Type 1 MI, there are other clinical conditions in which elevated cTn levels can be observed.

Central laboratory vs. point of care

The majority of cardiac troponin (cTn) assays performed in centralized laboratories fall into two categories: sensitive assays (which can detect cTn in around 20-50% of healthy individuals) and high-sensitivity assays (which can detect cTn in approximately 50-95% of healthy individuals). High-sensitivity assays are preferred over less sensitive ones due to their superior diagnostic accuracy, all while maintaining a similar cost. It's worth noting that most of the point-of-care (POC) tests currently in use do not meet the criteria for high-sensitivity assays. POC tests offer the advantage of providing faster results, but this benefit is counterbalanced by their lower sensitivity, reduced diagnostic accuracy, and diminished negative predictive value (NPV).

In a randomized trial involving low-risk chest pain patients with suspected NSTE-ACS and symptoms that had commenced at least 2 hours before arriving at the ambulance, it was reported that adopting a pre-hospital rule-out strategy (utilizing a single POC conventional troponin T test) resulted in a significant reduction in 30-day healthcare costs and a comparable rate of major adverse cardiovascular events (MACE) compared to an ER rule-out strategy following standard local procedures.[9,10]

Overall, automated assays have been subject to more extensive evaluation than POC tests and are currently the preferred choice. However, given the rapidly evolving nature of this field, it will be essential to re-evaluate this preference when highly validated high-sensitivity POC tests become clinically accessible.[11]

Confounders of cardiac troponin concentration

In patients presenting with suspected NSTE-ACS, there are four clinical variables that influence hs-cTn concentrations in addition to the presence or absence of MI. These variables include:

Age: Concentrations of hs-cTn can differ significantly between very young and very old individuals, with variances of up to 300% noted in healthy subjects.

Renal dysfunction: Patients with substantial differences in estimated glomerular filtration rate (eGFR), ranging from very high to very low, can exhibit variations of up to 300% in hs-cTn levels, even when they are otherwise healthy.

Time from chest pain onset: The duration of time elapsed since the onset of chest pain can impact hs-cTn levels by more than 300%.

Gender: While to a lesser extent, gender can also influence hs-cTn concentrations, causing approximately a 40% difference.

Despite the potential baseline variations in hs-cTn values associated with these four variables,

absolute changes in hs-cTn levels still hold diagnostic and prognostic significance. Therefore, until automated tools, such as risk assessment calculators, that consider the influence of all four clinical variables (age, eGFR, time from chest pain onset, and gender) become accessible, it is recommended to adhere to uniform cutoff concentrations as the standard approach for the early diagnosis of MI.[2,12]

Rapid 'rule-in' and 'rule-out' algorithms

Due to their heightened sensitivity and enhanced diagnostic accuracy in detecting MI upon presentation, the utilization of hs-cTn assays allows for a reduction in the time interval required for the second cTn assessment. This, in turn, significantly diminishes the delay in diagnosis, leading to shorter stays in the ER, reduced costs, and decreased diagnostic uncertainty for patients. The recommended approaches include the 0 h/1 h algorithm (preferred) or the 0 h/2 h algorithm (secondary choice). These algorithms have been established and validated through extensive multicentre diagnostic studies, employing central adjudication of the final diagnosis for all presently available hs-cTn assays. Optimal cutoff values for rule-out were selected to achieve a sensitivity and negative predictive value (NPV) of at least 99%. Conversely, optimal cutoff values for rule-in were chosen to attain a positive predictive value (PPV) of at least 70%. Notably, recent investigations have indicated that the ESC 0 h/3 h algorithm, considered as an alternative, may not strike the ideal balance between efficacy and safety when compared to swifter protocols employing lower rule-out concentrations, such as the ESC 0 h/1 h algorithm. The exceptional safety and effectiveness of the ESC 0 h/1 h algorithm have been reaffirmed in three real-world implementation studies, including one randomized controlled trial (RCT). Therefore, the ESC 0 h/3 h algorithm may be considered in cases where the ESC 0 h/1 h or 0 h/2 h algorithms are unavailable. It's essential to note that patients directed towards the 'rule-out' pathway using the ESC 0 h/1 h or 0 h/2 h algorithms exhibit a very low rate of clinical events within 30 days.[2,13]

The European Society of Cardiology (ESC) 0 h/1 h and 0 h/2 h algorithms are founded on two fundamental principles:

Continuous Variable: hs-cTn is recognized as a continuous variable, with the probability of MI increasing as hs-cTn values rise.

Early Absolute Changes: Early absolute changes in hs-cTn levels within 1 h or 2 h serve as proxies for absolute changes over a longer period (3 h or 6 h) and provide additional diagnostic value alongside the initial cTn assessment at presentation. The specific cutoff concentrations within the 0 h/1 h and 0 h/2 h algorithms are assay-dependent.

In the 'rule-out' pathway, the NPV for MI has consistently surpassed 99% in various extensive validation cohorts. Nevertheless, assignment to the 'rule-out' pathway does not invariably imply outpatient management. Instead, when coupled with clinical and ECG findings, the 0 h/1 h and 0 h/2 h algorithms facilitate the identification of suitable candidates for early discharge and outpatient care. Even after ruling out MI, further elective non-invasive or invasive imaging may be indicated based on clinical and risk assessments, and an alternative diagnosis should be determined.

Regarding the 'rule-in' pathway, studies have reported a PPV for MI in the range of approximately 70-75%. Many 'rule-in' pathway patients, even if diagnosed with conditions other than MI, still require specialized cardiology input and either coronary angiography or non-invasive imaging to establish a precise final diagnosis. Consequently, the vast majority of patients triaged towards the 'rule-in' pathway using these algorithms will necessitate hospital admission and invasive coronary angiography.

Patients who do not meet the criteria for either the 'rule-out' or 'rule-in' pathways are placed in the 'observe' pathway. This group encompasses diverse cases and has demonstrated a mortality rate comparable to that of 'rule-in' patients. Hence, individual assessments based on each patient's specific risk profile, such as risk scores, are crucial for those in this category. Additionally, it is

recommended to perform a third cTn measurement at 3 h (plus/minus echocardiography) as the subsequent step to guide further management.

In the 'observe' category, most patients with a strong clinical suspicion of ACS (e.g., a significant increase in cTn levels from presentation to 3 hours) may be potential candidates for invasive coronary angiography. Conversely, patients with a low to moderate likelihood of ACS, based on clinical judgment, are suitable candidates for non-invasive imaging after transitioning from the ER to the ward. Computed tomography (CT) angiography can assist in diagnosis and, notably, in identifying patients with unobstructed coronary arteries who may be discharged after ruling out other relevant conditions. CT angiography can also pinpoint patients with obstructive coronary disease where revascularization might be considered. In cases where alternative conditions have been identified to explain the cTn values (e.g., rapid ventricular rate response to atrial fibrillation, severe anaemia, or a hypertensive emergency), further diagnostic testing, may not be necessary.

The same principles apply to the 0 h/2 h algorithm. These ESC algorithms should always be integrated with a thorough clinical assessment and a 12-lead ECG. Repeat blood sampling is essential in cases where patients experience ongoing or recurrent chest pain. Recently, artificial intelligence models incorporating serial hs-cTn measurements in conjunction with individual risk profiles have been proposed to assist in personalized diagnostic evaluations for patients with suspected MI. Similarly, risk assessment models that combine hs-cTn values at presentation and after early or late resampling have been developed to predict MI events within the first 30 days.

For the effective implementation of the ESC 0 h/1 h algorithm, it is advisable to obtain blood samples for hs-cTn at 0 h and 1 h irrespective of other clinical details and pending results. While this may result in unnecessary cTn measurements in approximately 10-15% of patients with very low 0 h concentrations and chest pain onset exceeding 3 h, it significantly streamlines the process and enhances patient safety. Additionally, the 0 h blood sample should be promptly collected upon admission to the ED.[2]

Other biomarkers

Utilizing biomarkers other than cardiac troponin (cTn) for the diagnosis of ACS is discouraged, except in cases where cTn is unavailable. Among the multitude of additional biomarkers evaluated for the diagnosis of NSTEMI, only CK-MB, myosin-binding protein C, and copeptin may have clinical relevance when used in combination with (standard) cTn T/I, although in most clinical situations their incremental value above and beyond cTn is limited.[14]

BNP and NT-proBNP

These markers are employed for the diagnosis and assessment of the severity of congestive heart failure. N-Terminal brain natriuretic peptide (NT-proBNP) serves as an indicator in the bloodstream for brain natriuretic peptide (BNP), a hormone that increases during cardiac stress caused by the stretching of heart chambers. They also play a crucial role in monitoring the effectiveness of heart failure therapies. In a community-based study conducted in Japan, BNP was prospectively examined as a biomarker for cardiovascular events in 9625 patients with chronic kidney disease (CKD). Notably, participants with the highest serum BNP levels exhibited a significantly elevated risk of cardiovascular events.[15]

In another study involving 134 haemodialysis patients, Sommerer et al.[16] found that NT-proBNP plasma levels were elevated in 100% of cases, while approximately 40% had elevated cardiac troponin T (cTnT) levels, despite being asymptomatic. Importantly, both increased NT-proBNP and cTnT were strongly associated with adverse cardiovascular outcomes, including 23 deaths due to myocardial infarction (MI) and sudden cardiac death.

Recent research has revealed that both BNP and NT-proBNP exhibit similar long- and short-term prognostic capabilities in cases of acute MI with ST-segment elevation or without ST-segment elevation, both upon hospital admission and

during hospitalization.[17] Additionally, BNP and NT-proBNP have emerged as prognostic markers for long-term mortality after an acute coronary event. This association has been observed across various ACS scenarios, encompassing patients with STEMI, NSTEMI, unstable angina (UA), with or without elevated cardiac troponin, and with or without clinical signs of heart failure.[17]

Sub studies conducted within large-scale clinical trials have evaluated the prognostic value of BNP and NT-proBNP in patients presenting with non-ST-segment elevation acute coronary syndrome (NSTE-ACS).[18] In all of these studies, elevated levels of BNP and NT-proBNP consistently predicted adverse outcomes. A recent analysis conducted by the Sabatine[19] group included 450 patients from the OPUS-TIMI 14 trial and 1,635 patients from the TACTICS-TIMI 18 trial, both of which investigated an approach involving multiple markers in ACS without ST-segment elevation. The analysis found that BNP, CRP (C-reactive protein), and cTnI (cardiac troponin I) were all independent predictors of adverse outcomes. The incidence of adverse events not only correlated with the positivity of each marker but also with the number of positive markers. Patients with the worst prognosis who exhibited a relative risk of death at 30 days between 6.0 and 13.0, were those with a combined increase in levels of cTnI (indicative of thrombosis and myocardial necrosis), CRP (reflecting inflammatory status), and BNP (indicating myocardial dysfunction). More recently, plasma natriuretic peptide concentrations have also been linked to the risk of cardiovascular events and mortality in apparently asymptomatic individuals.[19]

Heart-type Fatty Acid-binding Protein (H-FABP)

Heart-type fatty acid-binding protein (H-FABP) is a compact, soluble protein with a molecular weight of 15 kDa. Comprising 132 amino acids, it ranks among the most abundant proteins found in the heart, constituting approximately 5 to 15% of the total cytosolic protein content in the aqueous cytoplasm. Glatz et al introduced this protein in 1988 as a potential novel biochemical marker for the early detection of acute myocardial infarction (AMI), a finding subsequently validated by other research studies. In physiological states, H-FABP remains absent from plasma or interstitial fluid but is released into the bloodstream following cardiac cellular injury. The ratio of H-FABP concentration within the cytoplasm compared to that in the vasculature is approximately 200,000 to 1. Typically, the concentration of H-FABP in plasma or serum is less than 5 ìg/L, rendering it a suitable indicator for the early identification and quantification of myocardial tissue damage.[20,21]

Research by Goìrski et al[22] revealed that both H-FABP and myoglobin concentrations were significantly elevated in individuals with renal failure. Importantly, the levels of these markers remained unaffected by dialysis treatment. It's worth noting that the effectiveness of H-FABP in diagnosing AMI is notably reduced in patients with renal failure.[20,21]

CONCLUSION

An ideal biomarker should be precise, reproducible, quickly measurable and assist in early diagnosis and disease management. Recently, a number of biomarkers have been studied in ACS. But cardiac troponins still remain the gold standard biomarker for diagnosis of ACS as well as for risk stratification of patients presenting to the ER with chest pain. Specially with the advent of high sensitivity troponins, which help in the triage of such patients leading to reduction in mortality, as well as a dramatic reduction in the turnaround time of chest pain patients, bringing down the overall healthcare costs.

REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD, Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). Circulation. 2018 Nov 13;138(20):e618-51.

2. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, Gilard M. 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). European Heart Journal. 2023 Aug 25:ehad191.

3. Biomarkers Definitions Working Group, Atkinson Jr AJ, Colburn WA, DeGruttola VG, DeMets DL, Downing GJ, Hoth DF, Oates JA, Peck CC, Schooley RT, Spilker BA. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clinical pharmacology & therapeutics. 2001 Mar;69(3):89-95.

4. Shah AS, Anand A, Strachan FE, Ferry AV, Lee KK, Chapman AR, Sandeman D, Stables CL, Adamson PD, Andrews JP, Anwar MS. High-sensitivity troponin in the evaluation of patients with suspected acute coronary syndrome: a stepped-wedge, cluster-randomised controlled trial. The Lancet. 2018 Sep 15;392(10151):919-28.

5. Twerenbold R, Boeddinghaus J, Nestelberger T, Wildi K, Rubini Gimenez M, Badertscher P, Mueller C. Clinical use of high-sensitivity cardiac troponin in patients with suspected myocardial infarction. Journal of the American College of Cardiology. 2017 Aug 22;70(8):996-1012.

6. Reichlin T, Hochholzer W, Bassetti S, Steuer S, Stelzig C, Hartwiger S, Biedert S, Schaub N, Buerge C, Potocki M, Noveanu M. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. New England Journal of Medicine. 2009 Aug 27;361(9):858-67.

7. Boeddinghaus J, Nestelberger T, Twerenbold R, Neumann JT, Lindahl B, Giannitsis E, Sörensen NA, Badertscher P, Jann JE, Wussler D, Puelacher C. Impact of age on the performance of the ESC 0/1h-algorithms for early diagnosis of myocardial infarction. European heart journal. 2018 Nov 7;39(42):3780-94.

8. Twerenbold R, Badertscher P, Boeddinghaus J, Nestelberger T, Wildi K, Puelacher C, Sabti Z, Rubini Gimenez M, Tschirky S, du Fay de Lavallaz J, Kozhuharov N. 0/1-Hour triage algorithm for myocardial infarction in patients with renal dysfunction. Circulation. 2018 Jan 30;137(5):436-51.

9. Mueller C, Giannitsis E, Möckel M, Huber K, Mair J, Plebani M, Thygesen K, Jaffe AS, Lindahl B, Biomarker Study Group of the ESC Acute Cardiovascular Care Association. Rapid rule out of acute myocardial infarction: novel biomarker-based strategies. European Heart Journal: Acute Cardiovascular Care. 2017 Apr;6(3):218-22.

10. Collinson PO, Saenger AK, Apple FS, IFCC C-CB. High sensitivity, contemporary and point-of-care cardiac troponin assays: educational aids developed by the IFCC Committee on Clinical Application of Cardiac Bio-Markers. Clinical Chemistry and Laboratory Medicine (CCLM). 2019 Apr 24;57(5):623-32.

11. Möckel M, Giannitsis E, Mueller C, Huber K, Jaffe AS, Mair J, Plebani M, Thygesen K, Lindahl B, Biomarker Study Group of the European Society of Cardiology Acute Cardiovascular Care Association. Editor's choice-rule-in of acute myocardial infarction: Focus on troponin. European Heart Journal: Acute Cardiovascular Care. 2017 Apr;6(3):212-7.

12. Reichlin T, Irfan A, Twerenbold R, Reiter M, Hochholzer W, Burkhalter H, Bassetti S, Steuer S, Winkler K, Peter F, Meissner J. Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction. Circulation. 2011 Jul 12;124(2):136-45.

13. Twerenbold R, Costabel JP, Nestelberger T, Campos R, Wussler D, Arbucci R, Cortes M, Boeddinghaus J, Baumgartner B, Nickel CH,

Bingisser R. Outcome of applying the ESC 0/1-hour algorithm in patients with suspected myocardial infarction. Journal of the American College of Cardiology. 2019 Jul 30;74(4):483-94.

14. Restan IZ, Sanchez AY, Steiro OT, Lopez-Ayala P, Tjora HL, Langørgen J, Omland T, Boeddinghaus J, Nestelberger T, Koechlin L, Collinson P. Adding stress biomarkers to high-sensitivity cardiac troponin for rapid non-ST-elevation myocardial infarction rule-out protocols. European Heart Journal Acute Cardiovascular Care. 2022 Mar 1;11(3):201-12.

15. Sakuma M, Nakamura M, Tanaka F, Onoda T, Itai K, Tanno K, Ohsawa M, Sakata K, Yoshida Y, Kawamura K, Makita S. Plasma B-type natriuretic peptide level and cardiovascular events in chronic kidney disease in a community-based population. Circulation Journal. 2010;74(4):792-7.

16. Sommerer C, Beimler J, Schwenger V, Heckele N, Katus HA, Giannitsis E, Zeier M. Cardiac biomarkers and survival in haemodialysis patients. European journal of clinical investigation. 2007 May;37(5):350-6.

17. Galvani M, Ottani F, Oltrona L, Ardissino D, Gensini GF, Maggioni AP, Mannucci PM, Mininni N, Prando MD, Tubaro M, Vernocchi A. N-terminal pro-brain natriuretic peptide on admission has prognostic value across the whole spectrum of acute coronary syndromes. Circulation. 2004 Jul 13;110(2):128-34.

18. White HD, French JK. Use of brain natriuretic peptide levels for risk assessment in non–ST-elevation acute coronary syndromes. Journal of the American College of Cardiology. 2003 Dec 3;42(11):1917-20.

19. Sabatine MS, Morrow DA, de Lemos JA, Gibson CM, Murphy SA, Rifai N, McCabe C, Antman EM, Cannon CP, Braunwald E. Multimarker approach to risk stratification in non-ST elevation acute coronary syndromes: simultaneous assessment of troponin I, C-reactive protein, and B-type natriuretic peptide. Circulation. 2002 Apr 16;105(15):1760-3.

20. Chacko S, Haseeb S, Glover BM, Wallbridge D, Harper A. The role of biomarkers in the diagnosis and risk stratification of acute coronary syndrome. Future science OA. 2017 Oct 27;4(1):FSO251.

21. Mohan G, Kaur R, Singh T. Cardiac biomarkers in acute coronary syndrome. Current Trends in Diagnosis and Treatment. 2017 Jul;1(2):80-8.

22. Goìrski J, Hermens WT, Borawski J, Mysliwiec M, Glatz JF. Increased fatty acid-binding protein concentration in plasma of patients with chronic renal failure. Clinical chemistry. 1997 Jan 1;43(1):193-5.

23. Angurana DK, Lone NA, Khan KA, Jalal S, Sangral R, Rather HA, Alai MS, Habib K, Bhogal BN, Jan VM. Rapid measurement of B-type natriuretic peptide in the diagnosis of congestive heart failure in patients presenting to the emergency department with acute shortness of breath. Int J Med Med Sci. 2011 Mar;3:77-82.

24. Morrow DA, Braunwald E. Future of biomarkers in acute coronary syndromes: moving toward a multimarker strategy. Circulation. 2003 Jul 22;108(3):250-2.

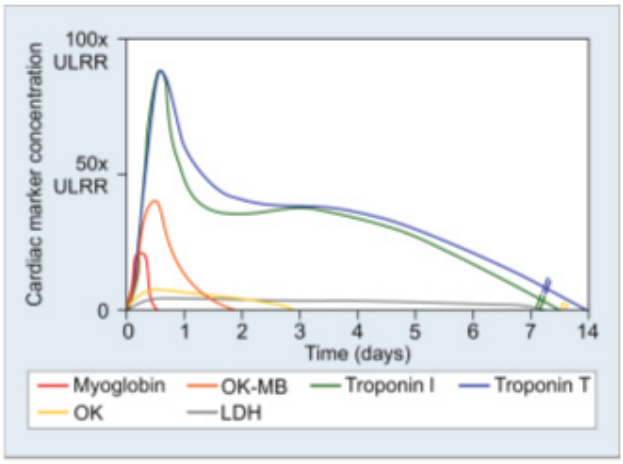


Figure 1. Cardiac markers change in level with time.[24]

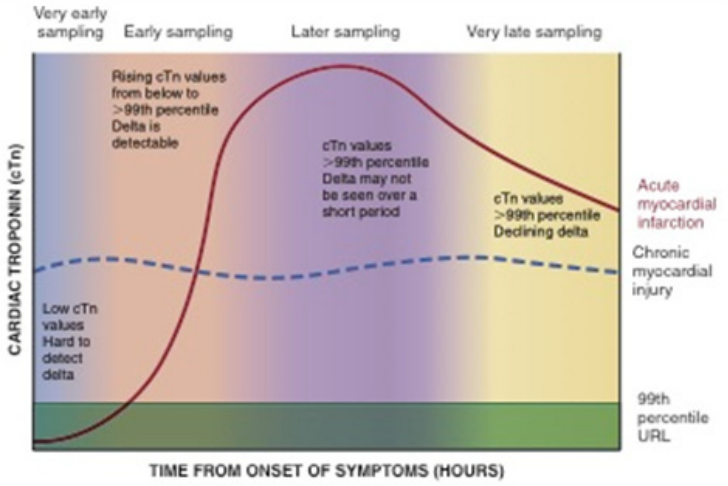


Figure 2. Timing of release of cardiac troponin.[1]

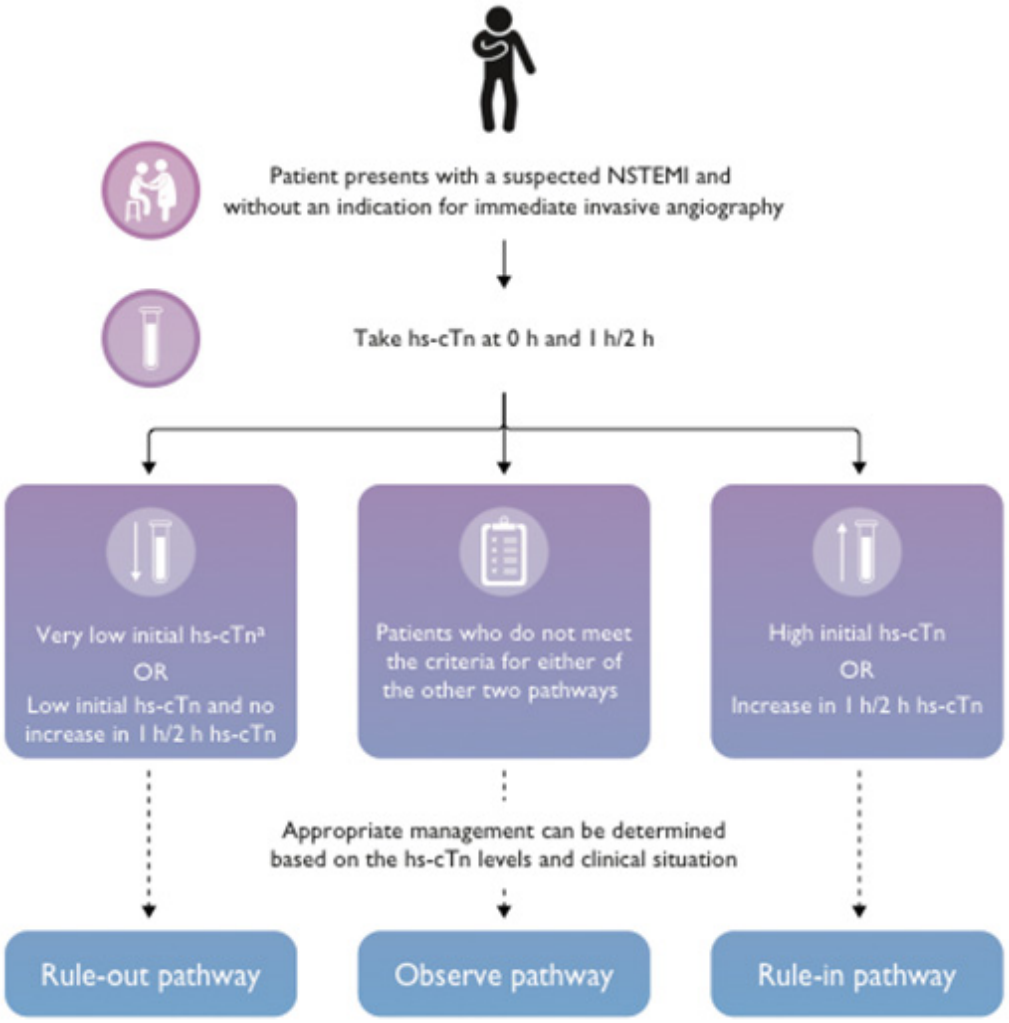


Figure 3 showing 0 h/1 h or 0 h/2 h rule-out and rule-in algorithms using high-sensitivity cardiac troponin assays.[2]

Role of Echocardiography in Acute Coronary Syndrome

Dr. Gopinath
Senior Interventional Cardiologist.
Rajiv Gandhi Superspeciality Hospital (Opec), Raichur, Karnataka

INTRODUCTION

Acute coronary syndrome" covers a spectrum of presentations, from unstable angina through to ST segment elevation myocardial infarction (STEMI)". A large number of patients present daily to the emergency department with the chief complaint of chest pain. Evaluation of coronary artery disease is the most common use of Echocardiography.

CLASSIFICATION OF ACS

Unstable angina	ECG changes Markers not raised
NSTEMI	ST depressions and/or T inversions
	Markers are elevated
STEMI	ST elevation Markers elevated

ISCHEMIC CASCADE

NORMAL FUNCTION
↓
PERFUSION ABNORMALITY
↓
DIASTOLIC DYSFUNCTION
↓
RWMA (REGIONAL WALL MOTION ABNORMALITY)
↓
ECG CHANGES
↓
ANGINA INFARCTION

Echocardiography in ACS is of great benefit under these scenarios

DIAGNOSIS OF CAD IN EMERGENCY IN THE PRESENCE OF *NONDIAGNOSTIC* OR *EQUIVOCAL ECGs*

RISK STRATIFICATION IN ACS

EVALUATION OF PATIENTS IN ACS

DIAGNOSIS AND EVALUATION OF COMPLICATIONS OF AMI

PROGNOSTIC DATA IN CAD

The challenge for the physician is to identify patients who require intervention, particularly when acute coronary syndromes (ACSs) present with atypical symptoms or non-diagnostic electrocardiogram (ECG) changes or normal cardiac enzyme levels.

Since the mortality and morbidity of ischemic heart disease improves following early treatment, timely diagnosis is of vital importance not only to help the patient but also to reduce hospital stay and economic costs.

Echocardiography gives structural, functional and hemodynamic information. It is the most frequently used cardiovascular diagnostic test after electrocardiography and chest X-ray. It is non-invasive, relatively cheap, and is an ideal portable imaging technique.

Newer imaging modalities, including myocardial contrast echo for the assessment of perfusion, hold great promise.

Transthoracic Echocardiography is essential both for diagnosing acute coronary syndrome, evaluation of ventricular systolic function, diastolic function, presence of regional wall motion abnormalities, and for ruling out other etiologies

of acute chest pain or dyspnea, including aortic dissection and pericardial effusion.

This chapter will concentrate on the current applications of echocardiography in patients with coronary artery disease

VARIOUS ECHO MODALITIES USED IN ACS

1. M-MODE
2. 2D-ECHOCARDIOGRAPHY
3. DOPPLER STUDY
4. CONTRAST ECHOCARDIOGRAPHY
5. SECOND HARMONIC IMAGING
6. TEE (RARELY)
7. STRESS ECHOCARDIOGRAPHY
8. 3D-ECHOCARDIOGRAPHY

Three dimensional echocardiography is more accurate than 2D echocardiography in the assessment of LV size and shape and may have a particular role in the evaluation of LV remodelling. It is a gold standard in research and is now coming into more routine clinical use, although the work involved in data acquisition and image reconstruction remains significant.

ECHOCARDIOGRAPHY IN THE EMERGENCY

The potential use of echocardiography for diagnosis of MI is based on observations of the effects of interruption of coronary flow.

Sequence of events seen in ACS are as follows

1. Left ventricular diastolic dysfunction occurs before systolic dysfunction;
2. Segmental wall motion abnormalities (RWMA) seen by echocardiography
3. ECG abnormalities and chest pain are relatively late events

In summary, echocardiography in the emergency room may facilitate early diagnosis and management in those patients with a high clinical suspicion of MI but a non-diagnostic ECG.

Regional wall motion should be assessed on multiple image views at the parasternal long-axis and short-axis views, apical four-chamber, two-chamber, and three-chamber views.

Subcostal views can prove extremely helpful, especially when parasternal or apical views are of poor quality (ex-Thick chest wall,COPD)

Second harmonic imaging with high signal-to-noise ratio can augment the clarity of the images.

RISK STRATIFICATION IN THE CORONARY CARE UNIT

Echocardiography is of tremendous value in risk stratification in ACS (MI and unstable angina)

- It is helpful for these patients to have assessment of LV function before angiography
- Identify unsuspected valvar abnormalities and
- Evaluate right heart function

Left ventricular angiography may not be appropriate in critically ill patients and it is easier to obtain accurate information before invasive testing.

All patients with acute MI should ideally have early echocardiography. In some patients it may assist in diagnosis;

It may also assist decision making if the appropriateness of reperfusion is uncertain by demonstrating the localisation and extent of wall motion abnormality.

Multiple indices of LV systolic and diastolic function have predictive value post-MI. Left ventricular wall motion score index (WMSI) is obtained by grading the motion of myocardial segments based on a standard model (Table 2).

Severe LV diastolic dysfunction tends to be associated with large infarctions, but a restrictive pattern is also independently associated with poor outcome.

ASESSMENT OF LV FUNCTION

GLOBAL LV FUNCTION

GIVES BOTH DIAGNOSTIC AND PROGNOSTIC INFORMATION

EJECTION FRACTION

VISUAL 'EYE BALL' METHOD (MANY STUDIES – SUPPORT)

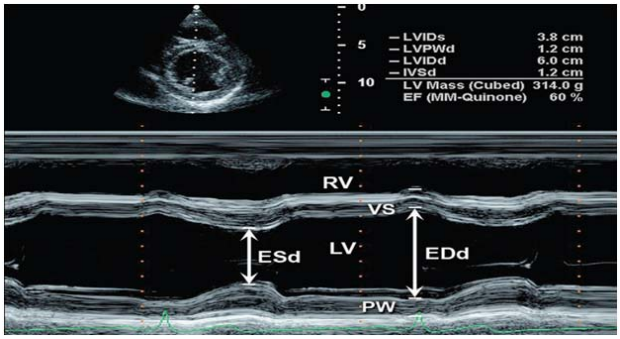
USING LV DIMENSIONS IN M-MODE

SIMPSON'S RULE OR RULE OF DISK

BIPLANE METHODOLOGY - MORE APPROPRIATE

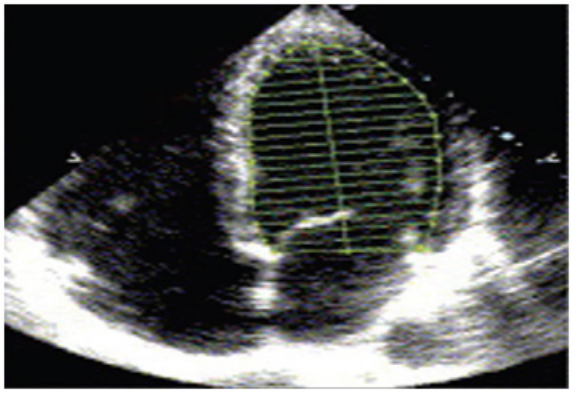
LV SYSTOLIC FUNCTION ASESSMENT (M-MODE)

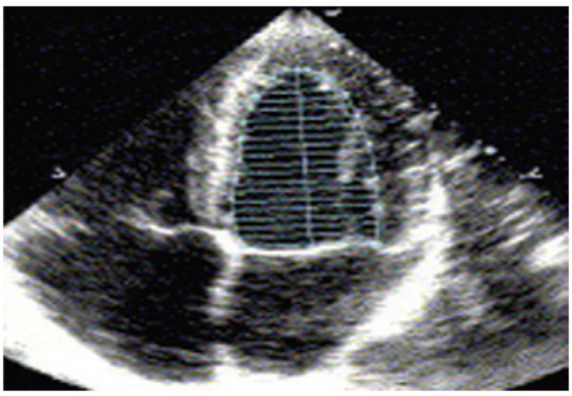
$$\frac{LVIDd - LVIDs}{LVIDd} X\ 100$$

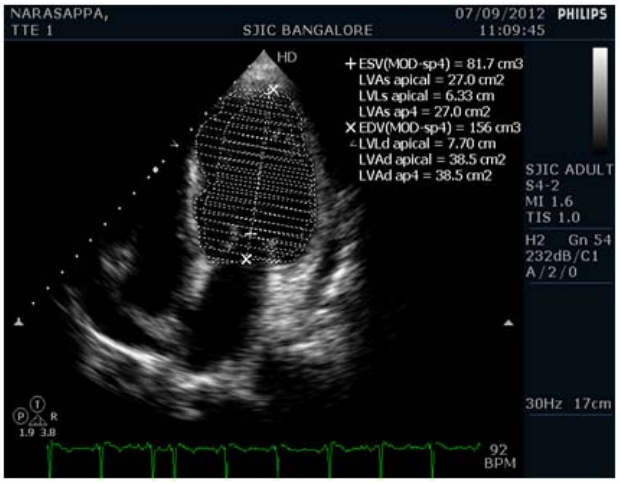


BIPLANE SIMPSON METHOD (USING 2D-ECHO)

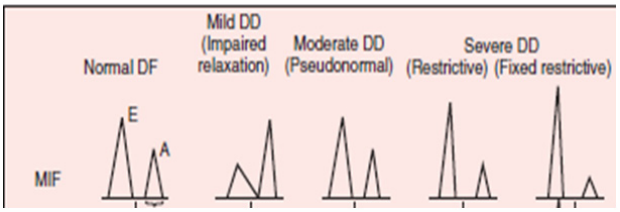
$$EF = \frac{EDV - ESV}{EDV} X\ 100$$







ASSESSMENT OF DIASTOLIC FUNCTION(USING DOPPLER)



There are many newer techniques that can be utilised for evaluation of LV function and ischaemia, including tissue Doppler imaging, strain rate imaging, and tissue characterisation; the discussion of these is beyond the scope of this review.

Exercise echocardiography is appropriate for patients who can walk on a treadmill. Pharmacological stress echo is indicated primarily in patients unable to exercise adequately for non-cardiac reasons and for assessment of viability.

The Role of Echocardiography in the Diagnosis of Coronary Artery Disease and Localization of Acute Myocardial Infarction

Evaluation of Myocardial Wall Motion Abnormalities

BASIC PRINCIPLES

Segmental WMA's correspond with the coronary blood supply

WMA more sensitive than ECG

RWMA: Hall Mark Of Acute Ischemic Syndrome

Initial hypokinesia/ akinesia	But Normal Wall Thickness
4-6 wks	Thinning And Increased Echogenicity
Transmural (>50% of wall thickness , q waves)	Definite Akinesis And Thinning

ACUTE INFARCTION

Wall thickness normal

Systolic thickening reduced or absent

OLD MI

Thinning

Abnormal motion

Absent wall thickening

Resting blood flow preserved until 90% lesion

>70% lesion	Ischemia with Exertion Exercise

In clinical practice, visual (eye ball) assessment via Two-Dimensional (2D) Echocardiography provides a rapid evaluation of regional systolic function. In each imaging plane, the left ventricle (LV) is divided into several segments, with each segment being scored a numerical value to signify the degree of contraction.

The American Heart Association recommended a 17-segment model (Figure 1). The locations of the segments follow the territory of the coronary arteries to expedite the evaluation of ischemia.

The severity of contractile dysfunction is, accordingly, scored visually in each segment as 1 for normal contraction or hyperkinesia, 2 for hypokinesis, 3 for akinesia, 4 for dyskinesia, and 5 for aneurysmal segments, and the global wall motion score is thereafter calculated by averaging the readings in all the segments.

A normal LV has a wall motion score index of 1, and the index increases as wall motion abnormalities increase in severity. There is a good correlation between the wall motion score index and functional impairment: a wall motion score index of 1.1–1.9 can predict a small infarct size, and an index equal to or greater than 2.0 can predict the occurrence of complications. (Table 2)

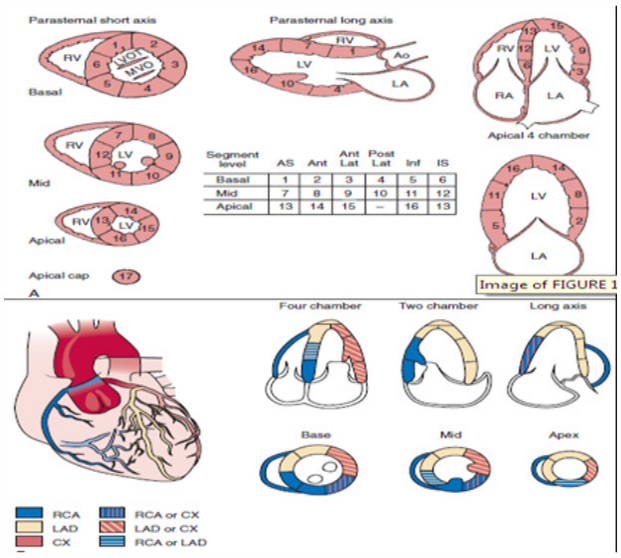
Table 2 : Qualitative scale for derivation of the echocardiographic wall motion score index

Score*	Wall motion	Definition
0	Hyperkinetic	Increased endocardial inward movement and systolic wall thickening
1	Normal	Normal endocardial inward movement and systolic wall thickening
2	Hypokinetic	Reduced endocardial inward movement and systolic wall thickening
3	Akinetic	Absence of endocardial inward movement; no systolic wall thickening
4	Dyskinetic	Outward wall movement in systole with absent wall thickening; often associated with myocardial thinning and fibrosis

*The score for each segment is divided by the number of segments visualised to obtain the wall motion score index.

SEGMENTAL APPROACH OF RWMA

17TH SEGMENT - TRUE APEX



Segment level	AS	Ant	Ant Lat	Post Lat	Inf	IS
Basal	1	2	3	4	5	6
Mid	7	8	9	10	11	12
Apical	13	14	15	–	16	13

Figure 1 : Segmental model for regional wall motion analysis. The left ventricle (LV) is divided into three levels: 6 basal; 6 mid; and 4 apical segments. LA, Left atrium; LV, Left ventricle; RA, Right atrium; RV, Right ventricle; Ao, Aorta; LVOT, Left ventricular outflow tract; MVO, Mitral valve orifice; AS, Anteroseptum; Ant, Anterior; Ant-Lat, Anterolateral; Post-Lat, Posterolateral; Inf, Inferior; IS, Inferoseptum on the basis of its contractile function as assessed visually

Normal (>40% thickening with systole)

Hypokinesia (10% to 40% thickening)

Severe hypokinesia to akinesia (<10% thickening)

Dyskinesia and Aneurysm

Localization of Infarction

The potential value of 2D Echocardiography as a diagnostic tool in acute myocardial infarction (AMI) was discovered very early, and a large number of studies reported its high sensitivity, both qualitatively and quantitatively.

Moreover, 2D Echocardiography is extremely accurate for the localization of the infarction.

There is a significant relationship between infarction and contractile dysfunction; consequently, the absence of wall motion abnormality or wall thinning rules out a clinically significant infarction.

Assessment of Infarct Size

As much as the pattern of dysfunction may be a reflection of the extent of an infarction, the circumferential extent of dysfunction could be more than the extent of the infarction, which might be in consequence of multi-vessel disease or a previous infarction. Ordinarily, wall motion analysis, in comparison with wall thickening, tends to overestimate the infarct size, but both parameters offer similarly close estimates of the infarct size.

Right Ventricular Infarction

Echocardiography is the imaging method of choice for the diagnosis of right ventricular (RV) infarction. The 2D Echocardiographic findings of RV infarction encompass RV dilation, RV systolic dysfunction, segmental wall motion abnormalities, and paradoxical septal motion. In many cases, inferior wall motion abnormality is likely to be subtle with a preserved overall LV function. TDI may provide complementary evidence of RV infarction.

The characteristic echocardiographic features of RV dysfunction in the setting of an RV infarction are increased right atrial pressure, begetting an interatrial septum shift toward the left atrium (LA), and dilation of the inferior vena cava with decreased (or lack of) inspiratory collapsibility, which correlates perfectly with the clinical status and prognosis.

Hemodynamic Assessment of Patients with Acute Myocardial Infarction Using Doppler Echocardiography

Patients with an AMI were classified into several groups based on the cardiac index and pulmonary capillary wedge pressure (PCWP) by Forrester and colleagues in 1976:

Group I: normal hemodynamics (cardiac index [CI] > 2.2 L/min/m^2, PCWP d 18 mmHg);

Group II: pulmonary congestion (CI > 2.2 L/min/m^2, PCWP > 18 mmHg);

Group III: peripheral hypoperfusion (CI d 2.2 L/min/m^2, PCWP d 18 mmHg); and

Group IV: pulmonary congestion and peripheral hypoperfusion (CI d 2.2 L/min/m^2, PCWP > 18 mmHg).

This classification is capable of predicting in-hospital mortality, irrespective of the patient's age, gender, precipitating factors, and location of the infarction.

In contrast, a meticulously performed Doppler echocardiographic examination can provide sufficient information to determine the hemodynamic category after an infarction without increased mortality.

CONTRAST ECHOCARDIOGRAPHY

First generation contrast agents such as agitated saline have been available for many years and are still useful for detection of intracardiac shunts. However these agents do not opacify the LV, as the bubbles cannot survive passage through the lungs. Second generation contrast agents incorporate high molecular weight gases which are more stable and can traverse pulmonary capillaries. Microbubble properties depend on bubble size, shell composition, and the gas used.

Myocardial contrast echocardiography

After many years of research, the assessment of coronary perfusion using myocardial contrast echocardiography (MCE) is starting to become a clinical reality. Visual assessment of myocardial perfusion from grey scale images is limited by the poor signal to noise ratio and the limited ability of the human eye to distinguish different shades of grey. Innovative ultrasound methods using harmonic imaging have been developed to exploit the interaction between microbubbles and ultrasound and enable assessment of perfusion. The use of contrast agents for LV opacification is very safe; the safety of MCE may depend on the type of contrast agent and mode of administration, and needs study in larger populations.

Myocardial perfusion has been extensively investigated by intracoronary injection, although no agents are specifically approved for intracoronary use. It is a reproducible and reliable technique for evaluation of the risk area after coronary occlusion, regional coronary flow reserve, myocardial viability, and the outcome of reperfusion.

Stress Echocardiography

Echocardiography is a valuable tool for the assessment of the cardiac structure and function in patients with coronary artery disease. Regional wall motion abnormalities correlate well with the significant stenosis of the coronary arteries; this becomes more evident during stress.

Stress (exercise or pharmacological) Echocardiography can be employed to demonstrate the presence of coronary artery disease by the induction of wall motion abnormalities.

Both exercise and pharmacologic stress echocardiographic examinations are well accepted and well tolerated by patients. Stress Echocardiography is suitable for symptomatic patients with an intermediate pretest probability of coronary artery disease and contraindication to regular treadmill stress testing.

Dobutamine Stress Echocardiography for Evaluation of Hibernating Viable Myocardium

Echocardiography is useful for the evaluation of myocardial viability and the demonstration of the magnitude of recovery after revascularization. Pharmacological Stress Echocardiography examines the "inotropic reserve" of the dysfunctional but viable myocardium through the administration of an inotropic agent. (Dobutamine is the most frequently used agent.) In response to inotrope administration, the viable myocardium exhibits an improved global or regional contractile function (inotropic reserve), which is assessed via simultaneous TTE.

Conclusion

Echocardiography is an accurate tool for the

evaluation of patients with known or suspected coronary artery disease. Every patient should be evaluated clinically for pretest probability of coronary artery disease and risk of future cardiac events. Patients with intermediate and high pretest probability could potentially benefit from testing for either diagnosis or prognosis.

COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION

This topic itself is a separate chapter, Hence it is covered briefly here. Echocardiography is the mainstay of diagnosis of mechanical complications of myocardial infarction (MI),and patients with unexplained haemodynamic deterioration should be immediately evaluated.

Cardiac Rupture

Many LV ruptures cause sudden death. However rupture may be subacute, allowing time for intervention. Direct visualisation of the rupture is often difficult as it may be only a "slit" in the myocardium and the location of pericardial fluid may not correlate with the area of rupture. However, intrapericardial thrombus is often present (fig 1)

An LV pseudoaneurysm forms when the rupture is contained, so that a cavity outside the LV develops lined by pericardium and often thrombus. (fig 2A, B).

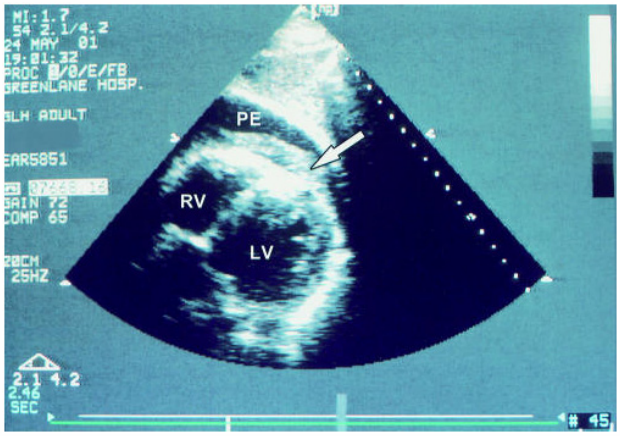


Figure 1 : Subcostal long axis transthoracic image showing a pericardial effusion (PE) and intrapericardial thrombus (arrow) in a patient with left ventricular rupture post-infarction. LV, left ventricle; RV, right ventricle.

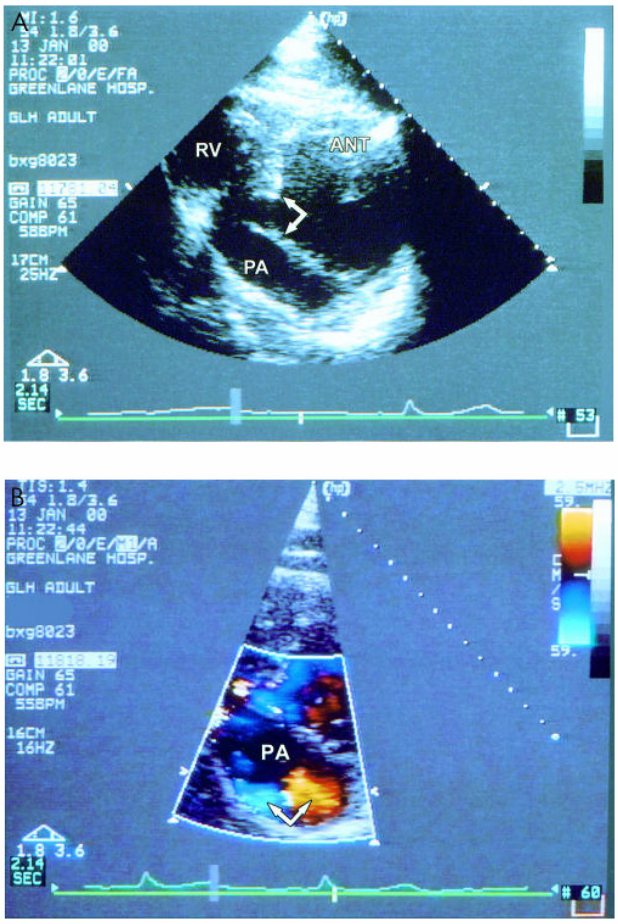


Figure 2 : (A) Parasternal short axis transthoracic image showing a pseudoaneurysm of the inferior wall. The arrows show the characteristic abrupt disruption of the inferior wall and a narrow neck leading to the pseudoaneurysm. (B) Parasternal short axis transthoracic image (same patient as in A) showing bidirectional flow (arrows) from colour Doppler. Ant, anterior left ventricular wall, RV, right ventricle. PA, pseudoaneurysm.

Ventricular septal rupture

Septal rupture may be difficult to distinguish clinically from mitral regurgitation (MR). From 2D echocardiography a discrete defect may be visible, but there may also be multiple serpiginous channels in the necrotic myocardium. The diagnosis can usually be made by TTE; experience is essential as the most useful views depend on the location of defect. Subcostal views are particularly useful in the critically ill, supine patient with inferior infarction (fig 3A).

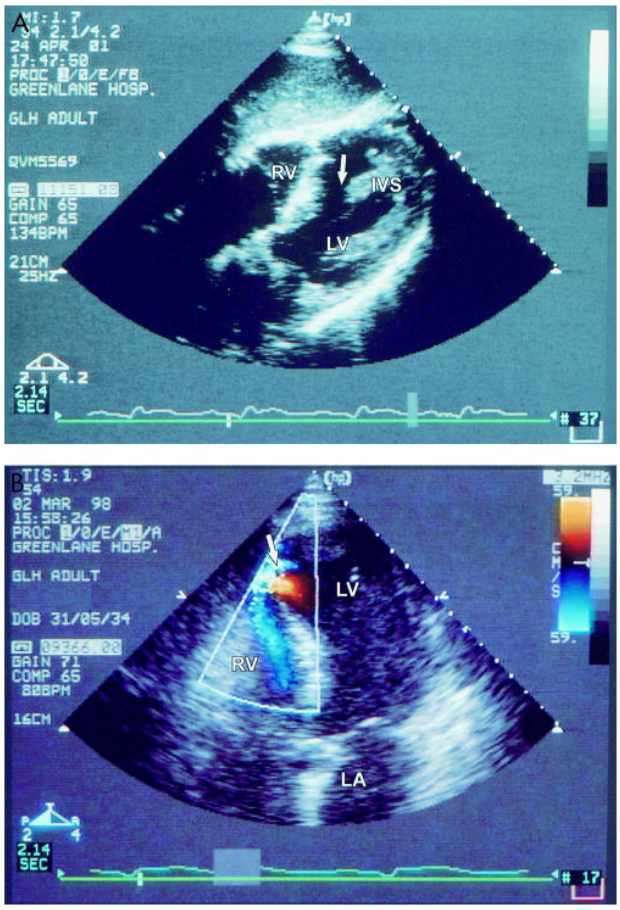


Figure 3 : (A) Subcostal long axis transthoracic image showing a large post-infarction rupture (arrow) in the mid inferior ventricular septum (IVS). (B) Apical four chamber transthoracic image showing colour Doppler flow (arrow) through a postinfarction apical ventricular septal defect. LA, left atrium; LV, left ventricle; RV, right ventricle.

Papillary muscle rupture

Papillary muscle rupture is the most serious mechanism of MR in acute infarction. It usually involves the posteromedial muscle which is perfused from the posterior descending artery, whereas the anterolateral muscle has blood supply from both diagonal and circumflex arteries. Rupture of a papillary muscle head causes severe MR; rupture of the entire trunk is generally fatal..

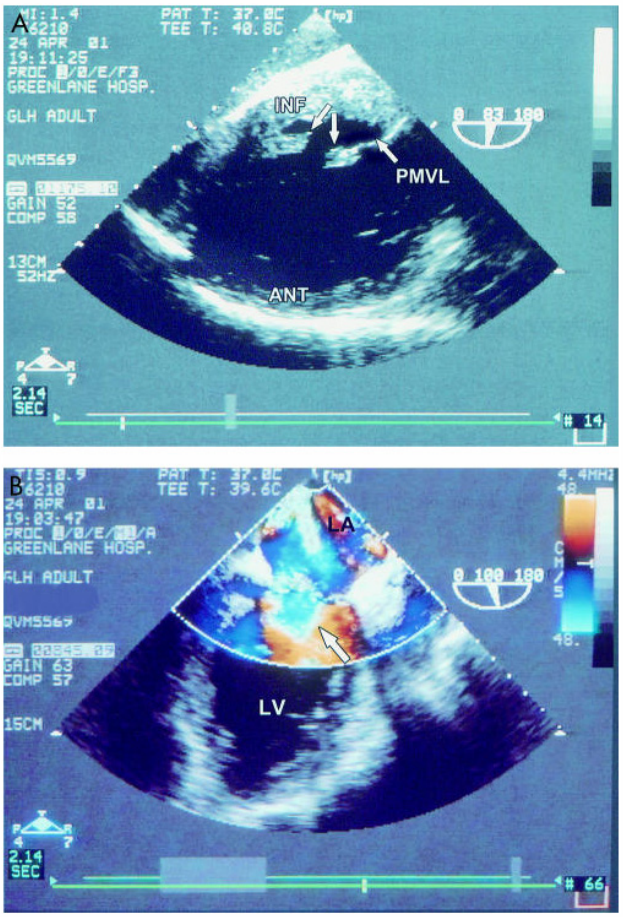


Figure 4 : (A) Transgastric image showing rupture of the posteromedial papillary muscle postinfarction. The arrows point to the separated portions of the trunk of the papillary muscle. (B) Transoesophageal image (same patient as in A) showing pronounced flow convergence from colour Doppler (arrow) as flow accelerates towards a regurgitant orifice; this is characteristic of severe mitral regurgitation. PMVL, posterior mitral valve leaflet; INF, inferior LV wall; ANT, anterior LV wall; LV, left ventricle; LA, left atrium.

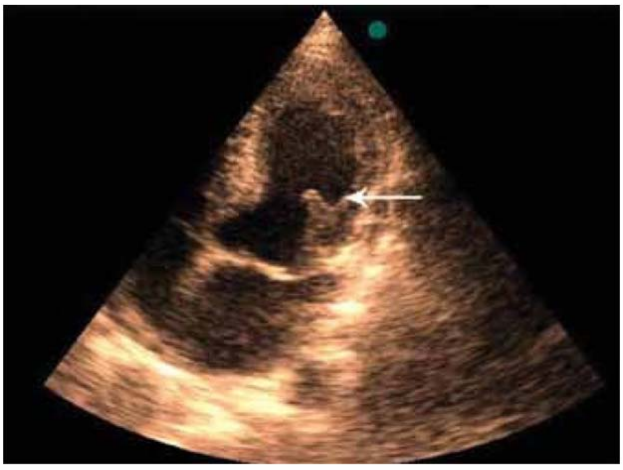


Figure 5 : Modified two-dimensional echocardiogram in the apical four-chamber view, showing the rupture of an anterolateral papillary muscle (arrow) in a patient who recently had a lateral myocardial infarction Rarely, multiple catastrophic mechanical complications of MI may occur in the same patient (figs 3A and 4A, B).

Aneurysm formation

True aneurysms complicate transmural infarction and are caused by dilatation of an area of scar (fig 6 and 7). An aneurysm is defined as deformation of both the diastolic and systolic LV contours with dyskinesis in systole. TTE is a sensitive tool for the diagnosis. .Aneurysm formation is a poor prognostic sign and is associated with congestive cardiac failure, arrhythmias, and thrombus formation.

Left Ventricular Thrombi

Before the reperfusion era, ventricular thrombi were reported in 25–40% of patients after an anterior MI. They were frequently reported with anteroapical MI and relatively extensive areas of abnormal wall motion. LV thrombus formation occurs in the regions of blood stasis (most commonly in the apex), but it may also be seen within aneurysms at the lateral and inferior walls. The peak timing of early thrombus formation is seventy-two hours; nevertheless, in larger MIs with large areas of akinesis and stagnant flow, thrombus formation tends to occur even within hours (Figures 6 and 8).

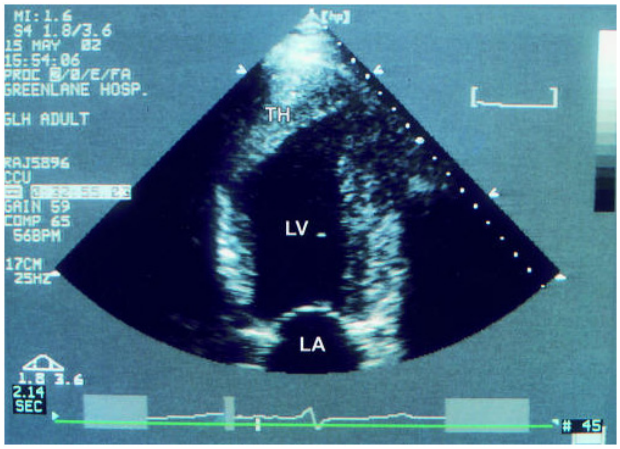


Figure 6 : Apical four chamber transthoracic image showing extensive thrombus in an apical aneurysm. TH, thrombus; LV, left ventricle; LA, left atrium.

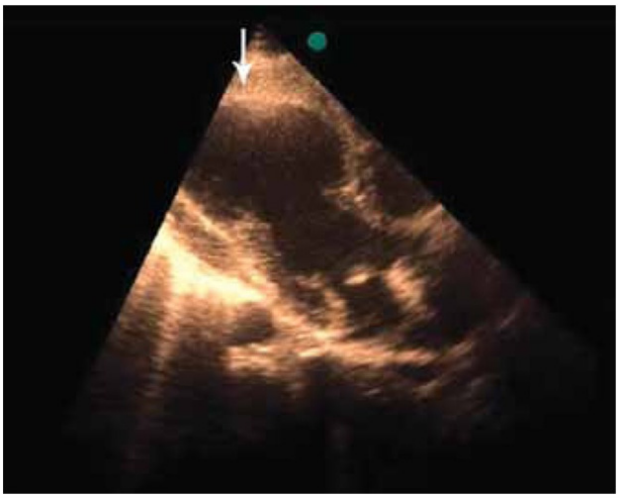


Figure 7 : Two-dimensional echocardiogram in the parasternal long-axis view, demonstrating a large true aneurysm in the left ventricle apex (arrow) in a patient who had a relatively old anteroapical myocardial infarction

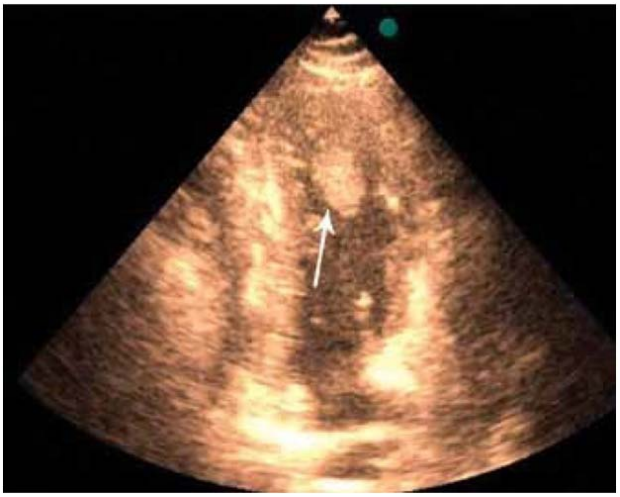


Figure 8 : Modified two-dimensional echocardiogram in the apical two-chamber view, revealing a large left ventricular apical clot (arrow) following a recent anterior myocardial infarction

Pericardial Effusion and Tamponade

The incidence of post-infarction pericardial effusion as detected by 2D Echocardiography is reported to be from 30–40% in patients with STEMI. The amount of effusion is minor, and the peak time for effusion to occur is three days after the infarction. The resolution is slow; effusion may

still be present six months after the infraction. Pericardial effusion occurs more frequently in patients who have had anterior MI and in those with heart failure. The cause of pericardial effusion is epicardial inflammation. Tamponade is rare in an uncomplicated MI. Larger effusion or effusion with a hemorrhagic appearance should always be considered a myocardial rupture(Figure-1).

Post-Infarction Pericarditis

Post-infarction pericarditis most often occurs between three and ten days in the wake of a Q wave MI with a mean incidence of 25% and is less common when thrombolytic therapy has been employed. An echocardiogram is often ordered in patients in whom pericarditis is suspected. No echocardiographic feature is diagnostic of the disease. Echocardiography is a sensitive technique for the diagnosis of pericardial effusion along with pericarditis; the absence of fluid, however, does not exclude pericarditis.

Echocardiography in acute coronary syndromes: key points

- Transthoracic and transoesophageal echocardiography are complementary techniques with different strengths
- Transoesophageal echocardiography is very safe, but does have potential complications and should be performed by experienced physicians
- Hand held cardiac ultrasound devices are likely to be increasingly used in both the emergency room and coronary care unit but remain controversial
- Echocardiography for diagnosis of myocardial infarction is most helpful in patients with a high clinical suspicion but a normal or non-diagnostic ECG
- Patients with unexplained haemodynamic deterioration postinfarction should be referred immediately for echocardiography
- Echocardiographic indices of left ventricular systolic and diastolic function provide prognostic information in unstable angina and myocardial infarction
- Contrast echocardiography for left ventricular opacification may be helpful in the evaluation of cardiac function in "technically difficult" subjects
- Myocardial contrast echocardiography can evaluate the success of reperfusion and assess myocardial viability
- Intravenous myocardial contrast echocardiography is likely to become a routine clinical tool

REFERENCES

1. **Premawardhana U**, Celermajer DS. Advances in echocardiography. *Aust NZ J Med* 2000;30:360–6.
2. **Daniel WG**, Erbel R, Kasper W, *et al*. Safety of transesophageal echocardiography. A multicenter survey of 10,419 examinations. *Circulation* 1991;83:817–21.
3. **Bonow RO**, Mann DL, Zipes DP, Libby P, editors. Braunwald's Heart disease, A Text book of Cardiovascular medicine, Twelth Edition
4. **Armstrong WF**, Ryan Thomas Feigenbaum's Echocardiography,Eighth Edition
5. **Saily C Greaves** et al Role of Echocardiography in acute coronary syndrome.**Heart** 2002;88(4):419-425
4. **Kishon Y**, Iqbal A, Oh JK, *et al*. Evolution of echocardiographic modalities in detection of post myocardial infarction ventricular septal defect and papillary muscle rupture: study of 62 patients. *Am Heart J* 1993;126(3 Pt1):667–75.
5. **Jugdutt BI**, Sivaram CA. Prospective two-dimensional echocardiographic evaluation of LV thrombus and embolism after acute myocardial infarction. *J Am Coll Cardiol* 1989;13:554–64.

6. **Goldberger JJ**, Himelman RB, Wolfe CL, *et al*. Right ventricular infarction: recognition and assessment of its hemodynamic significance by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1991;4:140–6.

7. **Peels KH**, Visser CA, Dambrink JHE, *et al* on behalf of the CATS Investigators Group. Left ventricular wall motion score as an early predictor of left ventricular dilation and mortality after first anterior infarction treated with thrombolysis. The CATS investigators group. *Am J Cardiol* 1996;77:1149–54.

8. **Feinberg MS**, Schwammenthal E, Shlizerman L, *et al*. Prognostic significance of mild mitral regurgitation by color Doppler echocardiography in acute myocardial infarction. *Am J Cardiol* 2000;86:903–7.

9. **Korup E**, Kober L, Torp-Pedersen C, *et al* on behalf of the TRACE Study Group. Prognostic usefulness of repeated echocardiographic evaluation after acute myocardial infarction. *Am J Cardiol* 1999;83:1559–62.

10. **Ioannidis JPA**, Salem D, Chew PW, *et al*. Accuracy of imaging technologies in the diagnosis of acute cardiac ischemia in the emergency department: a meta-analysis. *Ann Emerg Med* 2001;37:471–7.

11. **Zabalgoitia M**, Ismaeil M. Diagnostic and prognostic use of stress echocardiography in acute coronary syndromes including emergency department imaging. *Echocardiography* 2000;17:479–93.

12. **Trippi JA**, Lee KS, Kopp G, *et al*. Dobutamine stress tele-echocardiography for evaluation of emergency department patients with chest pain. *J Am Coll Cardiol* 1997;30:627–32.

13. **Mulvagh SL**, DeMaria AN, Feinstein SB, *et al*. Contrast echocardiography: current and future applications. *J Am Soc Echocardiogr* 2000;13:331–42.

14. **Kaul S**. Myocardial contrast echocardiography in acute myocardial infarction: time to test for routine clinical use? *Heart* 1999;81:2–5.

15. **Cerqueira MD,** Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. *Circulation*. 2002;105:539–542.

16. **Bhatnagar SK,** Al-Yusuf AR. Significance of early two-dimensional echocardiography after acute myocardial infarction. *Int J Cardiol*. 1984;5:575–584.

17. **Loh IK,** Charuzi Y, Beeder C, Marshall LA, Ginsburg JH. Early diagnosis of nontransmural myocardial infarction by two-dimensional echocardiography. *Am Heart J*. 1982;104:963–968.

18. **Otto CM**, Stratton JR, Maynard C, Althouse R, Johannessen KA, Kennedy JW. Echocardiographic evaluation of segmental wall motion early and late after thrombolytic therapy in acute myocardial infarction: the Western Washington Tissue Plasminogen Activator Emergency Room Trial. *Am J Cardiol*. 1990;65:132–138.

19. **Urheim S,** Edvardsen T, Torp H, Angelsen B, Smiseth OA. Myocardial strain by Doppler echocardiography. Validation of a new method to quantify regional myocardial function. *Circulation*. 2000;102:1158–1164.

20. **Giusca S,** Jurcut R, Ticulescu R, Dumitru D, Vladaia A, Savu O, Voican A, Popescu BA, Ginghina C. Accuracy of handheld echocardiography for bedside diagnostic evaluation in a tertiary cardiology center: comparison with standard echocardiography. *Echocardiography*. 2011;28:136–141.

21. **Sabia P**, Abbott RD, Afrookteh A, Keller MW, Touchstone DA, Kaul S. Importance of two-dimensional echocardiographic assessment of left ventricular systolic function in patients presenting to the emergency room with

cardiac-related symptoms. *Circulation*. 1991;84:1615–1624.

22. **Peels CH**, Visser CA, Kupper AJ, Visser FC, Roos JP. Usefulness of two-dimensional echocardiography for immediate detection of myocardial ischemia in the emergency room. *Am J Cardiol*. 1990;65:687–691.

23. **Horowitz RS**, Morganroth J, Parrotto C, Chen CC, Soffer J, Pauletto FJ. Immediate diagnosis of acute myocardial infarction by two-dimensional echocardiography. *Circulation*. 1982;65:323–329.

24. **Nieminen M,** Parisi AF, O'Boyle JE, Folland ED, Khuri S, Kloner RA. Serial evaluation of myocardial thickening and thinning in acute experimental infarction: identification and quantification using two-dimensional echocardiography. *Circulation*. 1982;66:174–180.

25. **Kozàkovà M**, Palombo C, Distante A. Right ventricular infarction: the role of echocardiography. *Echocardiography*. 2001;18:701–707.

26. **Goldberger JJ**, Himelman RB, Wolfe CL, Schiller NB. Right ventricular infarction: recognition and assessment of its hemodynamic significance by two-dimensional echocardiography. *J Am Soc Echocardiogr*. 1991;4:140–146.

27. **Forrester JS,** Diamond GA, Swan HJ. Correlative classification of clinical and hemodynamic function after acute myocardial infarction. *Am J Cardiol*. 1977;39:137–145.

28. **Gerber IL,** Foster E. Echocardiography in the coronary care unit: management of acute MI, detection of complication, and prognostic implications. In: Otto MC, editor. *The Practice of Clinical Echocardiography*. 3rd ed. Philadelphia/ China: Elsevier; 2007. pp. 305–315.

29. **Hozumi T,** Yoshida K, Mori I, Akasaka T, Takagi T, Kaji S, Kawamoto T, Ueda Y, Morioka S. Noninvasive assessment of hemodynamic subsets in patients with acute myocardial infarction using digital color Doppler velocity profile integration and pulmonary venous flow analysis. *Am J Cardiol*. 1999;83:1027–1032.

29. **Hass EE,** Yang EH, Gersh BJ, Robert A. O'Rourke ST-segment-elevation MI: clinical presentation, diagnostic evaluation, and medical management. In: Foster V, Walsh R, Harrington R, editors. *Hurst's the Heart*. 13th ed. New York/Chicago/San Francisco/ Lisbon/London/Madrid/Mexico City Milan/ New Delhi/SanJuan/Seoul/Singapore/ Sydney/Toronto: McGraw-Hill; 2011. pp. 1354–1385.

30. **Figueras J**, Barrabés JA, Serra V, Cortadellas J, Lidón RM, Carrizo A, Garcia-Dorado D. Hospital outcome of moderate to severe pericardial effusion complicating ST-elevation acute myocardial infarction. *Circulation*. 2010;122:1902–1909.

31. **Shiozaki AA**, Filho RA, Dallan LA, de Oliveira SA, Nicolau JC, Rochitte CE. Left ventricular free-wall rupture after acute myocardial infarction imaged by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2007;9:719–721.

32. **Koh AS**, Loh YJ, Lim YP, Le Tan J. Ventricular septal rupture following acute myocardial infarction. *Acta Cardiol*. 2011;66:225–230.

33. **Otsuji Y**, Handschumacher MD, Liel-Cohen N, Tanabe H, Jiang L, Schwammenthal E, Guerrero JL, Nicholls LA, Vlahakes GJ, Levine RA. Mechanism of ischemic mitral regurgitation with segmental left ventricular dysfunction: three-dimensional echocardiographic studies in models of acute and chronic progressive regurgitation. *J Am Coll Cardiol*. 2001;37:641–48.

Role of Intracoronary Imaging and Physiology in Acute Coronary Syndrome

Dr. Jayesh Prajapati
Professor and Head, Cardiology Department, U. N. Mehta Institute of Cardiology and Research Center, Ahmedabad, E-mail : drjsprajapati@gmail.com
Dr. Poojan Prajapati
Medical student, B. J. Medical college, Ahmedabad, poojan.prajapati19@gmail.com
Iva Patel
Research Associate, Research department, U. N. Mehta institute of cardiology and research center, Ahmedabad, E-mail : iva@unmicrc.org, ivabiotech@gmail.com

1. Background

Despite substantial advancements in pharmacological and interventional management methods, coronary artery disease (CAD) persists as the leading cause of death across the globe.(1) The most prevalent clinical presentation of CAD is acute coronary syndrome (ACS), encompassing ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris. CAD comprises various pathophysiological alterations to the intima and media of the coronary arterial wall, characterized by endothelial dysfunction, vascular inflammation, and the accumulation of lipids, calcium, and cellular debris. The predominant causes of ACS can be attributed to three primary mechanisms: plaque rupture (55–60%), plaque erosion (30–35%), and calcified nodule (2–7%).(2)

Coronary angiography, often regarded as the gold standard, has limitations in providing comprehensive insights into the biological activity and composition of atherosclerotic plaque.(1) Consequently, recent progress in intravascular imaging technologies has enabled a more thorough evaluation of culprit lesions in cases of ACS. The emergence of intracoronary imaging modalities like intravascular ultrasound (IVUS), optical coherence tomography (OCT), and near-infrared spectroscopy (NIRS) has proven instrumental in depicting the histological characteristics of plaque rupture, plaque erosion, and calcified nodules within the clinical context of ACS.

As per latest 2023 ESC guideline recommendations, intravascular imaging, especially OCT, is advised for guiding PCI in patients with ACS, receiving a Level II a recommendation (Class A). In cases where the culprit lesions are unclear, the use of intravascular imaging, including OCT, is suggested, albeit with a lower Level IIb recommendation (Class C).(3)

2. Intravascular Imaging Techniques

2.1. Optical coherence tomography

OCT provides very high-resolution details through a light-based, near-infrared spectrum emitted from a single fiber optic wire, rotating at high speed when pulled back into the vessel. OCT holds a special position among the available imaging techniques due to its remarkable axial and lateral resolution (10 and 70 µm). The main limitation of OCT is the penetration depth that decreases significantly in lipid plaques (0.2 mm), hindering efforts to assess plaque burden and measure the depth and volume of lipid pools. OCT requires a blood-free field during image acquisition. The second generation of OCT systems (Fourier domain OCT) enabled rapid imaging of the coronary arteries without occlusive acquisition, and images of long segments can be acquired, maintaining good longitudinal resolution during short contrast injections.(4) OCT stands out as the most reliable technique for assessing the intricate morphology of culprit lesions in ACS. Nevertheless, this approach does entail certain complex procedures, such as intracoronary contrast injection, to eliminate red blood cells during image acquisition.(5)

2.2. Intravascular ultrasound

IVUS is the first and most used real-time, high resolution intracoronary imaging technique which provides cross-sectional images of coronary arteries. IVUS enables real-time, tomographic examination of deep-seated plaque contents and the complete structural assessment of the blood vessel wall, encompassing the media and adventitia. Furthermore, it facilitates the evaluation of vascular remodeling. IVUS can easily penetrate plaque up to 10 mm; however, calcium inhibits the ultrasound signal and prevents it from being seen in IVUS.(4, 6, 7)

2.3. Near infrared spectroscopy

NIRS is a novel imaging modality based on spectroscopic analysis which recognizes lipid and plaque constituents through absorbed and scattered infrared light at different intensities and wavelengths. In human trials, NIRS exhibits accuracy and specificity exceeding 90% when it comes to identifying lipid components.(8) Diagnostic criteria for plaque rupture, erosion, and calcified nodules are illustrated in **Table 1**. And Comparison of IVUS and OCT presented in table 2. (9)

Table 1: Diagnostic criteria for plaque rupture, erosion, and calcified nodules.

	IVUS	OCT	NIRS
Plaque rupture	• Fibrous cap disruption • Intra-plaque cavity • Attenuated plaque	• Fibrous cap disruption • Intra-plaque cavity • Large lipid plaque • Macrophages • Vasa vasorum • Cholesterol crystals • Healed plaque	•High max LCBI 4mm (>400)
Plaque Erosion		• Intact fibrous cap • Fibrotic plaque	• Low max LCBI 4mm (<400)
Calcified Nodule	• Convex calcium • Large calcium sheet	• Convex calcium • Large calcium sheet	• Moderate max LCBI4mm

IVUS, intravascular ultrasound; LCBI, lipid core burden index; NIRS, near-infrared spectroscopy; OCT, optical coherence tomography.

Table 2 : Comparison of IVUS and OCT

Column1	Column2 IVUS	Column3 OCT
Technical features		
Waves	Ultrasound	Near-infrared light
Axial resolution(μm)	100–150	10–20
Lateral resolution(μm)	150–300	20–70
Tissue penetration(mm)	4–10	0.5–2
Need for blood clearance	no	yes
Lesion evaluation		
Ostial Left main	••	-
Large vessel diameter	••	•

Plaque burden	••	•
Lipid Core	•	••
Calcium depth	••	•••
Thrombus detection	•	•••
TCFA	-	•••
Macrophage infiltration	-	•••
Cholesterol crystals	-	•••
Microchannels	-	•••
Ease of image interpretation	•	•••
Acute stenting evaluation		
Stent expansion	•••	•••
Edge dissection	•	•••
Stent malposition	••	•••
Tissue protrusion	•	•••

3. Diagnosis and Treatment of Patients with Coronary Heart Disease by Intracoronary Examination

3.1. Accurate identification of culprit plaque

Intracoronary imaging can accurately show the continuity of vascular lumen, plaque disruption, and associated thrombus in patients with typical acute chest pain accompanying with ST-segment elevation in electrocardiogram to identify the underlying lesion. The most frequent cause of ACS is coronary atherosclerosis, whereby the normal triple-layered structure of the vessel wall is absent on the intracoronary image. OCT, with its superior resolution, permits clearer visualization and differentiation of various components within atherosclerotic plaques including lipid cores (which present as signal-poor areas with diffuse boundaries), thin fibrous caps (displaying homogeneous, signal-rich regions), and calcifications (which present as well-defined, signal-poor regions with sharp edges). However, due to the strong attenuation of the lipid component to the light signal, it is usually difficult to observe the posterior border of the lipid and the deep tissue components.(10, 11) Algorithm to guide intravascular imaging in patients with ACS is represented in **Figure 1**.

The detection of thrombus by intravascular ultrasound is more difficult (**Figure 2**), though it can be made easier by stationary imaging at the level of the suspected thrombus and a small injection of contrast to highlight the luminal contour. High-definition IVUS technology promises better resolution and enhanced diagnostic capabilities.(12)

The three most often occurring underlying mechanisms of coronary thrombosis that clinically present as ACS are plaque rupture, plaque erosion, and calcified nodules.(2, 12)

Figure 2: The role of intravascular imaging in delineating thrombus. Panel I: an angiographic image of a left anterior descending artery in a patient with ST-elevation myocardial infarction presentation and anterior ST-segment elevation. A hazy filling defect is evident in the proximal segment of the vessel, highlighted by white arrow A. Optical coherence tomography image (A) demonstrates red thrombus (red arrows) with an irregular surface and adherent to the lumen, attenuating the light, and obscuring deeper structures. Panel II: a 45-year-old woman was admitted with chest pain and anterior ST-elevation. Emergent angiography revealed a filling defect in the mid-left anterior descending artery. After thrombus aspiration angiography showed a

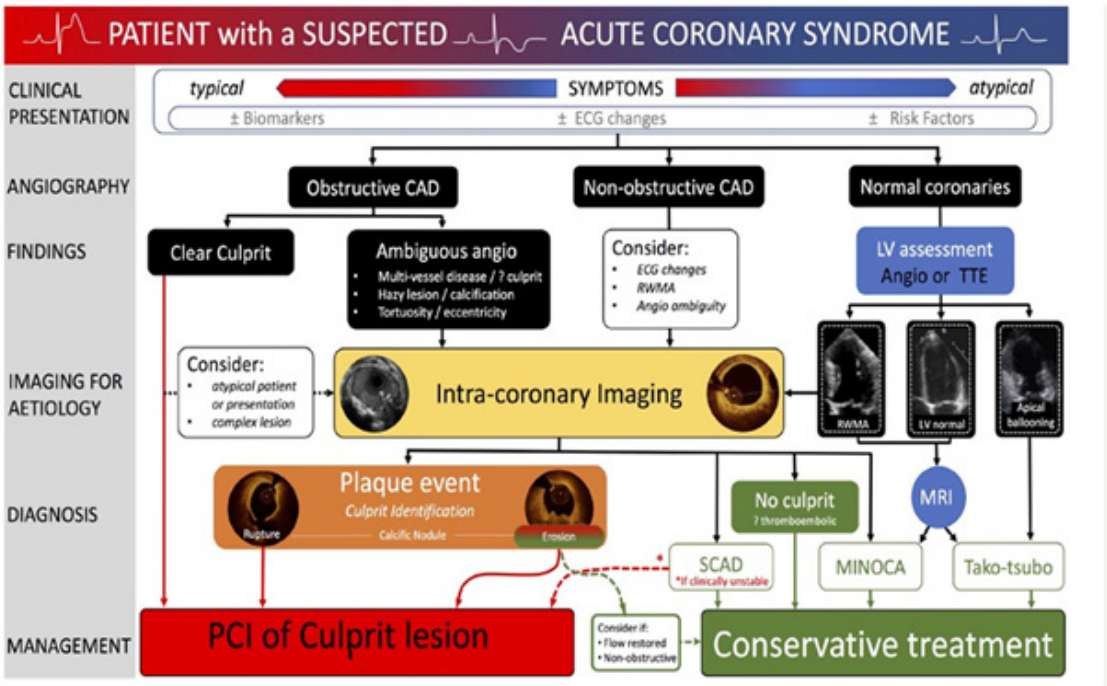
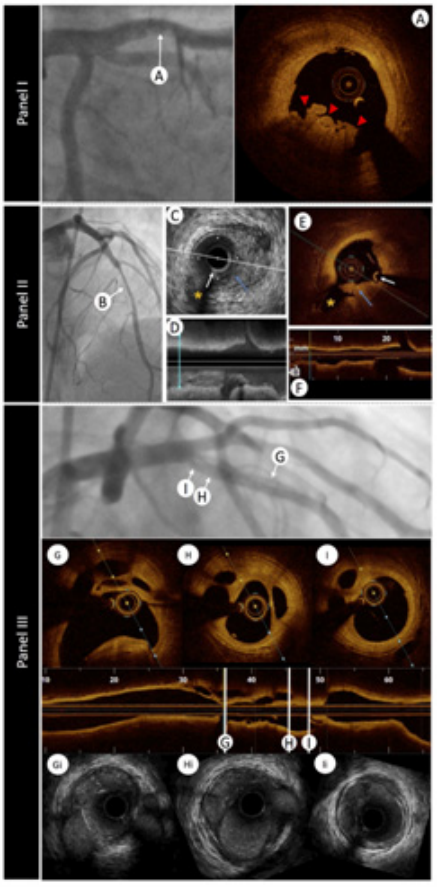


Figure 1: A treatment algorithm to guide the use of intravascular imaging in patients presenting with acute coronary syndromes. (Figure adapted from Johnson TW et al. Eur Heart J. 2019; 40(31):2566–2584.)



tubular stenosis in the mid-left anterior descending artery (B) that was investigated with intracoronary imaging to determine the substrate of the acute coronary syndromes. Corresponding intravascular ultrasound and optical coherence tomography images are shown. (C and D) Cross-sectional and longitudinal intravascular ultrasound images (40 MHz) demonstrating the presence of atherosclerotic plaque (visible in C from 2 to 6). Intraluminal material protruding towards a small side branch was visible (blue arrow). Optical coherence tomography (E and F) confirmed the presence of atherosclerosis (with lipid content given the attenuation observed) and demonstrated the presence of white thrombus (irregular mass protruding into the lumen with optical shadow). White arrow indicates the guidewire artefact. Asterisk indicates the side branch used for matching of corresponding cross-sections. Panel III: left anterior descending artery with mid-vessel filling defects secondary to a conservatively managed anterior ST-elevation myocardial infarction 10 years earlier. Longitudinal optical coherence tomography imaging with three representative optical coherence tomography

frames (G, H, and I) demonstrating re-canalized thrombus. Matched HD-IVUS (Boston Scientific) images (Gi, Hi, and Ii) demonstrating the superior delineation of structures with light-based imaging. (Figure adapted from Johnson TW et al. Eur Heart J. 2019; 40(31):2566–2584.)

3.1.1. Plaque rupture

Plaque rupture, which accounts for 55–80% of ACS cases, is the most often reported substrate for ACS.(2, 10) Plaque rupture is characterized by disruption of thin fibrous cap, resulting in the formation of a distinct cavity within the plaque. These components promote the formation of (generally red) thrombus, which is rich in red blood cells and leads to a sharp decrease in the lumen area. In this context, vasoconstriction and thrombosis may lead to acute cessation of the coronary blood flow and subsequent myocardial ischemia. Clinical management tends to recommend stent treatment for ruptured plaques. Compared with the other types of plaque, plaque rupture has more lipid components and worse prognosis.(10) During OCT imaging, the identification of plaque rupture is generally straightforward, primarily owing to several distinguishing features. These features include the presence of macrophages (recognized by their signal-rich, discrete or merging punctuate regions with shadowing), vasa vasorum (indicated by signal-poor, well-defined voids within the plaque), cholesterol crystals (discerned as thin, linear areas exhibiting high signal intensity within the lipid plaque), and healed plaques (designated as plaques that contain one or more layers displaying different optical density).(13, 14) Conversely, IVUS distinguishes plaque rupture as ulceration, characterized by a depression in the plaque that initiates at the luminal-intimal border. Lesions exhibiting plaque rupture typically feature a substantial plaque burden with positive vascular remodeling, resulting in the appearance of a hypoechoic plaque during IVUS imaging. This type of plaque, often referred to as an "attenuated plaque," produces an acoustic shadow stemming from the lipid core.(15-17)

3.1.2. Plaque erosion

Plaque erosion is the second most common lesion type, accounting for 30-35% of cases of ACS.(2, 10) Plaque erosion is usually characterized by a thicker and intact fibrous cap which accompanies with local platelet-rich white thrombus without superficial lipid or calcification. OCT is the only tool that may identify plaque erosion with its high resolution in clinical settings as the coarse resolution (100–200 ìm) of IVUS cannot determine the presence or absence of small rupture. As the OCT metrics of plaque erosion are different from the pathological definition, the OCT derived diagnostic criteria of plaque erosion are — i) "definite" OCT-derived plaque erosion (fibrous cap disruption, in a lesion frequently composed of fibrous tissue with overlying luminal white thrombus), and ii) "possible" OCT-derived plaque erosion (an irregular luminal surface without evident thrombus or an overlying thrombus with attenuation of the underlying plaque, without evidence of superficial lipid or calcification in the vessel upstream or downstream of the thrombus site).(18) At present, NIRS is accessible in the form of a combined catheter with IVUS, offering a solution to address IVUS's limitations in detecting plaque erosion.(2)

According to the latest EROSION III trial comparing angiography and OCT-guided PCI treatment, the number of stents implanted was reduced in the OCT group compared to angiography (15%), while similar prognosis was shown in both groups. This trial demonstrated the safety of non-stenting strategy and the importance of OCT for optimizing PCI strategies in patients with ACS.(19)

3.1.3. Calcified nodule

Calcified nodules are the least common cause of coronary thrombosis and usually occur in a coronary segment with extensive calcification which poses significant challenges for stent deployment and optimization. It occurs in 2-8% of patients with ACS and is typically more common among elderly males, patients with tortuous coronary arteries, diabetes mellitus, and chronic

renal failure.(2, 10) The lesions exhibit break in a calcified plate that disrupts the fibrous cap and are overlaid by thrombus. Identification of erupted calcific nodules is possible with IVUS and OCT. OCT can accurately identify the boundary and angle of calcification with sharp borders presenting with signal-poor regions when calcification is adequately thin to allow light penetration. OCT categorizes calcification into three types: eruptive calcified nodules, superficial calcific sheets, and calcified protrusions. However, most calcified nodules have superficially located large calcification. Within ACS culprit lesion, a large amount of thrombus may cause a strong attenuation of the near-infrared light and interfere with accurate OCT assessment of plaque morphology.(2, 10)

However, there are limitations to OCT imaging, for example, the presence of protruding calcium can pose challenges in tissue differentiation, particularly through attenuation of deeper structures resulting in misrepresentation as red thrombus and potential misdiagnosis of an acute culprit event. Similarly, distinguishing lipid core from calcium, if the boundaries are ill-defined, or detecting calcium when there is overlying thrombus can be better achieved with IVUS and virtual histology (VH)-IVUS.(20) Histopathological comparison has demonstrated that OCT can distinguish various types of coronary calcification and accurately detect calcific nodules. In clinical OCT studies, an eruptive calcific nodule has been defined as a lesion that exhibits evidence of fibrous cap discontinuity and/or thrombus, over a calcified plaque characterized by protruding calcification into the lumen, and the presence of substantive calcium proximal and/or distal to the lesion.(12) Multimodality imaging of plaque rupture, plaque erosion, and calcified nodule are represented in **Figure 3**.

Figure 3: Multimodality imaging of plaque rupture, plaque erosion, and calcified nodule. Plaque rupture (I) Angiogram shows occlusion of proximal LAD, the culprit lesion of STEMI **(A)**. IVUS

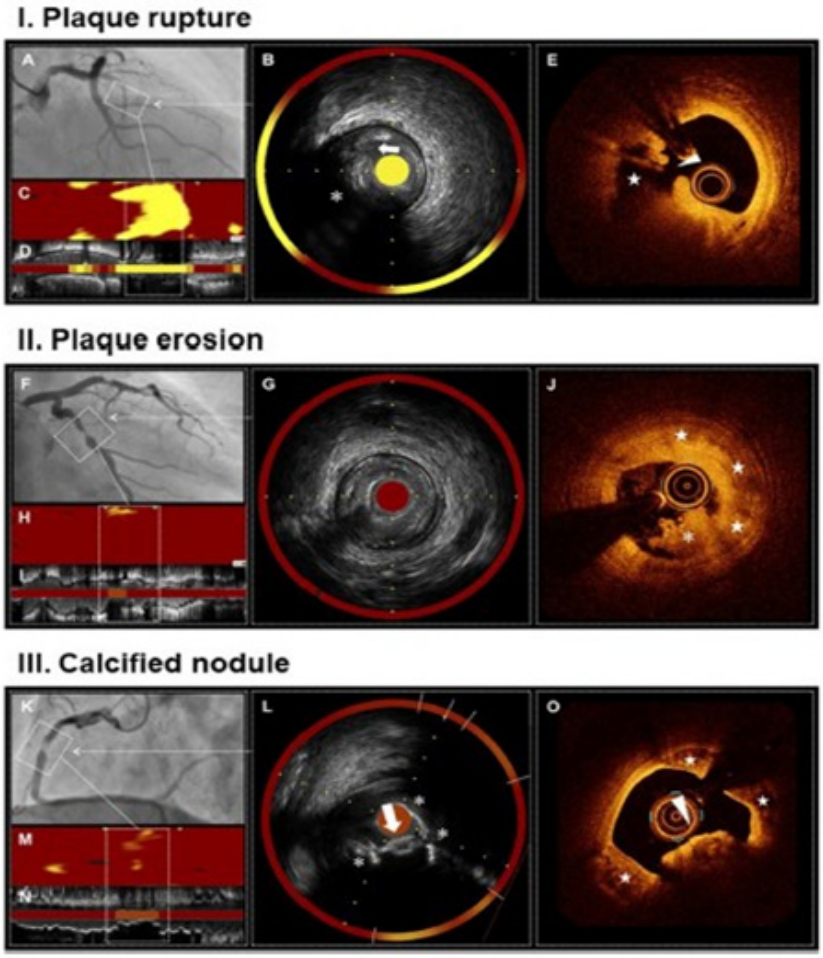


Figure 3

demonstrates ulceration (arrow) with a recess on the surface of attenuated plaque (asterisk) **(B,D)**. NIRS identifies a large lipid content (maxLCBI4mm = 920) **(B–D)**. OCT reveals plaque rupture characterized by a fibrous cap disruption (arrowhead) and a cavity (star) formation inside the plaque **(E)**. Plaque erosion (II) Angiogram shows severe stenosis in mid LCX, the culprit lesion of STEMI **(F)**. IVUS demonstrates the absence of plaque ulceration **(G,I)**. NIRS identifies a small lipid content (maxLCBI4mm = 129) **(G–I)**. OCT reveals plaque erosion characterized by the presence of attached thrombus (asterisk) overlying an intact fibrotic plaque (stars) **(J)**. Calcified nodule (II) Angiogram shows severe stenosis and intraluminal filling defect in mid RCA, the culprit lesion of non-STEMI **(K)**. IVUS demonstrates a convex calcium with irregular surface (arrow) and large superficial calcium (asterisks) **(L,N)**. NIRS identifies a moderate lipid content (maxLCBI4mm = 208) **(L–N)**. OCT reveals calcified nodule characterized by a protruding calcium with thrombi (arrowhead) and large superficial calcium (stars) **(O)**. IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCBI, lipid core burden index; LCX, left circumflex artery; NIRS, near-infrared spectroscopy; OCT, optical coherence tomography; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction. (Figure adapted from Kubo T, et al. Frontiers in Cardiovascular Medicine. 2022;8:824128.)

3.1.4. Myocardial infarction with non-obstructed coronary arteries (MINOCA)

Non-obstructive myocardial infarction (MINOCA) is another contributor to ACS, typically characterized by coronary stenosis of <50%. The most frequent culprits behind MINOCA include factors such as plaque rupture, plaque erosion, coronary artery spasm, coronary microvascular spasm, spontaneous coronary artery dissection, abnormal microcirculatory function.(12) Intracoronary imaging tools, particularly OCT, play a crucial role in detecting thrombosis in cases where prominent atherosclerotic plaques are absent. They also aid in identifying potential thromboembolism, vasospasm, and other non-atherosclerotic lesions. Consequently, for patients with atypical ACS presentations, intracoronary imaging proves invaluable in achieving an accurate diagnosis.(21) OCT enables the differentiation between culprit and non-culprit lesions which ultimately minimizes unnecessary exposure to antiplatelet medications and anticoagulants.

3.2. Accurate identification of vulnerable non-culprit lesions

The recurrence of adverse events in certain ACS patients following a procedure is commonly attributed to vulnerable plaques. In simpler terms, these plaques, characterized by a substantial lipid core, a thin fibrous cap, and an abundance of macrophages, are predisposed to rapid progression and may even trigger events, such as cardiac death, both in the short-term and during long-term follow-up. Common characteristics of vulnerable plaques on intracoronary imaging are depicted in **Figure 4**. Furthermore, it is noteworthy that these vulnerable plaques in ACS patients are typically located within segments of the epicardial coronary arteries that exhibit significant stenosis. An OCT-based experiments in ACS patients consistently confirmed that plaques with characteristics such as a maximum lipid angle >180° and a thinnest fibrous cap thickness <65 ìm causes a higher risk with a particular focus on thin fibrous cap thickness lesions in patients with STEMI showing more severe lesions.(22, 23) **(Fig. 4)**

Moreover, IVUS has been utilized for in vivo vulnerable plaque investigations over the last decade, and the recent integration of high-resolution intravascular ultrasound (HR-IVUS) featuring a 60-MHz capability has significantly supported plaque recognition sensitivity, despite IVUS having a lower lateral resolution when compared to OCT.(24, 25)

The lipid core burden index (LCBI), specifically Max LCBI4mm, is the primary measure for assessing vulnerable plaques through NIRS. A study involving 117 patients with ACS employing NIRS and IVUS revealed that a 100-unit increase in LCBI led to a 19% rise in the incidence of MACE, highlighting

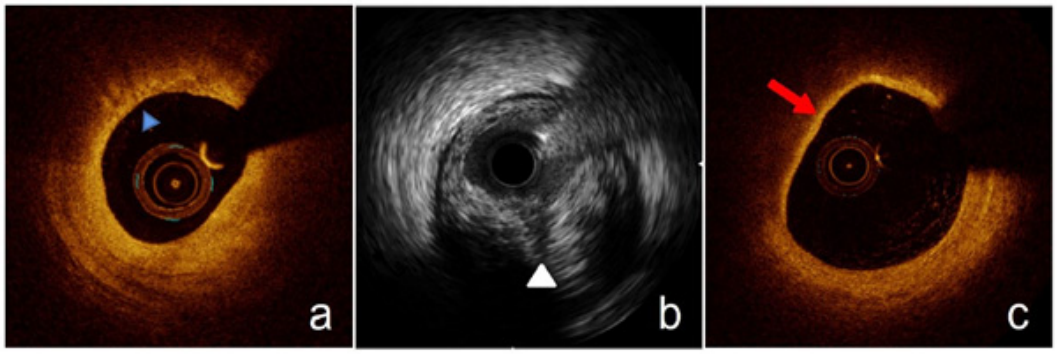


Figure 4: Common characteristics of vulnerable plaques on intracoronary imaging images. **(a)** Minimum lumen area = 2.51 mm^2 and macrophages (blue triangle) under OCT. **(b)** Low backscattering (white triangle) indicating PB >70% under IVUS. **(c)** A thin fibrous cap plaque delineating necrotic core with an overlying fibrous cap (red arrow) where the minimum thickness of the fibrous cap is less than 65 ìm defined by OCT. (Figure adapted from Sun Q et al. Reviews in Cardiovascular Medicine. 2023;24(2):45.)

the significant predictive role of lipid load in adverse outcomes.(26-28)

In addition to the single intracoronary imaging technology, several studies have employed combination of imaging tools and the findings of those illustrating vulnerable plaques identified by intracoronary imaging in ACS patients are summarized in **Table 2.**(29-32) The findings indicate that early interventional therapy for vulnerable plaques may further achieve better outcomes. By identifying vulnerable plaques and individuals with high-risk characteristics via intracoronary imaging technology, targeted treatment may be realized, such as reducing follow-up intervals and strengthening drug therapy. However, this superiority still needs to be confirmed by numerous large-scale trials in this field. Moreover, several studies have also employed the combination of OCT and IVUS to investigate the pathological characteristics of ACS patients.(30, 31, 33)

4. Coronary Physiology in Patients with ACS

4.1. Fractional flow reserve (FFR)

The concept of pressure derived FFR has been used in PCI guidance of simple and complex multi-

Table 2: The summary of studies illustrating vulnerable plaques identified by intracoronary imaging in ACS patients.

Study	Technology	Vulnerable Characteristics
ATHEROREMO-IVUS (28)	IVUS-NIRS	IVUS virtual histology-derived TCFA; PB >70%
PROSPECT II (29)	IVUS-NIRS	Max LCBI4mm >324.7? PB >70%
Wenbin Zhang et al.(30)	IVUS-OCT	ACS presentation was related to plaque vulnerability (more TCFA, more lipid and macrophages, larger PB and positive remodeling)
Francesco Prati et al.(31)	IVUS-OCT	MLA <4 mm2, FCT <75 µm predicts acute events

IVUS: Intravascular ultrasound; OCT: Optical coherence tomography; NIRS: Near InfraRed Spectroscopy; ACS: Acute Coronary Syndrome; MLA: minimum lumen area; FCT: Fibrous cap thickness; TCFA: Thin-cap fibroatheroma; LCBI: lipid core burden index; PB: Plaque burden

vessel diffuse lesions in clinical practice. FFR was calculated as the ratio of mean distal coronary artery pressure (Pd) to proximal coronary artery pressure (Pd/Pa) by injecting intracoronary adenosine under the condition of maximum myocardial filling. Generally, FFR >0.8 indicates FFR-negative lesion, FFR <0.75 indicates positive, while 0.75< FFR<0.8 is the gray area of measurement.(9)

4.2. Application of coronary physiological tools in ACS

Intracoronary physiology is progressively used in patients with ACS to evaluate the hemodynamic significance of intermediate severity non-infarct related artery (IRA) stenoses. In ACS, the infarct-related artery (IRA) is affected to a variable extent by microvascular obstruction. Intracoronary physiology has been used in small observational studies to assess the success of myocardial reperfusion by evaluating the degree of microcirculatory resistance.(3, 34) Approach towards the use of coronary physiology in different clinical scenarios in patients with ACS is depicted in Figure 6.

The invasive and time-consuming nature of FFR restricts its use in clinical settings. Moreover, some patients are intolerant of adenosine, and the results are easily affected by microcirculation conditions. As a result, new technologies such as transient waveform-free ratio (iFR), coronary angiography flow reserve fraction (CT-FFR), contrast agent-based FFR (QFR), OCT-based FFR (OFR) and IVUS-based FFR (UFR) are emerging as substitutes for FFR. In comparison to FFR, the majority of the new techniques have shown good accuracy and reproducibility.(35-41) Among these, CT-FFR is less accurate than FFR in the ACS group

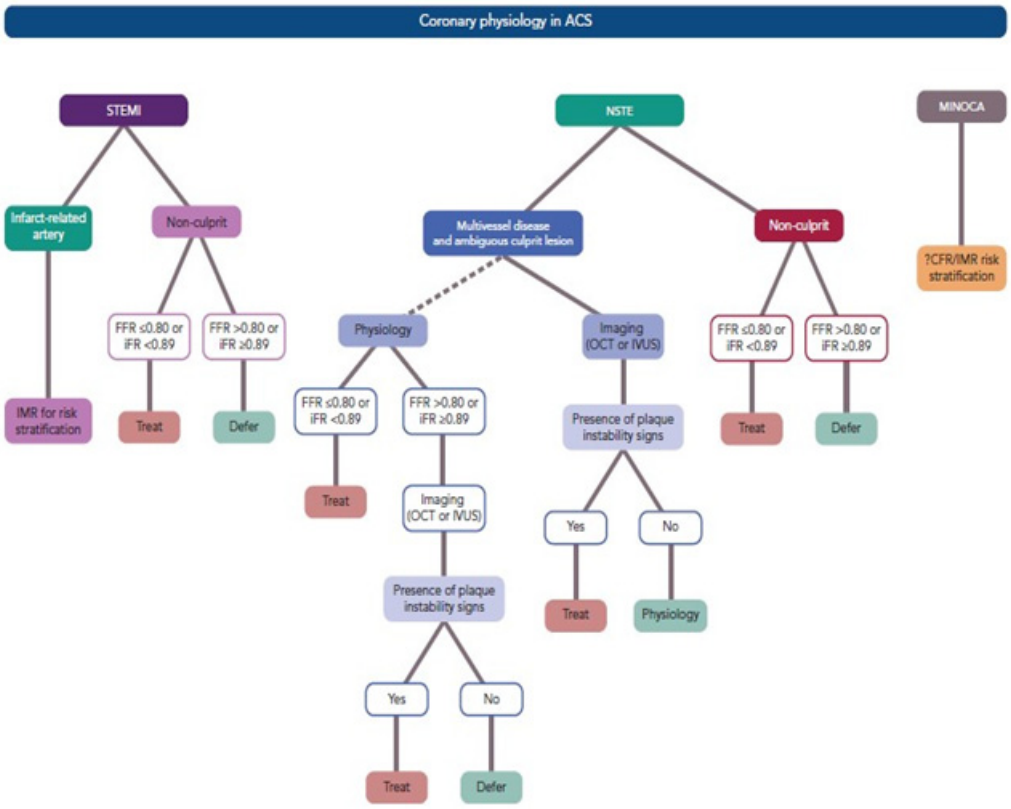


Figure 6: Use of Coronary Physiology in Different Clinical Scenarios in Patients with Acute Coronary Syndrome. ACS = acute coronary syndrome; CFR = coronary flow reserve; FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; IMR = index of microcirculatory resistance; IVUS = intravascular ultrasound; MINOCA = MI with non-obstructive coronary artery disease; NSTEMI = non-ST segment elevation MI; OCT = optical coherence tomography; STEMI = ST-elevation MI. (Figure adapted from Scarsini R et al. Interv Cardiol. 2020 Jun 4;15:e05.)

Table 3: Fractional flow reserve in acute coronary syndrome studies

Study	Sample Size	STEMI or NSTE-ACS	Main Findings
Ntalianis et al.(43)	101 patients, 112 lesions	STEMI and NSTE-ACS	Overall, FFR does not change when measured in the acute phase and at follow-up in non-culprit lesions
DANAMI-3-PRIMULTI (Engstrøm T, et al.)(44)	627 patients	STEMI	No significant difference was found between the two groups for all-cause mortality and non-fatal reinfarction at a median of 27 months follow-up, patients in the FFR-guided revascularization group had significantly fewer repeat revascularizations.
WAVE (Musto et al.)(45)	50 patients, 66 lesions	STEMI	No significant variations in FFR values between the acute and subacute phases (5–8 days)
Choi et al.(46)	100 patients	STEMI and NSTE-ACS	FFR decrease with worsening of lesion severity is similar in non-culprit artery and stable CAD
Van der Hoeven et al.(47)	73 patients	STEMI	Overall, FFR decreases from the acute phase to the 30-day follow-up (0.88 ± 0.07 versus 0.86 ± 0.09; p=0.001) 80.8% classification agreement between the acute phase and 30-day follow-up
Compare-Acute (Smits PC, et al.)(48)	885 patients	STEMI	FFR-guided complete revascularization during the index procedure was superior to IRA
Ahmed N, et al.(49)	648 patients	STEMI and NSTEMI	Guidewire-based measurement of FFR and IMR using i.v. adenosine was safe in patients with ACS
Hakeem A, et al.(50)	206 patients	STEMI and NSTEMI	Deferring PCI on the basis of non-ischemic FFR in patients with ACS is associated with significantly worse outcomes than in stable CAD. Caution is warranted in using FFR values derived from patients with stable CAD for clinical decision making in ACS patients
Layland J, et al.(51)	106 patients	NSTEMI	FFR in patients with recent NSTEMI showed high concordance with myocardial perfusion in matched territories as revealed by 3.0-T stress perfusion CMR

Layland J, et al.(52)	350 patients	NSTEMI	Angiographic-guided management was associated with higher rates of coronary revascularization when compared with FFR-guided
Cuculi F, et al.(53)	82 patients	STEMI	Coronary microcirculation begins to recover within 24 h and recovery progresses further for 6 months after MI. FFR significantly reduces from baseline to 6 months. The presence of MVO indicates a highly microvascular dysfunction
Samady H, et al.(54)	48 patients	STEMI and NSTEMI	FFR of the IRA identifies reversibility on noninvasive imaging early after MI

despite being noninvasive and superior to computed tomography angiography findings.(35, 41)

Interestingly, compared with FFR, iFR may even better reflect the actual state of epicardial blood flow in some cases, and the superiority of iFR has been confirmed in some literature. Furthermore, iFR does not require adenosine.(42) The list of studies that have employed FFR in ACS settings are summarized in Table 3.

STEMI: ST-segment elevation myocardial infarction; NSTEMI: Non-ST-segment elevation myocardial infarction; ACS: Acute coronary syndrome; IRA: infarct-related artery; FFR: Fractional flow reserve; MVO: microvascular obstruction; MI: Myocardial infarction; CMR: cardiovascular magnetic resonance imaging; CAD: Coronary artery disease

5. Optimization of Risk Stratification by Combining Multimodal Diagnostic Tools

It is not sufficient to guide the revascularization in patients with ACS only via intracoronary imaging or coronary physiological tools. Currently, a series of experiments combining plaque vulnerability characteristics and coronary physiology is being carried out to improve the prognostic risk classification of different patients.(10) In the PROSPECT ABSORB study (182 ACS patients, 25 months follow-up), performing PCI on angiographically mild lesions was safe and significantly increased the follow-up minimum lumen area (MLA).(55) In the COMBINE study (547 diabetic mellitus patients with stable angina pectoris or ACS, 18 months follow-up), patients with at least one FFR-negative lesion and TCFA positivity constituted 25% of the population and experienced a five-fold higher rate of major adverse cardiovascular events.(56)

6. Future Perspectives

Appropriate education on imaging interpretation represents a future challenge for intravascular imaging clinical implementation. The recent efforts have focused on developing data fusion methods and hybrid dual-probe catheter designs. Combining IVUS and OCT imaging provides a fused image with OCT's high-resolution capabilities for surface details and IVUS's deep imaging capacity. This combination enables a comprehensive depiction of coronary atherosclerotic plaque. Additionally, combining NIRS and OCT imaging allows the detection of lipid cores through spectroscopy and the assessment of structural characteristics, including

cap thickness, through OCT. This integrated approach will enhance the identification of thin-capped fibroatheroma, a recognized precursor to plaque rupture. Continued advancements in the technology, with higher resolution, faster image acquisition times, combined OCT/IVUS catheters, and more sophisticated co-registered image analysis, will facilitate greater adoption through ease of use and interpretation. Intracoronary imaging-guided PCI has an exciting future; however, randomized trials are needed for further validation and implementation in clinical practice.

7. Summary

Over the last decade, intracoronary imaging technology has played a pivotal role in enhancing the diagnosis and treatment of ACS patients, while coronary physiological tools have broadened our understanding of coronary lesions, shedding light on atherosclerosis pathogenesis and ACS pathophysiology. Nowadays, coronary intervention has transitioned from a 'one-size-fits-all' approach to a more precise intervention era. The amalgamation of multiple imaging methods offers comprehensive insights into atherosclerosis morphology and composition. The integration of both approaches is poised to become a clinically essential step in enhancing risk stratification for ACS patients and optimizing the PCI treatment process. This combined strategy, coupled with intracoronary imaging, represents a promising direction for guiding ACS in the future.

References

1. Batty JA, Subba S, Luke P, Gigi LWC, Sinclair H, Kunadian V. Intracoronary imaging in the detection of vulnerable plaques. Current cardiology reports. 2016;18:1-12.

2. Kubo T, Terada K, Ino Y, Shiono Y, Tu S, Tsao T-P, et al. Combined use of multiple intravascular imaging techniques in acute coronary syndrome. Frontiers in Cardiovascular Medicine. 2022;8:824128.

3. Byrne RA, Rossello X, Coughlan J, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). European Heart Journal. 2023:ehad191.

4. Aparisi Á, Cubero-Gallego H, Tizón-Marcos H. Intracoronary imaging: review and clinical use. REC Interv Cardiol. 2022;4:228-37.

5. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, Yamano T, et al. Assessment of culprit lesion morphology in acute myocardial infarction: ability of optical coherence tomography compared with intravascular ultrasound and coronary angioscopy. Journal of the American College of Cardiology. 2007;50(10):933-9.

6. Park S-J, Kim Y-H, Park D-W, Lee S-W, Kim W-J, Suh J, et al. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circulation: Cardiovascular Interventions. 2009;2(3):167-77.

7. Tan Q, Wang Q, Liu D, Zhang S, Zhang Y, Li Y. Intravascular ultrasound-guided unprotected left main coronary artery stenting in the elderly. Saudi medical journal. 2015;36(5):549.

8. Moreno PR, Lodder RA, Purushothaman KR, Charash WE, O'Connor WN, Muller JE. Detection of lipid pool, thin fibrous cap, and inflammatory cells in human aortic atherosclerotic plaques by near-infrared spectroscopy. Circulation. 2002;105(8):923-7.

9. Fabris E, Kedhi E, Verdoia M, Ielasi A, Tespili M, Guagliumi G, De Luca G. Current Role of Intracoronary Imaging for Implementing Risk Stratification and Tailoring Culprit Lesion Treatment: A Narrative Review. Journal of Clinical Medicine. 2023 May 10;12(10):3393.

10. Sun Q, Liu M, Zeng M, Jia H. Intracoronary Diagnostics in Patients with Acute Coronary

Syndrome. Reviews in Cardiovascular Medicine. 2023;24(2):45.

11. Fujii K, Kubo T, Otake H, Nakazawa G, Sonoda S, Hibi K, et al. Expert consensus statement for quantitative measurement and morphological assessment of optical coherence tomography. Cardiovascular Intervention and Therapeutics. 2020;35:13-8.

12. Johnson TW, Räber L, Di Mario C, Bourantas C, Jia H, Mattesini A, et al. Clinical use of intracoronary imaging. Part 2: Acute coronary syndromes, ambiguous coronary angiography findings, and guiding interventional decision-making: An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions: Endorsed by the Chinese Society of Cardiology, the Hong Kong Society of Transcatheter Endocardiovascular Therapeutics (HKSTENT) and the Cardiac Society of Australia and New Zealand. European heart journal. 2019;40(31):2566-84.

13. Tearney GJ, Regar E, Akasaka T, Adriaenssens T, Barlis P, Bezerra HG, et al. Consensus standards for acquisition, measurement, and reporting of intravascular optical coherence tomography studies: a report from the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation. Journal of the American College of Cardiology. 2012;59(12):1058-72.

14. Kubo T, Tanaka A, Ino Y, Kitabata H, Shiono Y, Akasaka T. Assessment of coronary atherosclerosis using optical coherence tomography. Journal of atherosclerosis and thrombosis. 2014;21(9):895-903.

15. Mintz GS, Nissen SE, Anderson WD, Bailey SR, Erbel R, Fitzgerald PJ, et al. American College of Cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (ivus) A report of the american college of cardiology task force on clinical expert consensus documents developed in collaboration with the european society of cardiology endorsed by the society of cardiac angiography and interventions. Journal of the American College of Cardiology. 2001;37(5):1478-92.

16. Saito Y, Kobayashi Y, Fujii K, Sonoda S, Tsujita K, Hibi K, et al. Clinical expert consensus document on standards for measurements and assessment of intravascular ultrasound from the Japanese Association of Cardiovascular Intervention and Therapeutics. Cardiovascular Intervention and Therapeutics. 2020;35:1-12.

17. Wu X, Mintz GS, Xu K, Lansky AJ, Witzenbichler B, Guagliumi G, et al. The relationship between attenuated plaque identified by intravascular ultrasound and no-reflow after stenting in acute myocardial infarction: the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial. JACC: Cardiovascular Interventions. 2011;4(5):495-502.

18. Jia H, Abtahian F, Aguirre AD, Lee S, Chia S, Lowe H, et al. In vivo diagnosis of plaque erosion and calcified nodule in patients with acute coronary syndrome by intravascular optical coherence tomography. Journal of the American College of Cardiology. 2013;62(19):1748-58.

19. Neumann F-J, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European heart journal. 2019;40(2):87-165.

20. Sawada T, Shite J, Garcia-Garcia HM, Shinke T, Watanabe S, Otake H, et al. Feasibility of combined use of intravascular ultrasound radiofrequency data analysis and optical coherence tomography for detecting thin-cap fibroatheroma. European Heart Journal.

2008;29(9):1136-46.

21. Häner JD, Duband B, Ueki Y, Otsuka T, Combaret N, Siontis GC, et al. Impact of intracoronary optical coherence tomography in routine clinical practice: A contemporary cohort study. Cardiovascular revascularization medicine. 2022;38:96-103.

22. Kubo T, Ino Y, Mintz GS, Shiono Y, Shimamura K, Takahata M, et al. Optical coherence tomography detection of vulnerable plaques at high risk of developing acute coronary syndrome. European Heart Journal-Cardiovascular Imaging. 2021;22(12):1376-84.

23. Kawasaki M, Bouma BE, Bressner J, Houser SL, Nadkarni SK, MacNeill BD, et al. Diagnostic accuracy of optical coherence tomography and integrated backscatter intravascular ultrasound images for tissue characterization of human coronary plaques. Journal of the American College of Cardiology. 2006;48(1):81-8.

24. Stone GW, Maehara A, Lansky AJ, De Bruyne B, Cristea E, Mintz GS, et al. A prospective natural-history study of coronary atherosclerosis. New England Journal of Medicine. 2011;364(3):226-35.

25. Ohashi H, Ando H, Takashima H, Waseda K, Shimoda M, Fujimoto M, et al. Diagnostic performance of high-resolution intravascular ultrasound for the detection of plaque rupture in patients with acute coronary syndrome. Circulation Journal. 2019;83(12):2505-11.

26. Kataoka Y, Puri R, Andrews J, Honda S, Nishihira K, Asaumi Y, et al. In vivo visualization of lipid coronary atheroma with intravascular near-infrared spectroscopy. Expert review of cardiovascular therapy. 2017;15(10):775-85.

27. Waksman R, Di Mario C, Torguson R, Ali ZA, Singh V, Skinner WH, et al. Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study. The Lancet. 2019;394(10209):1629-37.

28. Schuurman A-S, Vroegindewey M, Kardys I, Oemrawsingh RM, Cheng JM, de Boer S, et al. Near-infrared spectroscopy-derived lipid core burden index predicts adverse cardiovascular outcome in patients with coronary artery disease during long-term follow-up. European heart journal. 2018;39(4):295-302.

29. Cheng JM, Garcia-Garcia HM, de Boer SP, Kardys I, Heo JH, Akkerhuis KM, et al. In vivo detection of high-risk coronary plaques by radiofrequency intravascular ultrasound and cardiovascular outcome: results of the ATHEROREMO-IVUS study. European heart journal. 2014;35(10):639-47.

30. Erlinge D, Maehara A, Ben-Yehuda O, Bøtker HE, Maeng M, Kjøller-Hansen L, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study. The Lancet. 2021;397(10278):985-95.

31. Zhang W, Mintz GS, Cao Y, Matsumura M, Lee T, Hoshino M, et al. Clinical determinants of coronary artery disease burden and vulnerability using optical coherence tomography co-registered with intravascular ultrasound. Coronary Artery Disease. 2021;33(2):114-24.

32. Prati F, Gatto L, Romagnoli E, Limbruno U, Fineschi M, Marco V, et al. In vivo vulnerability grading system of plaques causing acute coronary syndromes: an intravascular imaging study. International journal of cardiology. 2018;269:350-5.

33. Abdelmonaem M, Abushouk A, Reda A, Arafa S, Aboul-Enein H, Bendary A. IVUS-guided versus OCT-guided PCI among patients presenting with acute coronary syndrome. The Egyptian Heart Journal. 2023;75(1):1-8.

34. Scarsini R, Terentes-Printzios D, De Maria GL, Ribichini F, Banning A. Why, When and How Should Clinicians Use Physiology in Patients with Acute Coronary Syndromes? Interventional Cardiology Review. 2020;15.

35. Jeremias A, Maehara A, Généreux P, Asrress KN, Berry C, De Bruyne B, et al. Multicenter core laboratory comparison of the instantaneous wave-free ratio and resting P d/P a with fractional flow reserve: the RESOLVE study. Journal of the American College of Cardiology. 2014;63(13):1253-61.

36. Gutiérrez-Chico JL, Chen Y, Yu W, Ding D, Huang J, Huang P, et al. Diagnostic accuracy and reproducibility of optical flow ratio for functional evaluation of coronary stenosis in a prospective series. Cardiology journal. 2020;27(4):350-61.

37. Yu W, Tanigaki T, Ding D, Wu P, Du H, Ling L, et al. Accuracy of intravascular ultrasound-based fractional flow reserve in identifying hemodynamic significance of coronary stenosis. Circulation: Cardiovascular Interventions. 2021;14(2):e009840.

38. Erbay A, Penzel L, Abdelwahed YS, Klotsche J, Schatz A-S, Steiner J, et al. Feasibility and diagnostic reliability of quantitative flow ratio in the assessment of non-culprit lesions in acute coronary syndrome. The International Journal of Cardiovascular Imaging. 2021;37:1815-23.

39. Ullrich H, Olschewski M, Belhadj K-A, Münzel T, Gori T. Quantitative flow ratio or angiography for the assessment of non-culprit lesions in acute coronary syndromes: Protocol of the randomized trial QUOMODO. Frontiers in Cardiovascular Medicine. 2022;9:815434.

40. Tu S, Westra J, Yang J, von Birgelen C, Ferrara A, Pellicano M, et al. Diagnostic accuracy of fast computational approaches to derive fractional flow reserve from diagnostic coronary angiography: the international multicenter FAVOR pilot study. Cardiovascular Interventions. 2016;9(19):2024-35.

41. Ahres A, Simon J, Jablonkai B, Nagybaczoni B, Baranyai T, Apor A, et al. Diagnostic Performance of On-Site Computed Tomography Derived Fractional Flow Reserve on Non-Culprit Coronary Lesions in Patients with Acute Coronary Syndrome. Life. 2022;12(11):1820.

42. Escaned J, Ryan N, Mejía-Rentería H, Cook CM, Dehbi H-M, Alegria-Barrero E, et al. Safety of the deferral of coronary revascularization on the basis of instantaneous wave-free ratio and fractional flow reserve measurements in stable coronary artery disease and acute coronary syndromes. JACC: Cardiovascular Interventions. 2018;11(15):1437-49.

43. Ntalianis A, Sels J-W, Davidavicius G, Tanaka N, Muller O, Trana C, et al. Fractional flow reserve for the assessment of nonculprit coronary artery stenoses in patients with acute myocardial infarction. JACC: Cardiovascular Interventions. 2010;3(12):1274-81.

44. Engstrøm T, Kelbæk H, Helqvist S, Høfsten DE, Kløvgaard L, Holmvang L, et al. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3-PRIMULTI): an open-label, randomised controlled trial. The Lancet. 2015;386(9994):665-71.

45. Musto C, De Felice F, Rigattieri S, Chin D, Marra A, Nazzaro MS, et al. Instantaneous wave-free ratio and fractional flow reserve for the assessment of nonculprit lesions during the index procedure in patients with ST-segment elevation myocardial infarction: the WAVE study. American heart journal. 2017;193:63-9.

46. Choi KH, Lee JM, Kim HK, Kim J, Park J, Hwang D, et al. Fractional flow reserve and instantaneous wave-free ratio for nonculprit

stenosis in patients with acute myocardial infarction. JACC: Cardiovascular Interventions. 2018;11(18):1848-58.

47. van der Hoeven NW, Janssens GN, de Waard GA, Everaars H, Broyd CJ, Beijnink CW, et al. Temporal changes in coronary hyperemic and resting hemodynamic indices in nonculprit vessels of patients with ST-segment elevation myocardial infarction. JAMA cardiology. 2019;4(8):736-44.

48. Smits PC, Abdel-Wahab M, Neumann F-J, Boxma-de Klerk BM, Lunde K, Schotborgh CE, et al. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. New England Journal of Medicine. 2017;376(13):1234-44.

49. White CW, Wright CB, Doty DB, Hiratza LF, Eastham CL, Harrison DG, et al. Does visual interpretation of the coronary arteriogram predict the physiologic importance of a coronary stenosis? New England Journal of Medicine. 1984;310(13):819-24.

50. Hakeem A, Edupuganti MM, Almomani A, Pothineni NV, Payne J, Abualsuod AM, et al. Long-term prognosis of deferred acute coronary syndrome lesions based on nonischemic fractional flow reserve. Journal of the American College of Cardiology. 2016;68(11):1181-91.

51. Layland J, Rauhalammi S, Watkins S, Ahmed N, McClure J, Lee MM, et al. Assessment of Fractional Flow Reserve in Patients With Recent Non-ST-Segment-Elevation Myocardial Infarction: Comparative Study With 3-T Stress Perfusion Cardiac Magnetic Resonance Imaging. Circulation: Cardiovascular Interventions. 2015;8(8):e002207.

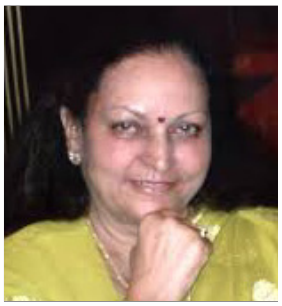
52. Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, et al. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS-NSTEMI randomized trial. European heart journal. 2015;36(2):100-11.

53. Cuculi F, De Maria GL, Meier P, Dall'Armellina E, de Caterina AR, Channon KM, et al. Impact of microvascular obstruction on the assessment of coronary flow reserve, index of microcirculatory resistance, and fractional flow reserve after ST-segment elevation myocardial infarction. Journal of the American College of Cardiology. 2014;64(18):1894-904.

54. Samady H, Lepper W, Powers ER, Wei K, Ragosta M, Bishop GG, et al. Fractional flow reserve of infarct-related arteries identifies reversible defects on noninvasive myocardial perfusion imaging early after myocardial infarction. Journal of the American College of Cardiology. 2006;47(11):2187-93.

55. Stone GW, Maehara A, Ali ZA, Held C, Matsumura M, Kjøller-Hansen L, et al. Percutaneous coronary intervention for vulnerable coronary atherosclerotic plaque. Journal of the American College of Cardiology. 2020;76(20):2289-301.

56. Kedhi E, Berta B, Roleder T, Hermanides RS, Fabris E, IJsselmuiden AJ, et al. Thin-cap fibroatheroma predicts clinical events in diabetic patients with normal fractional flow reserve: the COMBINE OCT-FFR trial. European heart journal. 2021;42(45):4671-9.



Management of Acute Coronary Syndrome

Dr. Lekha Adik Pathak
Director & Head of Department of Cardiology, Nanavati Max Super Speciality Hospital, Mumbai
Dr. Ronak V Ruparelia
Interventional Cardiologist, Bankers Super Speciality Hospital, Vadodara

Introduction:

Acute Coronary Syndrome (ACS) incorporate spectrum of clinical conditions namely acute myocardial infarction (AMI) and unstable angina. AMI can be further subdivided into ST elevation myocardial infarction (STEMI) and non-ST elevation ACS (NSTE-ACS). Unstable angina is defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury / necrosis. It is characterized by specific clinical finding of prolonged angina at rest, new onset of severe angina, angina that is increasing in frequency or angina that occurs after recent episodes of AMI. Diagnosis of AMI is made based on the fourth universal definition of MI. Although the term ACS is used interchangeably with AMI in clinical practice, both conditions differ from each other. AMI is defined as cardiomyocyte necrosis in clinical setting of acute myocardial ischemia. This chapter largely focuses on management of ACS.

Management of ACS:

I. History taking and physical examination

History taking and clinical examination plays a vital role in diagnosis and management of all diseases. Patient with ACS presents with broad range of clinical scenarios. A clinician should be very vigilant to diagnosis ACS early so that prompt treatment can be offered to the patient. The usual mode of presentation of ACS is anginal chest discomfort either at rest or on exertion. At times, elderly female and diabetic patients can have atypical presentation including dyspnea, easy fatigability, palpitation, giddiness, lethargy or uneasiness.

Assessment of vital signs is of utmost importance at first medical contact. That will guide clinician to determine whether patient is hemodynamically stable or not and whether patient requires intensive care unit admission or not. Focused clinical examination should include checking of all major pulses, blood pressure in both arms, auscultation of heart and lungs and assessing for sings of heart failure or circulatory compromise. At the same time, recording of electrocardiogram (ECG) is also equally important. ECG helps clinician to differentiate patients with STEMI from NSTE-ACS.

Another important diagnostic tool is cardiac biomarkers. After one has excluded STEMI and very high risk NSTE-ACS, cardiac biomarkers play a complementary role in diagnosis, risk stratification and management of ACS. High sensitivity Troponin (hs-cTn) is recommended as a diagnostic tool in management of ACS. At times serial estimation of cardiac biomarkers are needed for diagnosis of ACS. Time interval to second cTn assessment can be shortened with use of hs-cTn assays. It is recommended to use 0h/1h algorithm or the 0h/2h "rule-in" in pathway of ESC guidelines.

Another important diagnostic tool is transthoracic echocardiography (TTE). TTE can be performed by trained health care person serves an important tool to give exact estimation of cardiac functions and valvular dysfunction. It can also help at times to diagnosis dreadful complications or associations of ACS like cardiac tamponade,

acute valvular regurgitations or aortic dissection.

II. Pre-hospital Care or Primary Care:

Patient presenting to emergency team first should be categorized into STEMI and NSTE-ACS with the help of a 12 lead ECG. Initial diagnosis of STEMI suggests higher risk of immediate, life threatening complications such as ventricular arrhythmias. Such patients should be transferred as early as possible to the center with facility of cardiac cath lab. "Time is Muscle" holds true for patients with STEMI.

III. Acute pharmacotherapy

1. Oxygen: O2 supplementation is recommended in ACS patients with SpO2 < 90%. O2 supplement to patients without hypoxemia is not associated with clinical benefits

2. Nitrates: Sublingual nitrates helps to alleviate symptoms of ischemia. However, it is contraindicated in patients with inferior wall STEMI with RV infarction and in patients with hemodynamic instability (hypotension). It should also be avoided in patients with marked bradycardia or tachycardia. Use of phosphodiesterase 5 inhibitor in prior 24-48 hours also makes use of nitrates contraindicated.

3. Pain relief: Intravenous opioids (morphine) is considered as standard pain relief remedy in patients with AMI. However it can lead to nausea and vomiting and slows down gastrointestinal absorption of oral medicines like antiplatelets. Conversely, morphine has also been reported to reduce antiplatelet activity after administration of ticagrelor. Many articles has reported that morphine in addition to reducing absorption of antiplatelets, it also delay the onset of action and decrease the antiplatelet effect or P2Y12 inhibitors in patients with AMI. Further research is going on in this area, but at present it should be noted that currently available clinical data does not demonstrate any increase in risk of adverse clinical outcomes with morphine use.

4. Intravenous beta-blockers: Intravenous metoprolol is the most widely tested beta-blocker in trials. It is safe when used in patients without acute heart failure and has been associated with reduction in incidence of ventricular arrhythmias and microvascular obstruction in patients with STEMI. Administration of beta-blockers in patients with NSTE-ACS is not been evaluated.

IV. Selection of correct reperfusion therapy / strategy:

A patient with STEMI should undergo immediate PPCI (Primary Percutaneous Coronary Intervention) or fibrinolysis if PPCI is not possible within 120 minutes of diagnosis.

For patient with NSTE-ACS immediate invasive strategy is recommended when any very high risk feature is present. While early invasive strategy (within 24 hours) should be considered when high risk features are present. Very high risk features include hemodynamic instability or cardiogenic shock; recurrent or on going chest pain refractory to medical treatment; acute heart failure presumed secondary to ongoing myocardial ischemia; life threatening arrhythmias or cardiac arrest after presentation; mechanical complications recurrent dynamic ECG changes suggestive of ischemia. High risk features include confirmed diagnosis of NSTE-ACS; GRACE risk score > 140; Transient ST segment elevation; Dynamic ST segment or T wave changes.

- **PPCI or Fibrinolysis?** PPCI strategy is preferred mode of treatment with patients with STEMI if it can be performed in a timely manner (within 120 min of ECG diagnosis). It is superior to fibrinolysis in reducing mortality, non-fatal reinfarction and stroke. However, in certain circumstances immediate PPCI is not possible. Such patient can be subjected to pharmaco-invasive therapy provided the patient has presented within 12 hours of symptom onset. For

patients undergoing fibrinolysis, rescue PCI is indicated if fibrinolysis fails (i.e. ST segment resolution <50% within 60-90 min of fibrinolysis) or in presence of hemodynamic or electrical instability, worsening ischemia or persistent chest pain.

V. Fibrinolytic therapy:

Pharmacological therapy played a central role of treatment before invention of percutaneous coronary interventions. Fibrinolytic agents was vitally important as AMI pathophysiology involve thrombus genesis in coronary artery. Agents for fibrinolysis involves streptokinase (1st generation), alteplase (2nd generation), reteplase and tenecteplase (3rd generation). Fibrin specific 3rd generation fibrinolytic agents have shown to improve coronary flow rates and decrease reocclusion rates as compared to streptokinase. Although fibrinolysis does have its own limitations, namely, failed lysis in almost 15% of patients, reocclusion of infarct related artery resulting in re-myocardial infarction, increased risk of life threatening haemorrhage.

- **Pharmaco-invasive approach:** When PAMI cannot be performed within 120 mins of first medical contact, pharmaco-invasive approach can be applied to such patients for early revascularization of occluded artery in STEMI. This involves fibrinolysis at non-PCI capable centre followed by transfer to PCI capable centre for coronary intervention within 24h of fibrinolysis. This is different than a very popular alternate namely "Facilitated PCI". The rationale for this pharmaco-invasive approach is that initial fibrinolytic treatment is intended to restore the coronary blood flow and subsequent PCI maintain the patency of infarct related artery with coronary stenting. It is important to note that in pharmaco-invasive strategy, the time between fibrinolysis and PCI is crucial. Failure of facilitated PCI may have been attributed to fibrinolysis induced platelet activation, intraplaque haemorrhage of culprit lesion and increased bleeding risk. The optimal timing of routing coronary intervention for pharmaco-invasive strategy has not been determined, but it seems reasonable to perform coronary angiogram within 3 to 24 hours after successful fibrinolysis.

VI. Coronary Interventions

- **Stepping stones of STEMI management:** ISIS2 trial represented significant milestone in rapid treatment of AMI with streptokinase and aspirin. This trial was followed by GISSI study, which again proved the benefits of streptokinase. Streptokinase has many limitations like propensity to induce hypotension, high rates of allergy, prolonged anticoagulant effect and development of neutralizing antibodies. This paved the way for GUSTO trial series by introducing various tissue plasminogen activators (t-PA). September 1977 represented a golden milestone in STEMI management, when Andreas Gruntzig first performed balloon angioplasty. This has changed the priority of management of STEMI, which is being followed till date.

- **Thrombolysis to Coronary Interventions:** Thrombolytic agents dominated the management of STEMI during 1980s and 1990s. However, it had its own limitations like increasing bleeding risk and failed lysis in considerable number of cases. With advent of drug eluting stents and increasing number of cathlab across India, the paradigm of STEMI management started shifting towards coronary interventions. DANAMI-2, PRAGUE-2 and meta-analysis by Keeley et al made PPCI more widely acknowledge and the preferred method of revascularization. Both short term mortality (7% vs 9%) and MACE rate (8% vs 14%) are shown to be reduced by these trials. ACC/AHA and ESC/EACTS both recommended PPCI as class I/level of evidence A indication for the management of STEMI presenting within 12 hours. PPCI remains class I/level of evidence C for STEMI presenting beyond 12 hours while it becomes class IIa/level of evidence B for STEMI presenting late (24 – 48 hours after onset of symptoms).

- **Access Site:** Brachial approach for coronary interventions was originally described by Dr Werner Forssmann in 1929. Dr. Mason sones performed first cardiac catheterization via brachial route by arterial cut down technique. Lucien Campeau, in 1989, reported 100 trans radial angiography. The first radial intervention was performed by Kiemeneij and Laarman in 1993. In the early days of coronary interventions, femoral artery access was the preferred option. However, with advent of better hardware, now radial artery has replaced the femoral artery as preferred access site. The advantage of radial interventions remains less bleeding complication and early ambulation post interventions. Its safety has been established by trials in management of STEMI (STEMI-RADIAL & RIFLE-STEACS trials). Ultrasound guided arterial access has also made femoral puncture more safe and effective whenever required (e.g. IABP / LVAD insertion). More recently dorsal radial artery access has also gained popularity as it reduces long term hand complications related to radial interventions.

- Deferred vs. Immediate PCI in STEMI patients: Deferred stenting (initial opening of the occluded vessel with a balloon followed by stenting after 24 to 72 hours) did not reduce occurrence of no-reflow or slow flow, death, MI or repeat revascularization compared to immediate stenting in a meta-analysis. Hence majority of STEMI are being treated by immediate stenting.

- Single versus multivessel PCI: Four major RCTs (COMPLETE, CvLPRIT, DAnish & DANAMI3-PRIMULTI) have showed a benefit of complete revascularization as compared to Infarcted Related artery only PCI in patients with STEMI and multivessel disease. COMPLETE was a much larger RCA that showed MACE reduction. In terms of optimal timing of complete revascularization, the COMPLETE study showed no difference in outcomes whether the procedure was performed during the indexed hospital stay or a staged intervention within 45 days. In patients with AMI with cardiogenic shock and multivessel disease, CULPRIT SHOCK trial showed that a strategy with PCI of the culprit lesion only with possible staged complete revascularization determined a lower 30 day and 1 year risk of composite of all-cause mortality or severe renal failure compared with immediate multivessel PCI. In the light of this observation, immediate MVPCI is now not recommended by ESC guidelines.

- Current stents: The current generation DES (drug eluting stents) are based on thinner metallic struts with improved drug carrier (polymer) which releases drugs with improved antiproliferative agents. Early generation stent platforms were made up of stainless steel with strut thickness of 130-150 microns. Various studies indicated the advantages of thinner stent strut. Thinner struts tends to have less vessel cross sectional area loss and hence less in-stent restenosis. Newer generation DES have backbones made of novel metallic alloys such as cobalt chromium and platinum chromium. Their strut thickness has been reduced to 90 microns even though the radial strength is maintained. Furthermore, the older stents were coil tubes, which has been evolved to slotted tube stents. With technological advancements, this has been further modified to modular stent designs. These modifications have made stents more trackable and have given them more radial strength. This evolution in stent design has made a breakthrough in the management of STEMI. It has replaced Thrombolysis in centers where PCI facility is available or it is possible to transfer patients to PCI facility center.

- Facilitated PCI: It is defined as the use of pharmacological treatment (thrombolysis) as soon as possible after the onset of STEMI in an attempt to establish early reperfusion, followed by transport to an interventional laboratory for emergent mechanical reperfusion i.e. angioplasty. It is particularly

useful for patients presenting to center where PCI facility is not available and it is not possible to transfer patient to PCI enabled center within window period of 120 minutes. Early studies of facilitated PCI showed improvement in coronary blood flow during angiogram, however they failed to show improvement in clinical outcomes and major hemorrhagic complications were usually more frequent. More recent trials like PACT, GRACIA-2 and BRAVE also showed improvement in infarct artery patency in facilitated PCI. Larger clinical trials like ASSENT-4 and FINESSE evaluated tenectaplase and half dose reteplase + abciximab respectively in facilitated PCI. ASSNET-4 and FINESS both showed improvement in primary endpoint of death, shock and CHF at 90 days in facilitated PCI. CARESS-in-AMI, TRANSFER-AMI and NORDISTEMI all three large randomized trials noted no significant increase in major bleeding. A metanalysis of these trials showed significant reduction in re-infarction, recurrent ischemia and combined end point of death and re-infarction at 30 days. The clinician must choose the best reperfusion strategy in patients with STEMI presenting to non-interventional center based on an assessment of risk. This will include time from onset of symptom, time delay in transport for Primary PCI, risk of fibrinolytic therapy, presence of cardiogenic shock and cardiac arrhythmias.

- Late Presenters: Late presentation is associated with increased mortality. In the treatment of late-presenting STEMI patients, clinical evaluation and risk stratification represents paramount factors helping in decision. As recommended by recent guidelines, patients who are still early in the course of STEMI (12-48 hours) should undergo PCI. Those beyond 48 hours should undergo myocardial viability studies like Cardiac MRI, PET scan or SPECT scan. Patients presenting beyond 48 hours with evidence of silent ischemia or viability should also undergo PCI. Those with no evidence of silent ischemia or viability, can safely be treated with medical therapy.

VII. Periprocedural medications:

- **Antiplatelets:** It plays a key role in the acute phase of treatment of ACS. Many oral and intravenous antiplatelets are available. Choice of antiplatelet depends on bleeding risk of patient. Factors associated with increased bleeding risk have been given by the Academic Research Consortium on High Bleeding Risk (ARC-HBR). Presence of one major or two minor ARC-HBR risk factors indicate high bleeding risk.

  Efficacy of **Aspirin** was first demonstrated in the ISIS-2 Trial. Aspirin resulted in significant reduction in vascular mortality. Since then Aspirin remains the antiplatelet of choice to start as early as possible and to continue for life long even after coronary intervention. Loading dose of aspirin is 300 mg for all practical purpose followed by maintenance dose of 75-100 mg once a day.

  Use of **Clopidogrel**, a thienopyridine (pro-drug), evolved from initial trials like PCI CURE and PCI CLARITY. The recommended loading dose of clopidogrel in STEMI is 600mg. it should only be used when prasugrel or ticagrelor are contraindicated or not available or in some patients considered otherwise at high bleeding risk. In addition, the use of clopidogrel may be considered in older patients (>70 years)

  Prasugrel is a third generation thienopyridine. It achieves faster and more potent platelet inhibition compared to clopidogrel. Maximum plasma concentration of Prasugrel is achieved in 30mins in healthy volunteers. It also has very low rate of non-responders as compared to clopidogrel. Hence many interventional cardiologists prefer prasugrel over clopidogrel. Clinical superiority of prasugrel over clopidogrel in ACS is well demonstrated in TRITON TIMI 38 trial. Although, it is contraindicated in patients with prior stroke/TIA and is not recommended in patents aged e" 75 years or in patients with body weight < 60kg. A

reduced maintenance dose of 5 mg may be considered in these patients. Prasugrel should be considered in preference to ticagrelor for ACS patients who proceed to PCI. ISAR-REACT 5 RCT is largest head-to-head comparison of 1 year DAPT (Dual Antiplatelet Therapy) with prasugrel vs. DAPT with ticagrelor. Treatment with prasugrel significantly reduced the composite endpoint of death, MI or stroke without any increase in bleeding complications.

Ticagrelor is a drug of new class called Cyclo-Pentyl Triazolo Pyrimidine. It causes reversible inhibition of P2Y12 receptor and does not require hepatic metabolism for its activity. It provides more rapid, potent and consistent platelet inhibition. In recent era it has become the drug of choice for loading dose along with aspirin. PLATO trial demonstrated the safety and efficacy of ticagrelor. One of the common side effect responsible for discontinuation of the drug is Dyspnea.

Cangrelor is direct reversible, short acting P2Y12 receptor inhibitor that has been evaluated during PCI for CCS and ACS in clinical trials against clopidogrel in CHAMPION PCI, CHAMPION PLATFORM and CHAMPION PHOENIX. A meta-analysis of these trials showed that the benefit of cangrelor with respect to major ischemic endpoints was counterbalanced by increased minor bleeding complications. Due to its proven efficacy in preventing intra-procedural and post-procedural stent thrombosis, cangrelor may be considered on a case by case basis in P2Y12 receptor inhibitor naïve patients undergoing PCI.

Glycoprotein IIb/IIIa inhibitors provides rapid, potent platelet inhibition. Although it was being used in recent past by many interventionalists, its current use is restricted to "bailout" in the event of angiographic evidence of massive thrombus, slow/no-reflow or a thrombotic complication.

- **Antithrombotic agents:** Parenteral anticoagulation is recommended for patients with STEMI or NSTE-ACS undergoing PPCI. Unfractionated heparin remains the choice of anticoagulant at present. Enoxaparin and bivalirudin should be considered as alternative to UFH. Fondaparinux is not recommended. While in patients with NSTE-ACS not undergoing invasive treatment, fondaparinux is recommended in preference to enoxaparin. Although enoxaparin should be considered if fondaparinux is not available.

- **Maintenance antiplatelet / antithrombotic therapy after revascularization:** DAPT remains the preferred treatment for 12 months post angioplasty irrespective of stent type. Preferred DAPT regimen consists of a potent P2Y12 receptor inhibitor (Prasugrel or Ticagrelor) with Aspirin. In patients with high ischemic risk and low bleeding risk, DAPT may be extended beyond 12 months post intervention. More recently, short (3 months) and ultrashort (1 month) DAPT has also been recommended based on bleeding risk calculation by DAPT and PRECISE DAPT score. It is of utmost importance for cardiologist to balance the ischemic and bleeding risk and optimize duration of antiplatelet therapy. De-escalation is required at times from potent P2Y12 inhibitors to clopidogrel if patient develops bleeding complication or non-bleeding side effects (i.e. allergic reaction or dyspnea with ticagrelor). In TOPICAL-ACS trial DAPT de-escalation from prasugrel to clopidogrel was guided by platelet function testing and was found to be non-inferior to standard treatment with prasugrel at 1 year after PCI. TOPIC and TALOS-AMI trials investigated unguided de-escalation in ACS patient from ticagrelor/prasugrel to clopidogrel and concluded that unguided de-escalation significantly reduced net adverse clinical events and bleeding events. De-escalation of antiplatelet therapy in first 30 days is not recommended but may be considered as an alternative strategy beyond 30 days after and ACS in order to reduce the risk of

bleeding events. As suggested by DAPT and PEGASUS-TIMI 54 trials, a prolonged DAPT beyond 12 months can be considered in those with high thrombotic risk and without an increased risk of life threatening bleeding. Recently, 60mg BD ticagrelor was found to be associated with reduced bleeding as compared to 90mg BD ticagrelor and should be preferred for extended therapy beyond 12 months.

- **Dual Pathway Inhibition:** Newer oral anticoagulants (NOACs) are also gaining popularity in treatment post PCI. Very low dose rivaroxaban (2.5mg twice a day) with DAPT has been studied in ATLAS ACS 2-TIMI 51 trial. It showed reduction of ischemic event and CV mortality along with a higher risk of major intracranial bleeding. However, the trial was conducted with background of clopidogrel and data regarding ticagrelor / prasugrel with rivaroxaban is lacking.

  Combination of SAPT (aspirin) with NOAC (rivaroxaban), which acts on both platelet and fibrin together was evaluated in COMPASS trial. This study showed that aspirin + rivaroxaban reduced MACE rate significantly (4.1% vs 3.4%). This combination can be considered in place of DAPT beyond 12 months post ACS with high thrombotic risk.

  In special populations like patients with atrial fibrillation and STEMI, triple therapy for a short period of 1 to 4 weeks followed by SAPT + (N)OAC for 12 months has also been shown to be beneficial in AUGUSTUS Trial. Beyond 12 months (N)OAC monotherapy indicated as Class I for all patients.

VIII. Coronary Artery Bypass Grafting (CABG):

There are no dedicated RCT comparing percutaneous vs. surgical revascularization in patients with ACS. In patients with STEMI, CABG should be considered only when PPCI is not feasible. Even in high risk NSTE-ACS, PCI is usually preferred for reasons of timeliness, unless concomitant mechanical complication makes PCI contraindicated. In other ACS choice of CABG vs. PCI depends on presence of number of coronary involved.

IX. Long term treatment:

Secondary prevention after ACS plays a pivotal role to reduce morbidity and mortality. Life style modification and pharmacological therapy plays a central role in long term management post ACS

- **Life style modification:**

- Tobacco cessation is associated with reduced risk of reinfarction by 30-40% and death by 35-45%. Therefore smoking cessation is of utmost importance in management of ACS. Smoking cessation interventions includes combination of counselling and pharmacotherapy as and when required. Pharmacological interventions include nicotine replacement therapy, bupropion and varenicline. Varenicline is the most effective and safe medical treatment to support smoking cessation in ACS patients. E-cigarettes have also been tried. It does contain nicotine, but it do not contain as many tobacco chemicals as cigarettes. Caution should be given with respect to the use of E-cigarettes as current evidences suggests they are harmful to CV health.

o Physical activity and exercise: Sedentary behavior defined as time spent sitting or lying with low energy expenditure while awake is an independent risk factor for all cause mortality. General physical activity recommendations include a combination of regular aerobic physical activity and resistive exercise.

o Nutrition: Healthy diet and eating habits dramatically reduces CV risk.

o Alcohol consumption: Data suggest that alcohol abstinence has been associated with lowest risk of CV death. Weekly consumption of > 100 gm of alcohol is associated with decreased life expectancy.

- Psychological support: Anxiety and mood disorders are found to be very high in patients post ACS. Adequate use of psychological and pharmacological interventions are of utmost importance for such subset of patients.

- **Pharmacological treatment:**

- Lipid lowering therapy: Dyslipidemia should be managed with combination of lifestyle modifications, diet control and currently available pharmacological treatment. LDL-C levels after ACS are associated closely with mortality. Current treatment foal for secondary prevention is to lower LDL by e" 50% from baseline and achieve an absolute target of < 55 mg/dL. For patients who experience a second CV event within 2 years, a stringent LDL target of < 40 mg/dL is recommended. Lipid lowering therapy should be initiated as early as possible post ACS. High intensity statin (rosuvastatin and atorvastatin) are the first choice of drugs. Ezetimibe can be added if the target LDL is not achieved with high intensity statin therapy. PCSK 9 inhibitors can be considered as a third line of treatment for dyslipidemia post ACS. Treatment with PCSK 9 inhibitor has been shown to be safe and effective in LDL lowering.

- Beta-blockers: Benefit of beta blockers after ACS in patients with reduced LVEF is supported by evidence from contemporary trials. Pooled data suggests that beta blockers post MI reduces risk of death by >20%. However evidence for NSTEMI is less robust. The duration of beta-blockers after uncomplicated ACS is also controversial. Some observational studies suggesting that the clinical benefit of beta-blocker therapy is restricted to the first year after the event. There are 2 ongoing large scale RCTs testing impact of beta-blocker withdrawal after 6-12 months following uncomplicated ACS in patients with preserved LVEF.

- Nitrates and Calcium Channel blockers: Oral nitrates have no survival benefits in patients post ACS. Although it can be used at times as antianginal modality. Calcium channel blocker was also not associated with prognostic benefit in systematic review. It can be used in context of residual angina and blood pressure control.

- Renin angiotensin aldosterone system inhibitors: ACE inhibitors have been shown to improve outcome in post AMI patients with LVEF d" 40%, diabetes, CKD and / or hypertension. Early trials of ACE inhibitors in STEMI showed that ACE inhibitor use is associated with small but significant reduction in 30 day mortality. In VALIANT trial valsartan found to be non-inferior to captopril. ARNI have also been shown to be superior to ACE inhibitor in patients with established heart failure. However in more recent PARADISE-MI trial ARNI was not found to improve death from CV cause or incident HF in patients with recent ACS. In general ACE inhibitors are recommended for patients with HFrEF regardless of the etiology and it can be considered in patients with HFmrEF. ARBs are recommended in patients who cannot tolerate ACE inhibitors or ARNI.

Conclusion:

A clinician encounters Acute Coronary Syndrome very frequently in day to day practice. The key to success is early diagnosis and prompt treatment. A good clinical acumen is of utmost importance to diagnose ACS in scenario of atypical presentation. A 12 lead ECG is must for diagnosis and classification of ACS. Additionally high sensitive Troponin and echocardiography when available helps in prognostication as well as diagnosis of mechanical complications of AMI. In patients with STEMI, early PPCI remains the modality of treatment. When PPCI is not feasible in specified time interval, fibrinolysis or pharmcoinvasive approach should help. A very small subset of patients with STEMI and NSTE-ACS require CABG. Long term management of ACS involves a multimodality approach that involves pharmacological as well as non-pharmacological approach.

Antiplatelet agents

Dr. P.V. Nishanth
Consultant cardiologist,Trust multispeciality,Kakinada
Interventional cardiologist, Trust multispeciality hospital, Kakinada-5
Mail:mediconishnath@gmail.com

Acute coronary syndromes are a major cause of mortality and morbidity,antiplatelet agents are the cornerstone of therapy both in acute and chronic phases This review is a landscape view on the available antiplatelet agents and their application in treatment of acute coronary syndromes presented in a simple manner with relevant trial evidence

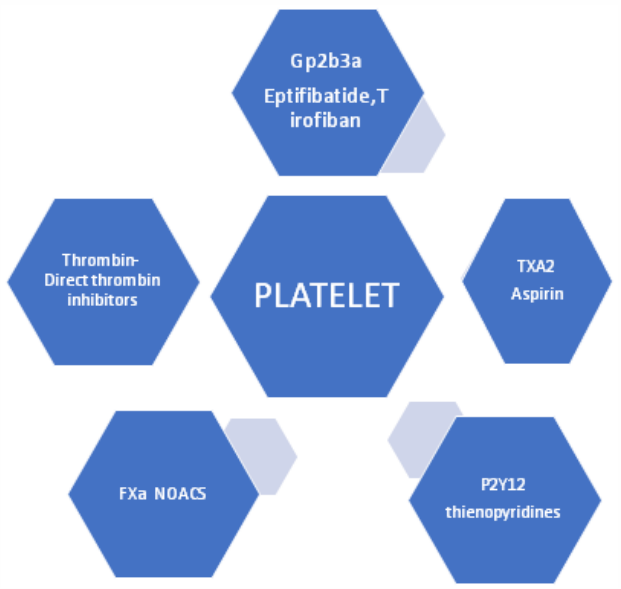
Epidemiology

India has highest burden of ACS in world.in Indian population STEMI incidence is higher than NSTEMI1. Data from few Indian registries is presented below

Study	Overall mortality/ STEMI/NSTEMI
CREATE,2001-2005(2)	6.6/3.7/5.8%
HP ACS2012-2014(3)	7.6/10.8/5%
PGIMER-ACS 2018-19(1)	7.6/8.7/4%

Pathophysiology of ACS

Mechanism of action of antiplatelet agents can only be understood by a review of pathophysiology of ACS .Central to pathophysiology is platelet activation which is triggered by a number of factors acting on platelet receptors. Various antiplatelet agents have been developed to act at different receptors to prevent platelet adhesion and aggregation



Aspirin

It is a reversible inhibitor of cyclooxygenase and has been the cornerstone of ACS management since 1988 after ISIS 2 trial(6)

The mechanism of action of aspirin even though well known is reiterated for the purpose of understanding the recommendation especially in regards to upper GI bleeding

1. Irreversible inhibition of cyclooxygenase therby inhibiting thromboxane and prostaglandin synthesis.(4,5)
2. Thrombaxanea2 inhibition in platelets and inhibition of thrombaoxane receptors required for activation of GP2b3a receptors(7).
3. It has systemic effects as it is not ionised in gastric lumen and is absorbed across gastric

mucosa and is trapped temporarily in gastric mucosal cells

4. Systemic and intragastric inhibition of cyclooxygenase prevent prostaglandin synthesis thereby the beneficial effects of prostaglandins in increasing bicarbonate secretion in gastric mucosa.

5. These topical and systemic effects can increase the risk of ulcer formation and bleeding from gastric ulcers(8)

Thenopyridines:

Clopidogrel:It is a irreversible antagonist of platelet adenosine di phosphate-p2y12.It is a prodrug needing hepatic conversion into an active metabolite(9).It s addition results in 20% reduction in ischemic events when combined with aspirin in ACS.Its safer than first generation ticlopidine.

It has no topical effects on gastric mucosa although it may lead to bleeding from pre formed ulcers

Prasugrel

It is a third generation drug that binds to same receptor as clopidogrel in an irreversible manner(10),It is a prodrug again requiring hepatic conversion which rose into prominence following concerns of variable bioavailabilty and resistance to clopidogrel(11)

Ticagrelor

It is a part of **cyclopentyltriazolopyrimidine** family acts by reversible binding to P2 Y12 inhibitor(12).it does not need activation in liver. Its rapid onset and offset of action necessitates a **twice daily** dosing

Cangrelor

It is an ***intravenous non thienopyridine*** platelet inhibitor with rapid onset and of set of action and short half life of approximately 5 minutes(12). Due to its unique metabolism it is suited to peri PCI and bridging periods.

GP 2b 3a inhibitors.

Abciximab, tirofiban and eptifibatide are IV inhibitors of GP2b 3a.Their use is limited to PCI with high thrombotic burden and in treatment of slow flow and no reflow.

CLINICAL EVIDENCE

Clopidogrel: Dose recommendation of 600mg loading and 75 mg maintainence is a result of 3 landmark trials (Table 1)

Prasugrel

The following are the 2 land mark trials with prasugrel (Table 2)

The beneficial effects of prasugrel over clopidogrel and ticagrelor could be due to enhanced endothelial function and decreased IL6 levels in addition to platelet inhibition(19)

Ticagrelor

Land mark trial with ticagrelor was the PLATO trial(20) (Table 3)

Table 1

Caprie trial(13)	Vs 325mg aspirin	Superior ischemic and bleeding outcomes	First trial
Cure trial(14)	NSTEMI With And without PCI	20 percent relative risk reduction with a 2.7 percent increase in major bleeding	DAPT duration between 3 to 12 months
CURRENT OASIS 7(15)	600VS 300mg clopidogrel	Significant reduction in stent thrombosis 1.6 vs 2.3 percent	Contributed to guideline reccommendation

Table 2

Principle timi 44(16)	60mg loading /10mg maitainence of prasugrel vs 600mg/75mg clopidogrel	Superior platelet inhibition and antiplatelet effects	Post PCI patients
TRITON TIMI 38(17)	VS Clopidogrel	9.9 vs 12.1 percent<.001 ischemic events 2.4 vs 1.8 percent bleeding	Prasugrel preferred over clopidogrel only when undergoing PCI. Clopidogrel preferred in stable ischemic heart disease
ISAR REACT 5(18)	VS ticagrelor	6.4 vs 9.3 %ischemic events 4.0 vs 5.4% bleeding events	ESC guideline changed to prasugrel over ticagrelor in NSTE ACS proceeding for PCI

Table 3

	Ticagrelor	Clopidogrel
Ischemic events	9.8%	11.3% (<.001)
Bleeding events	11.4	11.2
Vascular mortality	4	5.5%(<.001)
All cause mortality	4.5	5.9% (.001)

Ticagrelor is the only antiplatelet agent to demonstrate an all cause mortality benefit

Cangrelor

After futlility in demonstrating primary endpoint in CHAMPION PCI and CHAMPION PLATFORM trials (21)in 2009 Cangrelor rose again like the proverbial phoenix

In CHAMPION PHOENIX(22) trial it was superior to clopidogrel alone in patients undergoing elective pci(4.7 vs 5.5%)(22)

Societal guidelines

2023 ESC guidelines on acute coronary syndromes have proposed the following guidelines, regarding antiplatelet agents(23)

Dose regimen of antiplatelet agents (Table 4)

TIMING OF PRE TREATMENT WITH P2 Y12 INHIBITORS(23)

Pre treatment strategy refers to adminstsration of p2 y12 inhibitors before coronary anatomy is known. Evidence for this strategy is variable and following strategy is recommended

1. In patients with STEMI undergoing PPCI routine loading is preferable
2. In patients with NSTEMI,scheduled for early angio (<4 hrs),pretreatment without details of coronary anatomy is not recommended. f patient proceeds for PCI full loading is to be given at time of PCI
3. In NSTEMI ,with anticipated delay of >24 hrs pretreatment is to be given

MAINTAINENCE STRATEGY FOR ANTIPLATELET THERAPY

The recommended duration for antiplatelet therapy post intervention is 12 months with aspirin in combination with prasugrel or ticagrelor .Clopidogrel is to be substituted if bleeding rsik is higher.(23)

Table 4

Drug	Loading	Manitainiance	Special consideration
Aspirin	325mg	75m-150mg OD	No change in CKD
Clopidogrel	600mg/300mg for fibrinolysis	75mg OD	No change in CKD
Prasugrel	60mg	10mg/5mg in >75 yrs when deemed necessary	Contraindicated with history of stroke
Ticagrelor	180mg	90 mg BD	No change in CKD
Cangrelor	30mcg/kg IV bolus	4mcg/kg/min infusion for 2 hrs or duration of proceedure	Clopidogrel and prasugrel can be givena t end of infusion but ticagrelor should be given at start of PCI IN FULL LOADING DOSES

There are however two ways to shorten or change the antiplatelet strategy(24)

1. Shortened duration of DAPT
2. **Descalation** from one p2y12 inhibitor to another-this is needed for some **special situations**

a. High bleeding risk

b. Side effects(dysnea with ticagrelor)

c. Economic considerations

Descalation is not recommended in the first one month of ACS event as there is a potential risk of ischemic event

The decision to adapt either a regular strategy or an alternate strategy depends on balance between bleeding risk and ischemic risk

Ischemic risk estimation:

The following variables confer a high ischemic risk to the patient necessiaiting a stronger strategy(24)

1. History of STEMI or multivessel PCI or stent thrombosis
2. complex PCI like bifurcation, Left main ,CTO or last remaining coronary artery

The following scores have been used to estimate ischemic risk. (Table 5)

There are number of models available to assess bleeding risk **like PRECISE DAPT** and PRAISE. These are available online for application.

The widely used **PRECISE DAPT** (28)uses the following variables entered into a normogram

1.Age 2.WBCcount 3.Spontaneous bleeding 4.Creatinine clearance 5.Hemoglobin

Shortening duration of antiplatelet therapy duration was examined in a few trials. Thing to be borne in mind was these trials included only patients with moderate ischemic risk

1. **STOP DAPT2-ACS(29)** -strategy of stopping DAPT at 1 -2 month followed by clopidogrel monotherapy failed to demonstrate noninferiorty to standard therapy
2. **MASTER DAPT(30)-** I month DAPT followed by Aspirin or P2 Y12 inhibitor monotherapy vs standnard therapy in patients with high bleeding risk with a bisoreorbable polymer coated stent showed non inferiority in high bleeding risk patients with shortened DAPT
3. **TWILIGHT Trial(31)**-3 month vs standard DAPT with Ticagrelor monotherapy in shortened group. P atients were high risk ischemic patients with no bleeding or ischemic events in first 3 months following

Table 5

GRACE(25)	Systolic blood pressure Age, Killip class Heart rate, Cardiac arrest, Serum creatinine ST-segment deviation Cardiac biomarkerincrease a score of >140 benefit from early invasive strategy
PARIS CTE(26)	Diabetes, ACS, Smoker Creatinine clearance Prior PCI / prior CABG. Can predict risk of thrombotic events upto 2 years following stenting
DAPT(27)	Age >75 years −2 Age 65 to <75 years −1 Age <65 years -0 Current cigarette smoker 1 Diabetes mellitus 1 MI at presentation 1 Prior PCI or prior MI 1 Stent diameter <3 mm 1 Paclitaxel-eluting stent 1 CHF or LVEF <30% 2 Saphenous vein graft PCI 2 >2 Favors prolonged DAPT,<2 shortened DAPT

PCI.STEMI patients were excluded .Ticagrelor monotherapy was non inferior with fewer bleeding events in shortened duration group.

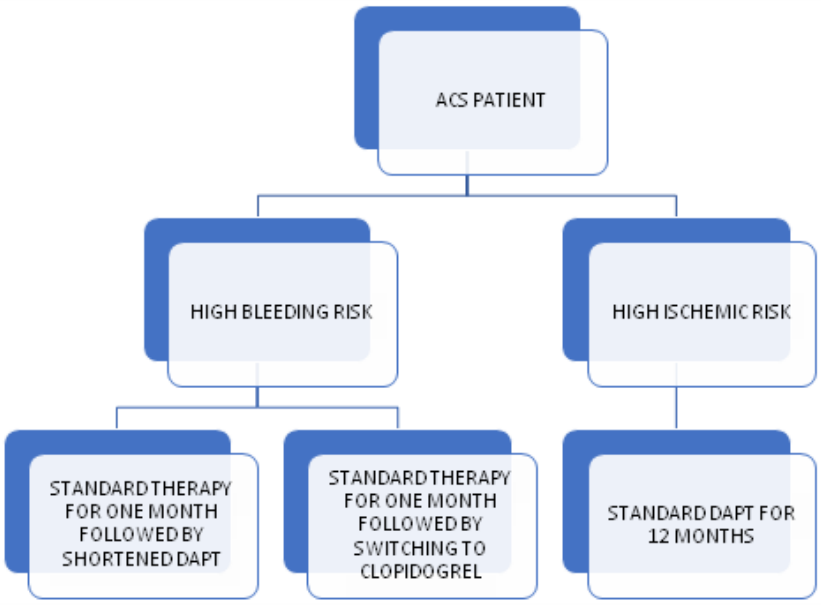
Descalation of antiplatelet therapy from potent p2y12 inhibitor to clopidogrel was tested in a few trials in with two startegies—**genetic guided vs unguided**

1. **Guided by genetic testing** a deescalation strategy of switching from prasugrel to clopidogrel at 2 weeks in **TROPICAL ACS** (32)and from ticagrelor/ prasugrel to clopidogrel at 48 hrs in **Popular Genetics(33)** was non inferior to standard therapy with lower incidence of bleeding
2. **TOPIC(34) and TALOS AMI(35)** tested **unguided descalation** from ticagrelor to clopidogrel at 1 month of DAPT with reduced net adverse and bleeding events without significant rsik of ischemic events
3. HOST-REDUCE-POLYTECH-ACS(37)- tested a dose de-escalation strategy of prasugrel from 10mg to 5 mg in patients <75 yrs of age at 1 month without significant increase in ischemic events

Recommendations for standard use of antiplatelet therapy in ESC 2023 guidelines on acute coronary syndrome(23)

Class1.

1. Asprin for all patients at a loading dose of 325 followed by 75-150mg for long term treatment
2. p2y12 inhibitor in recommended loading



and maintainence dose for 12 months unless there is high bleeding risk

3. Prasugrel at 60mg followed by maintainence of 10mg per day in all patients proceeding to PCI. DAose is 5 mg per day in patients >75kg or body weight less than 60 kg

4. Ticagrelor is recommended in both invasive and conservative groups

5. Clopidogrel is to be preferred with non availability of or intolerance to or contraindication for prasugrel and ticagrelor

6. Following CABG DAPT is to be continued for 12 months while stopping DAPT at time of surgery

Class2a

1. Prasugrel to be preferred over ticagrelor in setting of PCI

2. Gp2b3a inhibitors to be used in a case of no flow or thrombotic complication

Class2b.

1. Clopidogrel as the p2 y12 inhibitor in older patients with high bleeding risk

2. Cangrelor in p2y12 naïve patients proceeding for PCI

3.P retreatment with p2y12 inhibitor may be considered in patients undergoing primary PCI and patients with NSTE ACS in whom delayed angiography is planned at low bleeding risk

Class3

1. Routine pretreatment with GP2b 3a inhibitors

2. Pretreatment with p2 y12 inhibitor in NSTE ACS when early invasive startegy is planned

Shortening of antiplatelet therapy

Class2a

1. Low ischemic risk patients event free after 3-6 months of DAPT maybe considered for single antiplatelet therapy preferable with p2y12 inhibitor

Class2b

1. Switching to clopidogrel from more potent antiplatelet therapy to reduce bleeding risk

2. In high bleeding risk patients monotherapy with aspirin or monotherapy with p2y12 inhibitors after 1month of DAPT

Class3

1. Descalatation of antiplatelet therapy within 1 month of PCI is not recommended

Can aspirin be stopped early?

Cornerstone of ACS treatment for decades,aspirin monotherapy is a standard of care after 1 yr of DAPT. With prescence of potent p2 y12 inhibitors need for synergistic cyclooxygenase inhibition is being challenged.2 metaanalysis have shown p2 y12 monotherapy at 1-3 months of DAPT reduced bleedning risk by 50% without significant increase in ischemic risk. But recent ESC 2023 GUIDELINES still recommend Asprin monotherapy after 12 months of DAPT(23)

Prolonged anti thrombotic therapy after 12 months(23)

Esc 2023 guidelines have given following recommendations

1. Class1-Stop antiplatelet treatment at 12 months if patient is on OAC
2. Class2 a-If patient is at high ischemic risk and low bleeding risk a second antiplatelet maybe added to aspirin
3. Class2b-In patients with moderate ischemic risk bit low bleeding risk a second antiplatelet may be added
4. Class2b-Isolated p2 y12 inhibitor monotherapy.

Antiplatelet therapy in special situations

Patients receiving anticoagulants(23)

Class1

1. In patients with AF and CHADS2VASCF >1 in men and >2 in women following an ACS - 1 week of triple therapy with Asprin , Clopidogrel and NOAC followed by clopidogrel and NOAC for one year followed by NOAC alone
2. Bolus UFH IS is indicated in patients undergoing PCI if patient is on NOAC or INR <2.5 in VKA treated patients

Class2a

1. If patient needs VKA,INR should be 2-2.5 for 70% of time
2. Rivoroxaban 15mg in preference to 20mg for duration of DAPT in high bleeding risk patients
3. Dabigartan if used at 110mg BD instead of 150mg BD in high bleeding risk

Triple therapy with aspirin for one month if patient has high ischemic risk

Class2b-

Withdrawl of antiplatelet at 6 months while continuing antiplatelet therapy

Class3

Use of ticagrelor or prasugrel as a part of triple therapy is not considered

We review the trials which have led to the above recommendations

Metaanalysis of 4 NOAC based RCTS comparing DAT with Triple Therapy in AF patients undergoing PCI showed that double therapy with anticoagulant and single antiplatelet therapy reduced bleeding by 2.3% with a increase in stent thrombosis by 0.4% resulting in a neutral effect on mortality.

But the confounding factor was the use of VKA in TAT vs NOAC IN DAT group

Asprin used for one month in AUGUSTUS TRIAL did not reduce ischemic risk after 1 month but increased bleeding risk. Stent thrombosis ates were highest in first 30 months in non aspirin group.

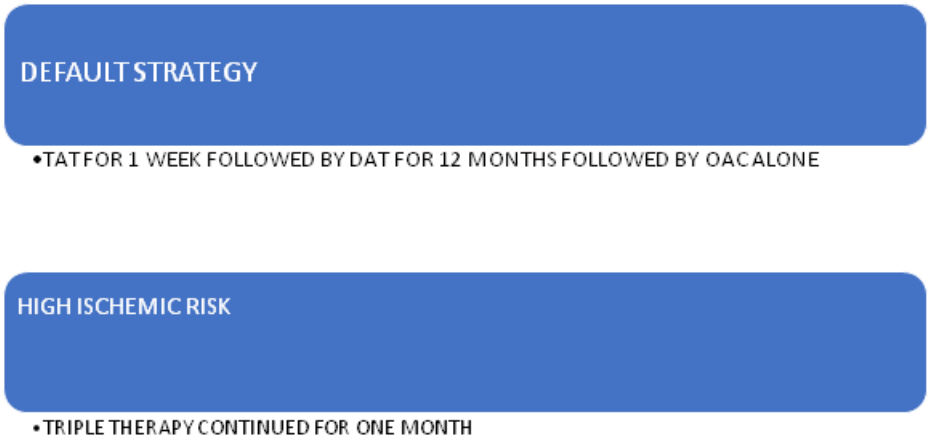
ANTIPLATELET THERAPY IN FIBRINOLYSIS(23)

Class1-Aspirin and Clopidogrel are recommended.

Results of TREAT study showed that switching from clopidogrel to ticagrelor did not increase 30 day mortality in patients treated by fibrinolysis..

Antiplatelet therapy in patients not undergoing reperfusion(24)

Usually a combination of **Aspirin and clopidogrel** is recommended .Prasugrel is only recommended for patients when CAD is cobnfirmed by angio.



Antiplatelet therapy in patients with GI bleeding

Gi bleed: patients with GI bleed the initial approach is to stop antiplatelets . Following cessation of bleeding the ischemic risk determines the choice of agent

1.As stated in beginning of article and interaction of Aspirin with GI mucosa the risk of rebleeding maybe marginally higher with aspirin than clopidogrel. Hence in these patients Clopidogrel montherapy to reduce risk of ischemic events is recommended.(8)

2.In patient s with prior MI less than 1 yr and stable IHD with PCI less than 6 months, it is recommended to continue DAPT while shortening duration to 6 months(8).

Dual pathway inhibition:

Based on the results of COMPASS trial dual pathway inhibition in the form of combiningAaspirin with Rivoraxaban at 2.5mg BD has shown to reduce cardiovascular events in high risk patients like those with prior CAD ,renal disease and peripheral vascular disease.(36)

How to transistion between P2Y12 inhibitors

1. Less than one month of PCI,full loading dose of new P2y12 inhibitor is to be given 24 hrs after last doseof prior agent .But when transistioning from clopidogrel ,the loading dose of ticagrelor and prasugrel should be given immediately and not after 24 hrs
2. After 30 days of PCI,transistion can be done with maintainence dose started after last dose of prior agent.but when changing from ticagrelor,which has a short half life a full loading dose of clopidogrel or prasugrel should be given 24 hrs after last dose of ticagrelor
3. If transistioning from cangrelor, clopidogrel, prasugrel loading doses should be given after the infusion and ticagrelor prior to termination of infusion due to variation in binding site with ticagrelor(37,38)

Conclusions:

This article is a an attempt at presenting the fundamental understanding of action ,dosing and considerations in prescribing antiplatelet s in CAD and special situations.this is an evolving topic and further research is needed on grey zones which may be answered in future.

DISCLOURES:NONE

Acknowledgements :

I thank my colleague Dr Pavan M.D D.M for his timely inputs and my wife Dr Madhuri for her encouragement in the preparation of the article .I have faithfully indexed all the articles which I verified in preparing this manuscript .Any failure in mentioning a article should be viewed as oversight and not infringement. I shall be happy to correct myself in case of any errors pointed.

LIST OF ABBREVIATIONS COMMONLY USED IN ARTICLE.

NOTE: With regards to clinical trials readers are referred to bibliography for the full forms of trials

ACS-ACUTE CORONARY SYNDROME

NOACS-NEWER ORAL ANTICOAGULANTS

PCI-PERRCUTANEOUS CORONARY INTERVENTION

DAPT-DUAL ANTIPLATELET THERAPY

TAT-TRIPLE ANTIPLATELET THERAPY

RCT-RANDOMISED CONTROLLED TRIALS

OAC-ORAL ANTICOAGLANTS\

TXA2-THROMBOXANE A2

CTO-CHRONIC TOTAL OCCLUSION

CHF-CONGESTIVE HEART FAILURE

BIBILOGRAPHY

1. Epidemiological profile, management and outcomes of patients with acute coronary syndrome: Single centre experience from a tertiary care hospital in North India Yash Paul Sharma*, Krishna Santosh Vemuri, Dinakar Bootla, Kewal Kanabar, C.R. Pruthvi, Navjyot Kaur, Krishna Prasad Nevali, Prashant Panda, G. Kasinadhuni, Lipi Uppal, Soumitra Mohanty

2. Xavier D, Pais P, Devereaux PJ, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet. 2008;371:1435e1442 (London, England)

3. Negi PC, Merwaha R, Panday D, Chauhan V, Guleri R. Multicenter HP ACS registry. Indian Heart J. 2016;68:118e127

4. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. Nat New Biol. 1971; 231: 232–5.

5. Roth GJ, Stanford N, Majerus PW. Acetylation of prostaglandin synthase by aspirin. Proc Natl Acad Sci U S A. 1975; 72: 3073–6.

6. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet. 1988 Aug 13;2(8607):349-60. PMID: 2899772.

7. Hamberg M, Svensson J, Samuelsson B. Thromboxanes: a new group of biologically active compounds derived from prostaglandin endoperoxides. Proc Natl Acad Sci U S A.1975; 72: 2994–8.

8. Pickett SJ, Levine GN, Jneid H, Bhatt DL, Nambi V. Is There an Optimal Antiplatelet Strategy after Gastrointestinal Bleeding in Patients with Coronary Artery Disease? Cardiology. 2021;146(6):668-677. doi: 10.1159/000517051. Epub 2021 Sep 14. PMID: 34521081.

9. Savi P, Heilmann E, Nurden P, Laplace M-C,Bihour C, Kieffer G, et al. Clopidogrel: an antithrombotic drug acting on the ADP-dependent activation pathway of human platelets. Clin Appl Thromb Hemost. 1996; 2(1): 35–42

10. Wiviott SD, Antman EM, Braunwald E. Prasugrel. Circulation. 2010;122(4): 394–403. https://doi.org/10.1161/CIRCULATIONAHA.109.921502

11 Wallentin L, Varenhorst C, James S, et al. Prasugrel achieves greater and faster P2Y12receptor-mediated platelet inhibition than clopidogrel due to more efficient generation of its active metabolite in aspirin-treated patients with coronary artery disease. Eur Heart J. 2008;29(1):21–30. https://doi.org/10.1093/eurheartj/ehm545

12 Steinhubl SR, Berger PB, Mann III JT, et al. Early and sustained dual oralantiplatelet therapy following percutaneous coronary

intervention: a randomized controlled trial. JAMA. 2002;288(19):2411–2420. https://doi.org/10.1001/jama.288.19.2411

13 CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet. 1996 Nov 16;348(9038):1329-39. doi: 10.1016/s0140-6736(96)09457-3. PMID: 8918275.

14. Gerschutz GP, Bhatt DL. The CURE trial: using clopidogrel in acute coronary syndromes without ST-segment elevation. Cleve Clin J Med. 2002 May;69(5):377-8, 380, 382 passim. doi: 10.3949/ccjm.69.5.377. PMID: 12022381.

15. Mehta SR, Tanguay JF, Eikelboom JW, Jolly SS, Joyner CD, Granger CB, Faxon DP, Rupprecht HJ, Budaj A, Avezum A, Widimsky P, Steg PG, Bassand JP, Montalescot G, Macaya C, Di Pasquale G, Niemela K, Ajani AE, White HD, Chrolavicius S, Gao P, Fox KA, Yusuf S; CURRENT-OASIS 7 trial investigators. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. Lancet. 2010 Oct 9;376(9748):1233-43. doi: 10.1016/S0140-6736(10)61088-4. PMID: 20817281.

16. Frelinger AL 3rd, Michelson AD, Wiviott SD, Trenk D, Neumann FJ, Miller DL, Jakubowski JA, Costigan TM, McCabe CH, Antman EM, Braunwald E. Intrinsic platelet reactivity before P2Y12 blockade contributes to residual platelet reactivity despite high-level P2Y12 blockade by prasugrel or high-dose clopidogrel. Results from PRINCIPLE-TIMI 44. Thromb Haemost. 2011 Aug;106(2):219-26. doi: 10.1160/TH11-03-0185. Epub 2011 Jun 28. PMID: 21713327.

17. Wiviott SD, Antman EM, Gibson CM, Montalescot G, Riesmeyer J, Weerakkody G, Winters KJ, Warmke JW, McCabe CH, Braunwald E; TRITON-TIMI 38 Investigators. Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet InhibitioN with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38). Am Heart J. 2006 Oct;152(4):627-35. doi: 10.1016/j.ahj.2006.04.012. PMID: 16996826.

18. Mayer K, Bongiovanni D, Karschin V, Sibbing D, Angiolillo DJ, Schunkert H, Laugwitz KL, Schüpke S, Kastrati A, Bernlochner I. Ticagrelor or Prasugrel for Platelet Inhibition in Acute Coronary Syndrome Patients: The ISAR-REACT 5 Trial. J Am Coll Cardiol. 2020 Nov 24;76(21):2569-2571. doi: 10.1016/j.jacc.2020.09.586. PMID: 33213734.

19. Schnorbus B, Daiber A, Jurk K, et al. Effects of clopidogrel vs. prasugrel vs.ticagrelor on endothelial function, inflammatory parameters, and plateletfunction in patients with acute coronary syndrome undergoing coronary artery stenting: a randomized, blinded, parallel study. Eur Heart J. 2020;41(33): 3144–3152. https://doi.org/10.1093/eurheartj/ehz917

20. James SK, Roe MT, Cannon CP, Cornel JH, Horrow J, Husted S, Katus H, Morais J, Steg PG, Storey RF, Stevens S, Wallentin L, Harrington RA; PLATO Study Group. Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATelet inhibition and patient Outcomes (PLATO) trial. BMJ. 2011 Jun 17;342:d3527. doi: 10.1136/bmj.d3527. PMID: 21685437; PMCID: PMC3117310.

21. Marino M, Rizzotti D, Leonardi S. Cangrelor: review of the drug and the CHAMPION programme (including PHOENIX). Curr Cardiol Rep. 2014;16(6):493. doi: 10.1007/s11886-014-0493-4. PMID: 24879371.

22. Cavender MA, Harrington RA, Stone GW, Steg PG, Gibson CM, Hamm CW, Price MJ,

Lopes RD, Leonardi S, Deliargyris EN, Prats J, Mahaffey KW, White HD, Bhatt DL; CHAMPION PHOENIX Investigators*. Ischemic Events Occur Early in Patients Undergoing Percutaneous Coronary Intervention and Are Reduced With Cangrelor: Findings From CHAMPION PHOENIX. Circ Cardiovasc Interv. 2022 Jan;15(1):e010390. doi: 10.1161/CIRCINTERVENTIONS.120.010390. Epub 2021 Dec 17. PMID: 34915723; PMCID: PMC8765214.

23. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, Gilard M, Hinterbuchner L, Jankowska EA, Jüni P, Kimura T, Kunadian V, Leosdottir M, Lorusso R, Pedretti RFE, Rigopoulos AG, Rubini Gimenez M, Thiele H, Vranckx P, Wassmann S, Wenger NK, Ibanez B; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Aug 25:ehad191. doi: 10.1093/eurheartj/ehad191. Epub ahead of print. PMID: 37622654.

24. Alexander Thomas, Mauro Gitto, Samit Shah, Yuichi Saito, Daniela Tirziu, Alaide Chieffo, Giulio G. Stefanini, Alexandra J. Lansky,Antiplatelet Strategies Following PCI: A Review of Trials Informing Current and Future Therapies,Journal of the Society for Cardiovascular Angiography & Interventions,Volume 2, Issue 3,2023

25 **Moscucci M**, Fox KA, Cannon CP, Klein W, López-Sendón J, Montalescot G, White K, Goldberg RJ. Predictors of major bleeding in acute coronary syndromes: the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J* 2003; **24**: 1815-1823 [PMID: 14563340 DOI: 10.1016/s0195-668x(03)00485-8]

25. **Baber U**, Mehran R, Giustino G, Cohen DJ, Henry TD, Sartori S, Ariti C, Litherland C, Dangas G, Gibson CM, Krucoff MW, Moliterno DJ, Kirtane AJ, Stone GW, Colombo A, Chieffo A, Kini AS, Witzenbichler B, Weisz G, Steg PG, Pocock S. Coronary Thrombosis and Major Bleeding After PCI With Drug-Eluting Stents: Risk Scores From PARIS. *J Am Col Cardiol* 2016; **67**: 2224-2234 [PMID: 27079334 DOI: 10.1016/j.jacc.2016.02.064]

26. **Yeh RW**, Secemsky EA, Kereiakes DJ, Normand SL, Gershlick AH, Cohen DJ, Spertus JA, Steg PG, Cutlip DE, Rinaldi MJ, Camenzind E, Wijns W, Apruzzese PK, Song Y, Massaro JM, Mauri L; DAPT Study Investigators. Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. *JAMA* 2016; **315**: 1735-1749 [PMID: 27022822 DOI: 10.1001/jama.2016.3775]

27. **Costa F**, van Klaveren D, James S, Heg D, Räber L, Feres F, Pilgrim T, Hong MK, Kim HS, Colombo A, Steg PG, Zanchin T, Palmerini T, Wallentin L, Bhatt DL, Stone GW, Windecker S, Steyerberg EW, Valgimigli M; PRECISE-DAPT Study Investigators. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. *Lancet* 2017; **389**: 1025-1034 [PMID: 28290994 DOI: 10.1016/S0140-6736(17)30397-5]

28. Watanabe H, Morimoto T, Natsuaki M, Yamamoto K, Obayashi Y, Ogita M, Suwa S, Isawa T, Domei T, Yamaji K, Tatsushima S, Watanabe H, Ohya M, Tokuyama H, Tada T, Sakamoto H, Mori H, Suzuki H, Nishikura T, Wakabayashi K, Hibi K, Abe M, Kawai K, Nakao K, Ando K, Tanabe K, Ikari Y, Morino Y, Kadota K, Furukawa Y, Nakagawa Y, Kimura T; STOPDAPT-2 ACS Investigators. Comparison of Clopidogrel Monotherapy After 1 to 2 Months of Dual Antiplatelet Therapy With 12 Months of Dual Antiplatelet Therapy in Patients With Acute Coronary Syndrome: The STOPDAPT-2 ACS Randomized Clinical Trial. JAMA Cardiol. 2022 Apr 1;7(4):407-417. doi: 10.1001/

jamacardio.2021.5244. PMID: 35234821; PMCID: PMC8892373.

29. Frigoli E, Smits P, Vranckx P, Ozaki Y, Tijssen J, Jüni P, Morice MC, Onuma Y, Windecker S, Frenk A, Spaulding C, Chevalier B, Barbato E, Tonino P, Hildick-Smith D, Roffi M, Kornowski R, Schultz C, Lesiak M, Iñiguez A, Colombo A, Alasnag M, Mullasari A, James S, Stankovic G, Ong PJL, Rodriguez AE, Mahfoud F, Bartunek J, Moschovitis A, Laanmets P, Leonardi S, Heg D, Sunnåker M, Valgimigli M. Design and rationale of the Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen (MASTER DAPT) Study. Am Heart J. 2019 Mar;209:97-105. doi: 10.1016/j.ahj.2018.10.009. Epub 2018 Nov 22. PMID: 30703644.

30. Baber U, Dangas G, Cohen DJ, Gibson CM, Mehta SR, Angiolillo DJ, Pocock SJ, Krucoff MW, Kastrati A, Ohman EM, Steg PG, Badimon J, Zafar MU, Chandrasekhar J, Sartori S, Aquino M, Mehran R. Ticagrelor with aspirin or alone in high-risk patients after coronary intervention: Rationale and design of the TWILIGHT study. Am Heart J. 2016 Dec;182:125-134. doi: 10.1016/j.ahj.2016.09.006. Epub 2016 Sep 28. PMID: 27914492.

31. Sibbing D, Aradi D, Jacobshagen C, Gross L, Trenk D, Geisler T, Orban M, Hadamitzky M, Merkely B, Kiss RG, Komócsi A, Dézsi CA, Holdt L, Felix SB, Parma R, Klopotowski M, Schwinger RHG, Rieber J, Huber K, Neumann FJ, Koltowski L, Mehilli J, Huczek Z, Massberg S; TROPICAL-ACS Investigators. Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial. Lancet. 2017 Oct 14;390(10104):1747-1757. doi: 10.1016/S0140-6736(17)32155-4. Epub 20(17)32155-4

32. Claassens DMF, Vos GJA, Bergmeijer TO, et al. A genotype-guided strategy for oral P2Y12 inhibitors in primary PCI. N Engl J Med. 2019;381(17):1621–1631. https://doi.org/10.1056/NEJMoa190709617 Aug 28. PMID: 28855078.

33. Cuisset T, Deharo P, Quilici J, et al. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. Eur Heart J. 2017;38(41):3070–3078

34. Kim CJ, Park MW, Kim MC, et al. Unguided de-escalation from ticagrelor to clopidogrel in stabilised patients with acute myocardial infarction undergoing percutaneous coronary intervention (TALOS-AMI): an investigator-initiated, open-label, multicentre, non-inferiority, randomised trial. Lancet. 2021; 398(10308):1305–1316

35. Kim HS, Kang J, Hwang D, et al. Prasugrel-based de-escalation of dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (HOST-REDUCE-POLYTECH-ACS): an open-label, multicentre, noninferiority randomised trial. Lancet. 2020; 396 (10257): 1079–1089.

36. Steffel J, Eikelboom JW, Anand SS, Shestakovska O, Yusuf S, Fox KAA. The COMPASS Trial: Net Clinical Benefit of Low-Dose Rivaroxaban Plus Aspirin as Compared With Aspirin in Patients With Chronic Vascular Disease. Circulation. 2020 Jul 7;142(1):40-48

37. De Luca L, Steg PG, Bhatt DL, Capodanno D, Angiolillo DJ. Cangrelor: clinical data, contemporary use, and future perspectives. J Am Heart Assoc. 202110(13), e022125.

38. Franchi F, Rollini F, Rivas A, et al. Platelet inhibition with cangrelor and crushedticagrelor in patients with ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Circulation. 2019;139(14):1661–1670.

Fibrinolytic Strategy for ST-Segment– Elevation Myocardial Infarction

Dr. Omer Mustafa Hassan
Director, Interventional Cardiology
Allahabad Heart Centre, Prayagraj

Abstract

Thrombolysis revolutionized the treatment of acute ST elevation myocardial infarction in the latter part of the last century and has been in use for more than two decades. Use of thrombolytic therapy is widespread owing to its safety, efficacy, ease of use, and affordability. Thrombolytic therapy has several limitations, many of which have been overcome with the adoption of percutaneous coronary intervention techniques in recent years. Primary percutaneous intervention is currently the preferred form of reperfusion therapy in the management of ST elevation myocardial infarction. However, thrombolytic therapy continues to have a role in many situations even in this era of intervention.

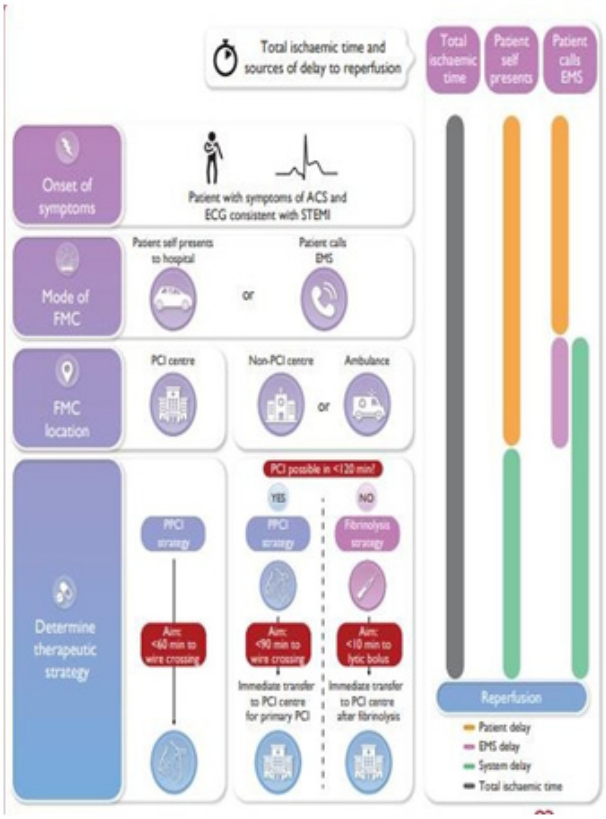
"A short distance from its origin, the left coronary artery was completely obstructed by a red thrombus that had formed at a point of great narrowing¦ The hope for the damaged myocardium lies in the direction of securing a supply of blood."

- James B Herrick. 1912

A cute myocardial infarction is usually due to disruption of an atherosclerotic plaque in a coronary artery followed by thrombus formation.1,2 The complete occlusion of the lumen of a major epicardial coronary artery leads to acute ST Elevation Myocardial Infarction (STEMI). Prompt, complete and sustained restoration of antegrade flow in the infarct related artery is essential to salvage the myocardium at risk, improve ventricular function and reduce short term morbidity and mortality.

There are two methods of achieving reperfusion of the myocardium at risk in acute STEMI. It is either by pharmacological therapy by using thrombolytic agents or by mechanical means by way of primary percutaneous coronary intervention (Primary PCI). Primary PCI has proved to be the superior, and therefore preferred, reperfusion strategy. Based on evidence, all major scientific organizations in their guidelines recommend Primary PCI as the reperfusion therapy of first choice for the management of acute STEMI.3-5 Consequently, the number of patients worldwide that receive Primary PCI for STEMI has been steadily increasing. However, Primary PCI has major logistic limitations of availability, accessibility and affordability.

STEMI – Management



Primary PCI for the treatment of acute STEMI in India is being practiced in several centers. However, availability of this treatment has been largely urban- centric and limited to the affordable and the insured. Thrombolytic therapy continues to be the most used management strategy for acute STEMI in our country and, indeed, in most parts of the world.

THROMBOLYTIC THERAPY IS BENEFICIAL

Since the time of De Wood and colleagues6who convincingly established the prevalence of total thrombotic coronary occlusion during the early hours of acute trans-mural myocardial infarction, reperfusion therapy has evolved, over the years, from intra-coronary thrombolysis to intravenous thrombolysis and now to mechanical reperfusion.

It was the Italian study in 1986 that established streptokinase as an effective thrombolytic agent when used intravenously.7 Thrombolytic therapy using streptokinase rapidly became the preferred strategy for the management of acute myocardial infarction.8 Many new thrombolytic agents were developed in due course to overcome some of the limitations of streptokinase like antigenicity, allergic reactions, and systemic fibrinogen depletion. These newer thrombolytic agents could be administered as a bolus as opposed to Streptokinase which needs to be administered as an infusion.

Thrombolytic Agents

Streptokinase:

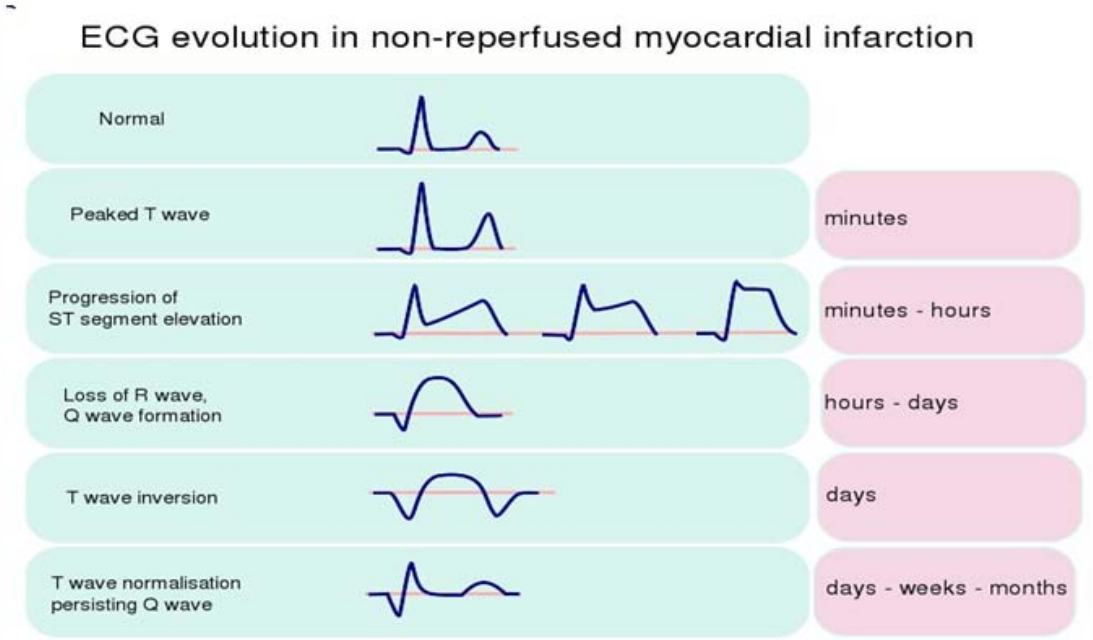
This was the first thrombolytic to be used in the management of STEMI, initially by the intracoronary route and subsequently as an intravenous infusion. Streptokinase is isolated from bacteria and hence is antigenic. It should not be reused in any patient for a second STEMI, since pre formed antibodies can neutralize the standard doses of streptokinase. Therefore, repeat thrombolysis, when required, should be carried out using a non - immunogenic agent.

Tissue Plasminogen Activator (t- PA, alteplase):

It is a non - antigenic, second generation thrombolytic and produces only mild systemic fibrinogen depletion. t-PA is administered in an accelerated dose regimen over 90 minutes. Modification of t-PA has led to the development of third generation thrombolytic agents like reteplase and tenecteplase, which have prolonged plasma clearance and could therefore be administered as a bolus.

Reteplase:

It is are combinant mutant form of t- PA. The GUSTO-III trial, which compared reteplase with t-PA in 15059 patients, did not demonstrate superiority of reteplase over or equivalence with



t-PA.9 However, many experts consider these two agents to be equivalent, and reteplase has the advantage of a 'double bolus' administration (10 + 10 units).

Tenecteplase:

It is a third generation thrombolytic, a mutant of t-PA, modified in such a way that it has decreased plasma clearance, increased fibrin specificity and reduced sensitivity to plasminogen activator inhibitor-1. ASSENT 2 compared single bolus tenecteplase with accelerated dose t-PA in 16,949 patients of STEMI.10 Tenecteplase proved to be equivalent to t- PA with respect to 30 day mortality and major bleeding. However, in patients who were treated after 4 hours of onset of symptoms, mortality rate was significantly less with tenecteplase as compared to t- PA (7.0 % with tenecteplase versus 9.2 % with t-PA, p = 0.018).

With the introduction of an indigenous preparation of tenecteplase in India, a number of Indian studies have established the safety and efficacy of tenecteplase in the treatment of Indian patients with STEMI.11,12

I'he Evidence foí I'híombolytic theíapy

When administered in appropriately selected patients early after the onset of acute STEMI, the benefits of thrombolytic therapy have been established beyond doubt. FTT collaborative study13 included in their analysis all trials that randomized at least 1000 patients of suspected MI. In all, 9 trials and 58,600 patients formed the study material. Major adverse events during hospitalization and deaths during the first five weeks after MI were analysed. Though there was an excess of death during days 0 - 1, especially amongst the elderly and those presenting after 12 hours, there was an abundantly clear overall benefit outweighing the "early hazard". The benefit was evident in patients with ST elevation and those with new onset LBBB, irrespective of age, gender, blood pressure, heart rate, prior MI and diabetes. The absolute mortality reduction was 30 per 1000 patients presenting within 0 - 6 hours and 20 per 1000 patients presenting between 7 and 12 hours. Beyond 12 hours, the benefit was uncertain.

So, the earlier the treatment is administered, greater is the benefit.

Alteplase is more fibrin-specific and non-antigenic, and mortality with accelerated infusion of alteplase was less when compared with streptokinase. Reteplase has ease of administration, but has no additional advantage over alteplase.9 Tenecteplase, which can be given as a single intravenous bolus was equivalent to accelerated t-PA and had significantly lower rate of non - cerebral hemorrhage.10 Tenecteplase was superior to t-PA in a subgroup of patients who were treated after a time window of 4 hours, mortality rate being 7.0% vs 9.2% in favour of tenecteplase.

In an observational registry from India,12 data of 6000 patients of STEMI receiving tenecteplase showed that thrombolysis was successful in 90.9%, the overall in-hospital mortality was 3.2% and the incidence of intracranial hemorrhage was 0.62%.

The earlier the thrombolytic therapy is administered, the more beneficial is the therapy. A meta - analysis of 22 studies showed a substantially larger mortality benefit in patients treated within 2 hours of onset of STEMI than in those treated later.14

Limitations of Thrombolysis

1. Contraindications

Despite the benefits of thrombolytic therapy and its ease of administration, there are a number of contraindications forbidding its use.15 TIMI 9 registry has shown that 10.3% of patients had contraindications for the use of thrombolytic therapy.16

The absolute contraindications are:

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischemic stroke in preceding 6 months
- Central nervous system trauma or neoplasms
- Recent major trauma / surgery / head injury within preceding 3 months

- Gastrointestinal bleeding within the last month • Known bleeding disorder
- Aortic dissection
- Non-compressible punctures (eg. Liver biopsy, lumbar puncture)
- The relative contraindications are:
- Transient ischemic attack in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week postpartum
- Uncontrolled hypertension (BP > 180/110 mmHg)
- Advanced liver disease • Infective endocarditis
- Peptic ulcer
- Refractory resuscitation

2. Elderly population

There is an increase in mortality rate as the age increases.17 More evidence and clearer guidelines are required for thrombolytic therapy in patients of STEMI who are 85 years or older.

A scientific statement from the American Heart Association council for clinical cardiology18 summarized the thrombolytic treatment for the elderly STEMI population as follows:

i. Thrombolytic therapy as compared to no reperfusion therapy offers mortality benefit (that includes treatment-related deaths due to intra- cranial haemorrhage, stroke, shock and myocardial rupture) in the elderly population up to the age of 85 years

ii. Nonfatal strokes are rare (less than 3%) even amongst the subjects 85 years or older

iii. Reduced dosing of unfractionated heparin or adjusted doses of low molecular weight heparin minimize the risks of bleeding

iv. The risk of thrombolytic therapy in subjects 85 years or older remains high and more data is needed for clear guidelines

3. Time Sensitivity

Time sensitivity of thrombolytic therapy is well established. The earlier the treatment is instituted the greater is the benefit. In a meta-analysis of 22 trials comprising of 50,246 patients, the relationship between time delay in thrombolytic therapy and short term outcome in the form of 35 - day mortality was analysed. The results of thrombolytic therapy were substantially superior in patients presenting within 2 hours of onset of symptoms as compared to those presenting later.14 Thrombolytic therapy is more "time sensitive" as compared to primary PCI.

4. Bleeding

Hemorrhage is another important issue with thrombolytic therapy. Intracranial bleed is seen in 0.9 to 1.0 % of the total population studied.9,10 Major non-cerebral bleed occurs in 4 to 13% of patients treated with thrombolytics.10,19 The significant predictors of intracranial hemorrhage are old age, lower body weight, female gender, prior cerebrovascular disease and hypertension on admission.20

5. Infarct Related Artery Patency

The issue of "Illusion of reperfusion" has often been raised (Figure 1). The 90 - minute patency rates vary from 50% with streptokinase to 75% with newer thrombolytics, whereas TIMI grade 3 flow correspondingly is seen in only 32% to 63% of those treated. It is also clear that a patent epicardial coronary artery does not always mean effective tissue perfusion. Even with a patent coronary artery, there may be a decline in the benefit due to insufficient recanalization, TIMI grade 2 flow, residual stenosis, poor tissue perfusion, subsequent re-occlusion and reperfusion injury.21

6. Re-infarction and Recurrent Ischemia

Following thrombolytic therapy, there is a pro- thrombotic period. Re- occlusion rate

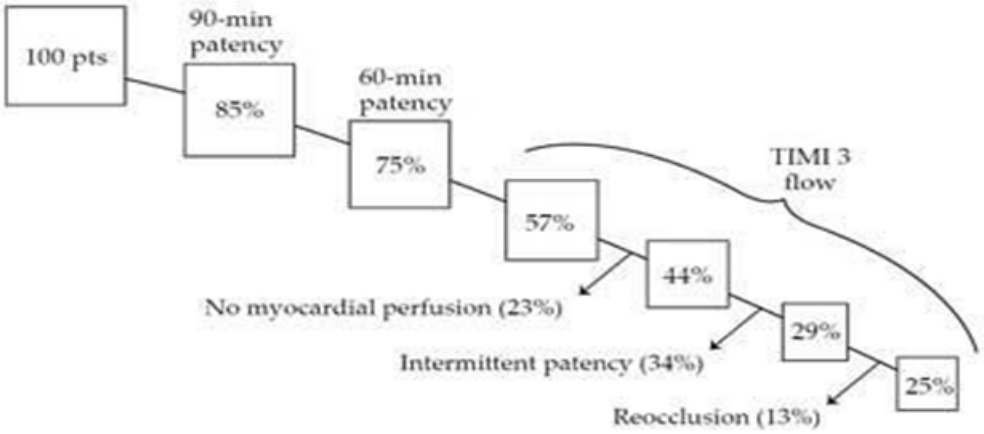


Fig. 1[21] : Infarct related artery patency

of the infarct related artery may be as high as 10% in hospital, and up to 30% by 3 months.22 Re-infarction rates have been reported to be around 5% in hospital and 7% within the first year of thrombolysis. Advances in adjunctive antiplatelet and anticoagulant therapies and close follow up have been able to overcome many of these problems.

Adjunctive anti thrombotic therapy is indicated to increase the efficacy of thrombolysis and also minimise the risk of re occlusion.23 The benefit of Aspirin in the management of STEMI is long established and is unequivocal.24 The CLARITY TIMI 28 as well as the COMMIT trials demonstrated the benefit of adding clopidogrel to aspirin and thrombolytic therapy.25,26 Heparin has long been used in the treatment of STEMI in association with thrombolysis, and has been shown to improve coronary patency following thrombolysis with tPA. The low molecular weight heparin, enoxaparin, has substantial evidence in its favour for its use in the treatment of STEMI.27-29 Newer agents like Fondaparinux have also improved patient outcomes by preventing deaths and re infarction, especially in those that receive Streptokinase.30 These adjunctive therapies have further enhanced the benefits of thrombolytic therapy.

Thrombolysis vs Primary PCI

Over the last several years, the field of Interventional Cardiology has demonstrated the superiority of primary PCI over thrombolytic therapy in the management of acute STEMI.

Benefits Coronary flow restoration is achieved in a higher number of patients with primary PCI as compared to thrombolytic therapy. Widimsky et al31 and Anderson et al32 have shown that while primary PCI restores coronary flow in 90% of patients of acute STEMI, it is seen in only 40-60% of patients treated with thrombolytic therapy. A quantitative review of 23 randomised trials clearly demonstrated a significant mortality benefit with primary PCI (5%) when compared with thrombolytic therapy(7%).

LimitationsLack of primary PCI facility and capability in majority of centres globally in general and in India in particular is a major drawback. It is also a more expensive therapeutic strategy, which many in our country can ill afford. Due to infrastructural constraints, many centres may not have PCI facility available round the clock, and some centres may not be achieving the ideal door to balloon time or first medical contact to balloon time. Another major impediment would be the distance to travel from non-PCI capable centre to PCI-capable centre. Streamlined STEMI care and medical networking in the health care system are yet to catch the imagination our health care authorities, especially in our country.Data from

CREATE registry from India34 gives an insight into the role of reperfusion therapies in STEMI in India. In a study population of 20,468 patients who had a definitive diagnosis of acute coronary syndrome, the median time from symptom onset to hospitalisation was 360 minutes; of patients who had STEMI, 58.5% received thrombolytic therapy and 15.3% received primary PCI. 72.1% of patients came from lower middle class and poor class.

Current Scope of Thrombolysis

Considering the relative advantages and disadvantages of thrombolysis and Primary PCI, one has to individualize the choice of therapy of each patient. The following need to be borne in mind while considering the option of thrombolytic therapy in any patient.

1. Thrombolytic therapy is beneficial, easily accessible and affordable. Even in the elderly, thrombolysis is clearly better than no treatment.
2. Thrombolytic agents can be administered as a bolus.
3. When transfer delay is a problem, thrombolysis is a good option. In such situations, how quickly the reperfusion therapy is delivered is more important than which reperfusion therapy is offered.
4. Primary PCI has constraints in terms of cost, availability, accessibility and expertise while at the same time delivering better patient outcomes.

What do the Guidelines Say?

Guidelines for managing patients with STEMI are available from various professional bodies, notably from the American College of Cardiology / American Heart Association (ACC / AHA),4 the European Society of Cardiology (ESC),5 and the Association of Physicians of India (API)3

Guidelines from Association of Physicians of India lay down the indications for thrombolytic therapy in STEMI as follows:

1. Early presentation (3 hours or less from symptom onset and there is a delay in invasive therapy)
2. Invasive strategy is not an option:
   - Catheterization laboratory not available / occupied.
   - Financial reasons
   - Lack of access to a skilled PCI laboratory
   - Vascular access difficulties
3. Delay to invasive strategy
   - Prolonged transport: (door to balloon) (door to needle) time is >1 hr
   - Medical contact to balloon or door to balloon time is > 90 minutes

ACC/AHA Guidelines (2007 STEMI Focused update recommendations) are as below:

Class I Recommendations are:

1. STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 minutes of first medical contact as a systems goal. (Level of Evidence: A)
2. STEMI patients presenting to a hospital without PCI capability and who cannot be transferred to a PCI center and undergo PCI within 90 minutes of first medical contact should be treated with thrombolytic therapy within 30 minutes of hospital presentation as a systems goal unless thrombolytic therapy is contraindicated. (Level of Evidence: B)

ESC Guidelines state the following for thrombolytic therapy in patients with STEMI:

Thrombolytic therapy should be used in the absence of contraindications and if primary PCI cannot be performed within the recommended time (I A)

A fibrin-specific agent should be given (I B)

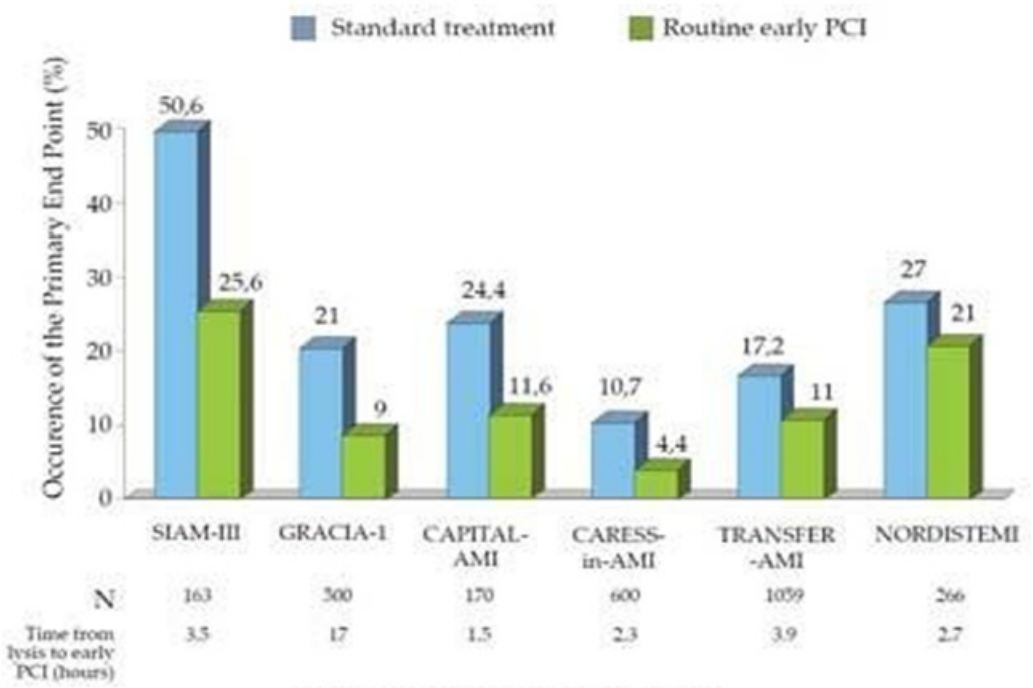


Fig. 2[44] : Fibrinolysis vs PCI

Recommendations for reperfusion therapy and timing of invasive strategy

Recommendations	Class[a]	Level[b]
Recommendations for reperfusion therapy for patients with STEMI		
Reperfusion therapy is recommended in all patients with a working diagnosis of STEMI (persistent ST-segment elevation or equivalents[c]) and symptoms of ischaemia of ≤12 h duration.[51,182]	I	A
A PPCI strategy is recommended over fibrinolysis if the anticipated time from diagnosis to PCI is <120 min.[52,218,219]	I	A
If timely PPCI (<120 min) cannot be performed in patients with a working diagnosis of STEMI, fibrinolytic therapy is recommended within 12 h of symptom onset in patients without contraindications.[176,183]	I	A
Rescue PCI is recommended for failed fibrinolysis (i.e. ST-segment resolution <50% within 60–90 min of fibrinolytic administration) or in the presence of haemodynamic or electrical instability, worsening ischaemia, or persistent chest pain.[184,185]	I	A
In patients with a working diagnosis of STEMI and a time from symptom onset >12 h, a PPCI strategy is recommended in the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias.[220]	I	C
A routine PPCI strategy should be considered in STEMI patients presenting late (12–48 h) after symptom onset.[189–191,221]	IIa	B
Routine PCI of an occluded IRA is not recommended in STEMI patients presenting >48 h after symptom onset and without persistent symptoms.[189,192,193]	III	A

Pre-hospital initiation of thrombolytic therapy (IIa A)

These guidelines clearly state that "The emphasis on primary PCI should not obscure the importance of thrombolytic therapy." The critical factor in reducing morbidity and mortality is the time to treatment from onset of symptoms of STEMI.

Many centres treating STEMI in our country and also globally do not have PCI capability and many interventional cardiology centres do not meet the time goal for primary PCI. Thrombolytic therapy is preferred under these circumstances.

Innovations in Thrombolytic Therapy

There are two well-defined areas where thrombolytic therapy may continue to have a prominent place.

A. Píe - hospital >híombolysis

B. Phaímaco-invasive theíapy.

Pre - hospital Thrombolysis:

Since "time is muscle and muscle is life", it is logical to raise the issue of the role of pre-hospital thrombolysis. Several registries, post-hoc analyses, randomized control trials and meta- analysis have shown that pre-hospital thrombolysis is feasible and clinically useful in improving the outcome of patients with STEMI.One study involving more than 6000 patients showed that pre-hospital thrombolysis as compared to in-hospital thrombolysis was associated with a significant 17% reduction in early mortality. A meta-analysis of 22 trials highlighted the larger mortality reduction in patients treated within 2 hrs of onset of symptoms than in those treated later.A 5-yr follow up of CAPTIM trial concluded that mortality is similar for primary PCI as compared to the use of a policy of pre - hospital thrombolysis followed by transfer to a PCI capable centre. It also showed that patients treated within 2 hrs of symptoms had a lower 5-year mortality with pre-hospitalthrombolysis.

Pharmaco-Invasive Therapy

We also need to overcome another limitation of the thrombolytic therapy, and that is "reocclusion" of the infarct related artery leading to re-infarction and poor outcome.The re-occlusion rate following thrombolysis is 10 % in-hospital and 30 % during the first year. Apart from the adjunctive therapy with anti-platelets and anti- thrombotics.A routine PCI after 3 hours and before 24 hours is an attractive option.5 In CARESS trial,37 a more conservative strategy (i.e. angiogram only in cases of failed thrombolysis) was associated with a worse clinical outcome than the strategy of angiogram and intervention (if indicated) in all cases following thrombolysis (the pharmaco - invasive strategy).

TRANSFER AMI study38 showed that patients coming to non-PCI centres when transferred for PCI within 6 hours of thrombolysis had fewer ischemic complications than those patients receiving standard treatment(i.e. rescue PCI or delayed angiography). A meta-analysis demonstrated significant mortality benefit at 30 days and one year with early transfer of patients for PCI subsequent to thrombolysis as compared to ischemia guided intervention.39

NORDISTEMI trial40 also showed a significant reduction in the composite of death, re-infarction, stroke or recurrent ischemia at one year in the group of patients undergoing immediate transfer and PCI following thrombolysis as compared to those in the conservative treatment arm.

Conclusion

Thrombolytic therapy will continue to have a major role in the management of STEMI patients for many years to come. Where Primary PCI facilities are not available or time delay to PCI is expected to be too long, thrombolytic therapy should be offered promptly. After thrombolysis, whether pre or in - hospital, the patient should be transferred to a PCI facility immediately. A system for STEMI care with networking of centres and streamlining of procedures should evolve to enable optimal management of patients with STEMI.

References

1. Falk E, Shah PK, Fuster V. Coronary plaque disruption. Circulation 1995;92:657 671.

2. Antman EM and Braunwald E. ST elevation myocardial infarction: Pathology, Pathophysiology and Clinical Features in Braunwald's Heart Disease A textbook of Cardiovascular Medicine. 8th Edition, Published by Elsevier 2008;1210.

3. Sharma S et al. API expert consensus document on management of ischemic heart disease. JAPI 2006;54:469-480.

4. Antman et al 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial InfarctionJ. Am. Coll. Cardiol 2008;51;210-247.

5. Van de Werf F, Bax J, Betriu A, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008;29:2909 2945.

6. DeWood MA, Spores J, Notske R, Mouser LT, Burroughs R, Golden MS, Lang HT. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980;303:897 902.

7. GruppoItaliano per lo Studio dellaStreptochinasinell'InfartoMiocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986;1:397 402.

8. Laffel GL, Braunwald E. Thrombolytic therapy. A new strategy for the treatment of acute myocardial infarction. N Engl J Med 1984;311:710 7.

9. The Global Use of Strategies to Open Occluded Coronary Arteries GUSTO III Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. N Engl J Med 1997;337:1118-1123.

10. Assessment of the safety and efficacy of a New Thrombolytic Investigators. Single bolus tenecteplase compared with front loaded alteplase in acute myocardial infarction: the ASSENT- 2 double blind randomized trial. Lancet 1999;354:716-722

11. Sathyamurthi I, Srinivasan KN, Jayanthi K et al. Efficacy and safety of tenecteplase in Indian patients with STEMI. Indian Heart J 2008;60:554-557 12.Iyengar SS, Nair T, Sathyamurthi et al. Efficacy and safety of tenecteplase in STEMI patients from ELAXIM Indian Registry. Indian Heart J 2009;61:480-481.

13. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet 1994;19;343:742.

14. BoresmaE, Mass ACP, Decker JW and Simon ML. Early thrombolytic therapy in acute myocardial infarction. Lancet 1996;348:771-775

15. Van de Werf F et al Management of acute myocardial infarction in patients presenting with persistent ST elevation. Eur Heart J 2008;29:2909 2945.

16. Cannon CP, Bahit M, Haugland JM, et al. Under utilization of evidence based medications in acute ST elevation myocardial infarction. Results of the TIMI 9 registry. Crit Pathways Cardiol 2002;I;44-52

17. Kunadian V, Michael Gibson C. Thrombolytics and Myocardial Infarction. Cardiovascular Therapeutics. 29:no.doi: 10.1111/j.1755 5922.2010.00239.x

18. Alexander et al. Acute coronary care in the elderly, Part II. ST segment elevation myocardial infarction. A scientific statement for healthcare professionals from American Heart Association Council on clinical cardiology. Circulation 2007;115:2570-89

19. Berkowitz SD, Granger CB, Pieper KS et al. Incidence and predictors of bleeding after contemporary thrombolytic therapy for myocardial infarction. The Global Utilization of Streptokinase and Tissue Plasminogen activator for Occluded coronary arteries (GUSTO) I Investigators. Circulation 1997;95:2508 2516.

20. Gore JM, Granger CB, Simoons ML et al. Stroke after thrombolysis. Mortality and functional outcomes in the GUSTO-I trial. Global Use of Strategies to Open Occluded Coronary Arteries. Circulation 1995;92:2811 2818.

21. Lincoff AM and Topol EJ. Illusion of reperfusion. Does anyone achieve optimal reperfusion during acute myocardial infarction? Circulation 1993;88:1361-1374

22. Antman E M, Braunwald E. Acute Myocardial Infarction. In Heart Disease.

Braunwald, Zipes, Libby ed. 6th Ed. W B Saunders Company. Page 1150 23.De Luca G, Marino P. Advances in antithrombotic therapy as adjunct to reperfusion therapies for ST segment elevation myocardial infarction. Thromb Haemost 2008;100:184 195.

24. ISIS-2 Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988;2:349 360

25. Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med 2005;352:1179 1189.

26. Chen ZM, Jiang LX, Chen YP, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo- controlled trial. Lancet 2005;366:1607 1621.

27. ASSENT-3 Investigators. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. Lancet 2001;358:605 613.

28. Antman EM, Morrow DA, McCabe CH, et al. Enoxaparin versus unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction. N Engl J Med 2006;354:1477 1488.

29. Sabatine MS, Morrow DA, Dalby A, et al. Efficacy and safety of enoxaparin versus unfractionated heparin in patients with ST-segment elevation myocardial infarction also treated with clopidogrel. J Am CollCardiol 2007;49:2256 2263.

30. Yusuf S, Mehta SR, Chrolavicius S, et al. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. J Am Med Assoc 2006;295:1519 1530.

31. Widimsky P, Budesinsky T, Vorac D, et al. Long distance transport for primary angioplasty vs immediate fibrinolysis in acute myocardial infarction. Final results of the randomized national multicentre trial-PRAGUE-2. Eur Heart J 2003;24:94 104.

32. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003;349:733 742.

33. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous fibrinolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003;361:13 20.

34. Xavier D, Pais P, Devereaux PJ, et al. Treatment and Outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet 2008;371:1435-42

35. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta- analysis. JAMA 2000;283:2686 2692.

36. Bonnefoy E, Steg PG, Boutitie F et al. Comparison of primary angioplasty and prehospital fibrinolysis in acute myocardial infarction (CAPTIM). Euro Heart J 2009;30:1598-1606

37. Di Mario C, Dudek D, Piscione F, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the CARESS in AMI study: An open, prospective, randomized, multicentre trial. Lancet 2008;371:559-568

38. Cantor WJ, Fitchett D, Borgundvaag, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. New Engl J Med 2009;360:2705- 2718

39. Wijeysundera HC, You JJ, Nallamothu BK et al. An early invasive strategy versus ischemia guided management after fibrinolytic therapy for ST segment elevation myocardial infarction: A meta analysis of contemporary randomized controlled trials. Am Heart J 2008;156:564-572

40. Bohmer E, Hoffmann P, Abdelnoor M, et al. Efficacy and safety of immediate angioplasty versus ischemia guided management after thrombolysis in in acute myocardial infarction in areas with very long transfer distances results of the NORDISTEMI. J Am CollCardiol 2010;55:102-110

41. Sezer M, Oflaz H, Goren T, et al. Intracoronary streptokinase after primary percutaneous coronary intervention. N Engl J Med 2007;356:1823-34

42. Sezer M, à‡imen A, Aslanger E, et al. Effect of Intracoronary Streptokinase Administered Immediately After Primary Percutaneous Coronary Intervention on Long-Term Left Ventricular Infarct Size, Volumes, and Function. J Am CollCardiol 2009;54:1065 71

43. Kelly RV, Crouch E, Krumnacher H, et al. Safety of adjunctive intracoronary thrombolytic therapy during complex percutaneous coronary intervention: initial experience with intracoronary tenecteplase. Catheter CardiovascInterv 2005;66:327-32.

44. Halvorsen H, Huber K. The role of fibrinolysis in the era of primary percutaneous coronary intervention. ThrombHaemost 2011:105:390-395.

Role of Anticoagulants and GpIIb/IIIa in Acute Coronary Syndrome

Prof Dr Satyanarayan Routray
DM Cardiology
Dr Sradhananda Rout
Senior Resident , Cardiology

In this modern day of diabetes and hypertension pandemics, epidemic of Acute Coronary Syndrome (ACS) is hammering on the limited resources of a developing nation like INDIA. Acute coronary syndrome (ACS) consists of unstable angina (UA), non–ST- segment elevation myocardial infarction (NSTEMI) and ST- segment elevation MI (STEMI) . The 12- lead electrocardiogram (ECG) distinguishes patients from STEMI and NSTEMI-ACS. Besides reliving pain and symptoms, pharmacological anticoagulation and anti platelet therapy forms the backbone of ACS Management.

Anticoagulant and Antiplatelet Therapy

Anticoagulant Therapy

Immediate Anticoagulant therapy institution to patients with ACS serves the purpose of

1. Establishing and maintaining patency of the infarct- related artery
2. preventing deep venous thrombosis
3. preventing pulmonary embolism
4. ventricular thrombus formation
5. cerebral embolization
6. Favourable myocardial remodelling
7. Decreasing major adverse cardiac events(MACE)

Anticoagulants commonly used in ACS[1, 2]

1. Unfractionated Heparin(UFH)
2. Low- molecular- weight heparins/ Enoxaparin (LMWHs)
3. Hirudin and Bivalirudin (Direct Thrombin Inhibitors)
4. Parenteral Factor Xa Antagonists(Fondaparinux)

The following figure-1 from European society of cardiology(ESC) 2023 ESC Guidelines for the management of acute coronary syndromes provides fundamental pharmacological anticoagulation approach in different ACS :

Unfractionated heparin(UFH)

Unfractionated Heparin(UFH) is the choice of anticoagulant in patients with STEMI undergoing Primary Percutaneous coronary intervention(PPCI) due to mountains of evidence and favourable risk/ benefit profile. The most recent recommendations of Unfractionated Heparin(UFH) as per European

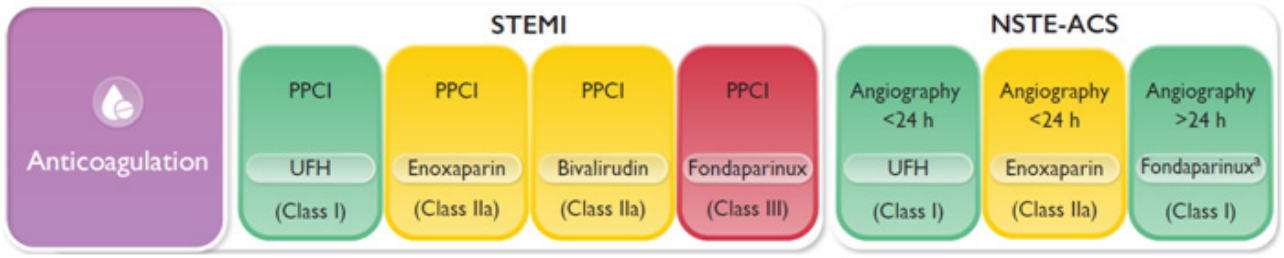


Figure – 1 - [1]Byrne RA, Rossello X, Coughlan JJ, Barbato E et al. ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Aug 25. Primary Percutaneous coronary intervention(PPCI)

Society of Cardiology (ESC) [figure -2] and American Heart Association (AHA)[figure – 3] are given below :

One of the standard regimens of an IV UFH bolus is of 60 units/kg to a maximum of 4000 units, followed by an initial infusion at 12 units/kg/hr to a maximum of 1000 units/hr for 48 hours, adjusted to maintain the APTT at 1.5 to 2 times control (approximately 50 to 70 seconds), is effective in patients receiving fibrinolytic therapy for STEMI.[11]

In patients with NSTE-ACS who are anticipated to undergo immediate or early (i.e. <24 h from the time of diagnosis) invasive angiography and PCI if indicated, parenteral anticoagulation at the time of diagnosis is recommended, and UFH has been historically established as the anticoagulant of choice.[11]

Anticoagulant therapy		
Parenteral anticoagulation is recommended for all patients with ACS at the time of diagnosis.[255,296]	I	A
Routine use of a UFH bolus (weight-adjusted i.v. bolus during PCI of 70–100 IU/kg) is recommended in patients undergoing PCI.	I	C
Intravenous enoxaparin at the time of PCI should be considered in patients pre-treated with subcutaneous enoxaparin.[256,261,297]	IIa	B
Discontinuation of parenteral anticoagulation should be considered immediately after an invasive procedure.	IIa	C
Patients with STEMI		
Enoxaparin should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.[258,261,298]	IIa	A
Bivalirudin with a full-dose post PCI infusion should be considered as an alternative to UFH in patients with STEMI undergoing PPCI.[259,299,300–303]	IIa	A
Fondaparinux is not recommended in patients with STEMI undergoing PPCI.[260]	III	B
Patients with NSTE-ACS		
For patients with NSTE-ACS in whom early invasive angiography (i.e. within 24 h) is not anticipated, fondaparinux is recommended.[262,304]	I	B
For patients with NSTE-ACS in whom early invasive angiography (i.e. within 24 h) is anticipated, enoxaparin should be considered as an alternative to UFH.[256]	IIa	B

Figure-2- [1]Byrne RA, Rossello X, Coughlan JJ, Barbato E et al. ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Aug 25

Complications/Disadvantages of Unfractionated Heparin (UFH)

The most serious complication of any anticoagulant therapy is bleeding especially intracranial hemorrhage. Major hemorrhagic events occur more frequently in patients with low body weight, advanced age, female sex, marked prolongation of the activated partial thromboplastin time (APTT) (>90 to 100 seconds), and performance of invasive procedures.[3] Frequent monitoring of the APTT reduces the risk for major hemorrhagic complications in patients treated with heparin. During the first 12 hours after fibrinolytic therapy, however, the APTT may be elevated as a result of the fibrinolytic agent alone (particularly if streptokinase is administered), thus making it difficult to interpret accurately the effects of a heparin infusion on the patient's coagulation status.

Potential disadvantages of unfractionated heparin (UFH) include dependency on antithrombin III for inhibition of thrombin activity, sensitivity to platelet factor 4, inability to inhibit clot- bound thrombin, marked interpatient variability in therapeutic response, and the need for frequent monitoring of the APTT.

Heparin Induced thrombocytopenia is not uncommon with UFH.

Low- Molecular- Weight Heparins(LMWHs)

Advantages of low-molecular- weight heparins (LMWHs) include a stable, reliable anticoagulant effect, high bioavailability permitting administration via the subcutaneous (SC) route, and a high anti- Xa/anti- IIa ratio producing blockade of the coagulation cascade in an upstream location and greatly reducing thrombin generation. The ATOLL (STEMI Treated With Primary Angioplasty and Intravenous Lovenox or Unfractionated Heparin) trial reported a reduction in the primary endpoint at 30 days (incidence of death, complication of MI, procedure failure, or major bleeding) with enoxaparin in comparison to UFH in patients with STEMI undergoing PPCI.[4]

Recommendations for Heparin, Low-Molecular-Weight Heparin, and Bivalirudin in Patients Undergoing PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 35.

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients undergoing PCI, administration of intravenous unfractionated heparin (UFH) is useful to reduce ischemic events.
1	C-LD	2. In patients with heparin-induced thrombocytopenia undergoing PCI, bivalirudin or argatroban should be used to replace UFH to avoid thrombotic complications (1,2).
2b	A	3. In patients undergoing PCI, bivalirudin may be a reasonable alternative to UFH to reduce bleeding (3-12).
2b	B-R	4. In patients treated with upstream subcutaneous enoxaparin for unstable angina or NSTE-ACS, the use of intravenous enoxaparin may be considered at the time of PCI to reduce ischemic events (13-17).
3: Harm	B-R	5. In patients on therapeutic subcutaneous enoxaparin, in whom the last dose was administered within 12 hours of PCI, UFH should not be used for PCI and may increase bleeding (14,18,19).

Figure- 3 - [2]Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 Jan 18;79(2):e21-e129. doi: 10.1016/j.jacc.2021.09.006. Epub 2021 Dec 9. Erratum in: J Am Coll Cardiol. 2022 Apr 19;79(15):1547. PMID: 34895950.

In a meta-analysis of trials comparing UFH with enoxaparin, mortality and major bleeding was not different between both agents in patients with NSTE-ACS or stable patients scheduled for PCI.[5] Therefore, enoxaparin should be considered as an alternative to UFH in these patients (especially in cases where monitoring of clotting times is complex).

In the ASSENT (Assessment of the Safety and Efficacy of a New Thrombolytic) 3 trial, enoxaparin (30- mg IV bolus, followed by SC injections of 1 mg/kg every 12 hours until discharge from the hospital) reduced 30- day mortality, in- hospital reinfarction, or in- hospital refractory ischemia compared with UFH (RR, 0.74; 95% CI 0.63 to 0.87) in STEMI patients .[6] The rate of intracranial hemorrhage was similar with UFH and enoxaparin (0.93% versus 0.88%; *P* = 0.98). In the ExTRACT-TIMI 25 (Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment–Thrombolysis in Myocardial Infarction 25) trial, a strategy of enoxaparin administered for the duration of the index hospitalization was superior to the conventional antithrombin strategy of UFH administration for 48 hours after fibrinolysis, with a 33% reduction (*P* = 0.001) in reinfarction and a nonsignificant favorable trend on overall mortality (*P* = 0.11). This improvement in recurrent MI was balanced by an increase in the incidence of major bleeding (1.4% and 2.1%, *P* = 0.001). In a meta- analysis of trials of LMWH versus UFH, LMWH clearly reduced recurrent MI but with a pattern of increased bleeding. [6]

Most recent AHA/ESC guidelines on LMWHs are given in the table above . [1,2]

Hirudin and Bivalirudin (Direct Thrombin Inhibitors)

In patients undergoing fibrinolysis, direct thrombin inhibitors such as hirudin or bivalirudin reduce the incidence of recurrent MI by 25% to 30% compared with heparin. In the Bivalirudin with prolonged full-dose Infusion during primary PCI versus Heparin Trial 4 (**BRIGHT-4**), 6016 patients with STEMI undergoing PPCI were randomized to either bivalirudin (with a full dose post-PCI infusion) or UFH.[7] The primary endpoint (a composite of all-cause mortality or Bleeding Academic Research Consortium [BARC] type 3–5 bleeding at 30 days), the individual components of the primary endpoint, and definite or probable stent thrombosis were all significantly reduced in the

bivalirudin group. [7] Based on the totality of the available data, bivalirudin with a full-dose post-PCI infusion should be considered as an alternative to UFH, although further studies to confirm these findings in non-East Asian populations are required. Bivalirudin is also the recommended alternative to UFH in patients presenting with ACS who have a history of heparin-induced thrombocytopaenia. [7]

When administered for a short period as an adjunct to primary PCI in the **HORIZONS- AMI** (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial, bivalirudin (open label), versus heparin plus glycoprotein (GP) IIb/IIIa inhibitors, reduced the 30- day rate of major bleeding or major adverse CV events, including death, reinfarction, target vessel revascularization for ischemia, and stroke (RR, 0.76; 95% CI 0.63 to 0.92; *P* = 0.005), driven by a significant 40% reduction in major bleeding. Treatment with bivalirudin significantly reduced mortality at 30 days and at 1 year but increased the early risk for stent thrombosis.[8]

In the EUROMAX (European Ambulance Acute Coronary Syndrome Angiography) trial, when started during transport for primary PCI in STEMI, bivalirudin reduced the primary outcome of death or major bleeding compared to heparin with optional GP IIb/IIIa, with a reduction in major bleeding but increase in stent thrombosis.[8]

Most recent AHA/ESC guidelines on Direct Thrombin Inhibitors are given in the table above . [1,2]

Parenteral Factor Xa Antagonists (Fondaparinux)

Based on the results of the OASIS-6 (The Safety and Efficacy of Fondaparinux Versus Control Therapy in Patients With ST Segment Elevation Acute Myocardial Infarction) trial, fondaparinux is not recommended in patients with STEMI undergoing PPCI.[9] NSTE-ACS patients who do not undergo early invasive angiography (i.e. within 24 h of diagnosis) will have an extended initial treatment phase consisting of only pharmacological treatment. In these patients, fondaparinux therapy is recommended in preference to enoxaparin while awaiting invasive angiography, based on the favourable outcomes demonstrated with fondaparinux in comparison to enoxaparin in the Fifth Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS-5) trial.[10] Of note, guiding catheter thrombus formation was of concern with fondaparinux and, therefore, a full-dose bolus of UFH should be given if the patient proceeds to PCI.

Most recent AHA/ESC guidelines on Fondaparinux are given in the table above . [1,2]

Anticoagulation With Fibrinolysis.

Both the ExTRACT- TIMI 25 and the OASIS- 6 trials indicated that prolonged administration of an anticoagulant for the duration of hospitalization is beneficial compared with the previous practice of administering UFH only for 48 hours unless clear-cut indications for discontinuing anticoagulation were present. Accordingly, patients managed with pharmacologic reperfusion therapy should receive anticoagulant therapy for a minimum of 48 hours and preferably for the duration of hospitalization after STEMI, up to 8 days. Enoxaparin is preferred when the administration of an anticoagulant for longer than 48 hours is planned in patients with STEMI treated with a fibrinolytic. Enoxaparin should be administered according to age, weight, and creatinine clearance and be given as an IV bolus, followed in 15 minutes by SC injection for the duration of the index hospitalization, up to 8 days or until revascularization.[11]

Antiplatelet Therapy(GP IIb/IIIa inhibitors)

Platelets play a major role in pathogenesis of ACS. So its timely inhibition is of utmost significance. In the coagulation cascade, glycoprotein receptors have two subunits, α, and β, which are responsible for platelet aggregation and adhesion. They are present on the platelet plasma membrane and undergo a conformational change upon platelet activation, allowing them to adhere to each other. Glycoprotein IIb/IIIa receptor inhibitors are direct acting antiplatelet agents targeting the glycoprotein IIb/ IIIa platelet receptor. GP IIb/IIIa

inhibitors bind to the receptor and prevent fibrinogen and von Willebrand factor (vWF) from binding to the receptors.

Many of the trials of glycoprotein IIb/IIIa inhibitors in the setting of ACS were conducted in an era before the use of potent P2Y12 inhibitors or before routine stenting. In the contemporary era of shorter revascularization times and use of potent DAPT, the benefit of glycoprotein IIb/IIIa receptor inhibitor agents is diminished . The use of glycoprotein IIb/IIIa receptor inhibitors in the era of more potent antiplatelet agents is generally reserved for patients with a large thrombus burden or no-reflow or slow flow that is believed to be attributable to distal embolization of thrombus.

The available GP IIb/IIIa inhibitors include Tirofiban and Eptifibatide, Abciximab.

Currently, the American College of Cardiology/ American Heart Association(Figure-3) as well as European College of cardiology(Figure-4) recommends the use of GP IIb/IIIa inhibitors in ACS as per the table below [1,2] . Intracoronary infusion of GP IIb/IIIa inhibitors in multiple trials had shown improvement in epicardial and myocardial perfusion with fewer adverse events. However, clinical trials did not find a significant improvement in outcomes or recurrent MI.

Tirofiban has a half-life of 2 hours, and its duration of action is 4 hours. It is 65% protein-bound, and its Volume of distribution is 22 to 42L. About 65% of tirofiban clearance is through urine and 25% through feces.[12] Its clearance is 213 to 314 mL/min. It is dialyzable. .The dosage of **eptifibatide** requires adjustment in patients with CrCl <50 mL/min; ACS: 180 mcg/kg IV, and then continuous infusion 1 mcg/kg/min; PCI: 180 mcg/kg IV, and then continuous infusion 1 mcg/kg/min with another 180 mcg/kg IV bolus 10 minutes after the first one. The safety and use during hemodialysis remain unestablished.[12] The GP IIb/IIIa inhibitors (tirofiban and eptifibatide) are only available as intravenous agents. However, tirofiban and eptifibatide require a reduction in dosing for renal impaired patients.

Major and minor bleeding contributes to the majority of adverse events of GP IIb/IIIa inhibitors, ranging from 1 to 10%. Cardiovascular side effects such as hypotension and bradycardia were reported as well. Thrombocytopenia contributes to about 1 to 5% of adverse reactions.[13]

Recommendations for Intravenous Glycoprotein IIb/IIIa Inhibitors in Patients Undergoing PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 34.

COR	LOE	RECOMMENDATIONS
2a	C-LD	1. In patients with ACS undergoing PCI with large thrombus burden, no-reflow, or slow flow, intravenous glycoprotein IIb/IIIa inhibitor agents are reasonable to improve procedural success (1,2).
3: No Benefit	B-R	2. In patients with SIHD undergoing PCI, the routine use of an intravenous glycoprotein IIb/IIIa inhibitor agent is not recommended (3-5).

Figure-3 : [2]Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 Jan 18;79(2):e21-e129. doi: 10.1016/j.jacc.2021.09.006. Epub 2021 Dec 9. Erratum in: J Am Coll Cardiol. 2022 Apr 19;79(15):1547. PMID: 34895950.

GP IIb/IIIa receptor antagonists should be considered if there is evidence of no-reflow or a thrombotic complication during PCI.	IIa	C

Figure-4 : [1]Byrne RA, Rossello X, Coughlan JJ, Barbato E et al. ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Aug 25

Hypersensitivity and local injection site complications are less frequent.

Absolute contraindications includes, Major bleeding diathesis and active major internal bleeding, and history of hemorrhagic stroke within 30 days. Relative contraindications: History of thrombocytopenia, stroke, major surgery within six weeks, and severe hypertension. Intracranial disease and renal impairment require review on a case-to-case basis. Reports exist of acute thrombocytopenia within 24 hours. If platelet count drops below 100,000/mm during the infusion, discontinue the GP IIb/IIIa inhibitor. Usually, platelet count normalizes between 1 to 2 weeks. The clinician should have the patient's coagulation parameters and platelet count checked before and during infusion. Platelet count should be checked 2 to 4 hours after the beginning of infusion and at 24 hours.

Conclusion

With advent of newer pharmacological anticoagulants, fibrin specific thrombolytics with primary PCI, "TIME and Resource" are limiting factors for a large population developing country like INDIA. So judicious and timely use of anticoagulants, proper training and increasing health expenditure with respect to gross GDP may help us fighting the epidemic of ACS and atherosclerosis cost effectively.

References

1. Byrne RA, Rossello X, Coughlan JJ, Barbato E et al. ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Aug 25:ehad191. doi: 10.1093/eurheartj/ehad191. Epub ahead of print. PMID: 37622654.

2. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 Jan 18;79(2):e21-e129. doi: 10.1016/j.jacc.2021.09.006. Epub 2021 Dec 9. Erratum in: J Am Coll Cardiol. 2022 Apr 19;79(15):1547. PMID: 34895950.

3. Bhatt DL, Hulot JS, Moliterno DJ, Harrington RA. Antiplatelet and anticoagulation therapy for acute coronary syndromes. *Circ Res*. 2014;114:1929–1943.

4. Montalescot G, Zeymer U, Silvain J, Boulanger B, Cohen M, Goldstein P, *et al*. Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label ATOLL trial. *Lancet* 2011;**378**:693–703. https://doi.org/10.1016/s0140-6736(11)60876-3

5. Silvain J, Beygui F, Barthélémy O, Pollack C, Cohen M, Zeymer U, *et al*. Efficacy and safety of enoxaparin versus unfractionated heparin during percutaneous coronary intervention: systematic review and meta-analysis. *BMJ* 2012;**344**:e553. https://doi. org/10.1136/bmj.e553

6. Onwordi EN, Gamal A, Zaman A. Anticoagulant therapy for acute coronary syndromes. *Interv Cardiol*. 2018;13:87–92.

7. Li Y, Liang Z, Qin L, Wang M, Wang X, Zhang H, *et al*. Bivalirudin plus a high-dose infusion versus heparin monotherapy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a randomised trial. *Lancet* 2022;**400**:1847–1857. https://doi.org/10.1016/s0140-6736(22)01999-7

8. Stone GW, Mehran R, Goldstein P, et al. Bivalirudin versus heparin with or without glycoprotein IIb/IIIa inhibitors in patients with STEMI undergoing primary percutaneous coronary intervention: pooled patient- level analysis from the HORIZONS-AMI and EUROMAX trials. *J Am Coll Cardiol*. 2015;65:27–38.

9. Yusuf S, Mehta SR, Chrolavicius S, Cohen M, Grines CL, Goodman S, *et al*. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. *JAMA* 2006;**295**: 1519–1530. https://doi.org/10.1001/jama.295.13.joc60038

10. The Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. *N Engl J Med* 2006;**354**:1464–1476. https://doi.org/10.1056/NEJMoa055443

11. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST- elevation myocardial infarction: a report of the American College of Cardiology Foundation/ American Heart Association task force on practice guidelines. *J Am Coll Cardiol*. 2013;61:e78–e140.

12. Tummala R, Rai MP. Glycoprotein IIb/IIIa Inhibitors. [Updated 2023 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554376/

13. Schrör K, Weber AA. Comparative pharmacology of GP IIb/IIIa antagonists. J Thromb Thrombolysis. 2003 Apr;15(2):71-80

Role of Coronary Angiogram in Acute Coronary Syndrome

Dr. Ravi Shankar Sharma
Professor and HOD Medicine,
SS. Medical College Jabalpur, MP
Email: docrssharma@gmail.com

The spectrum of acute coronary Syndrome (ACS) includes ST segment elevation myocardial infarction (STEMI) and the non ST segment elevation acute coronary syndromes (NSTE-ACS) and unstable angina (USA) which may have similar clinical presentations in initial evaluation. The 12 lead ECG and markers of myocardial necrosis are essential in distinguishing between three types of ACS mentioned above. Patients with typical symptoms without persistent (> 20 minutes) ST elevation in atleast 2 contiguous ECG leads, but with elevation of myocardial markers are classified as NSTEMI. Patients with typical symptoms and serial negative markers of myocardial necrosis are classified as having UA (18).

More than half of patients with NSTE-ACS may have normal or non-diagnostic ECGs. Ischemia may occur in territory that is not well represented in standard 12 lead ECG or because patient may have episodic ischemia missed in initial ECG.

Patients with baseline conduction disturbances and rhythms represent particular challenges for diagnosing myocardial ischemia by ECG. Comparison with a prior tracing when the patient was asymptomatic and recording an ECG with the pacing function temporarily switched off (in patients who are no pacemaker dependent) may be helpful.

Coronary angiography identifies a culprit lesion in the circumflex coronary artery in one-third of patients with high risk NSTE-ACS. Because the standard 12- lead ECG does not represent the territory supplied by the circumflex coronary artery well, assessment of posterior leads V_7 through V_9, (with the gain increased to 20 mm/mV) should be considered in patients with a history suggestive of ACS and a non-diagnostic initial ECG. Similar, ACS caused by isolated involvement of an acute marginal branch of the right coronary artery is often not apparent on the standard 12-lead ECG but may be suspected from leads V_3R and V_4R. Therefore, it is useful to obtain these extra leads in patients suspected of having ACS but with normal findings on a 12-lead ECG. Continuous, monitoring of the ECG in the days following NSTE-ACS can identify patients at higher risk for recurrent events. ST-segment depressions noted on such monitoring within the first week after NSTE- ACS are associated with an increased risk for reinfarction and death,. Hence coronary angio done early in such cases may be very useful (18).

Invasive coronary angiography has been the standard technique for imaging the coronary arterial tree for nearly six decades. The culprits lesion in NSTE-ACS typically exhibits an eccentric stenosis with scalloped or overhanging edges and a narrow neck. These angiographic findings may represent disrupted atherosclerotic plaque or thrombus. Features suggesting thrombus include globular intraluminal masses with a rounded or polypoid shape; "haziness" of a lesion suggests the presence of thrombus, but this finding is not specific.

Approximately 90% of patients with a clinical diagnosis of NSTE-ACS have significant coronary obstruction i.e., >50% stenosis of luminal diameter in at least one major coronary artery. Most have obstructive disease in multiple epicardial arteries (approximately 10% have left main [LM] CAD) often accompanied by multivessel CAD. Among patients without LM disease, about 35% have three-vessel disease, and 25% two- vessel disease, whereas

only approximately 20% have single- vessel disease. The remaining 10% have no significant coronary obstruction, a finding that is more common in women and minorities than in white men. In such patients, NSTE-ACS may be related to microvascular coronary obstruction, endothelial dysfunction, or coronary artery spasm and may have a more favorable prognosis. In 38,101 patients enrolled in eight clinical trials of NSTE-ACS, the 30 day rate of death or MI was 2.2% in those with no obstructive CAD compared with 13.3% in patients with obstructive disease. (1).

Intravascular ultrasound (IVUS) and OCT are two invasive cross-sectional imaging techniques that can provide details regarding plaque morphology. In the clinical setting, IVUS or OCT are used most commonly to guide coronary stent placement. These techniques and others (e.g., near-infrared spectroscopy,; intravascular CMR, angioscopy) can provide detailed plaque morphology and establish the pathphysiologic etiology of ACS, although the clinical utility of such additional information is uncertain.

Optimal Timing of an Invasive Strategy in Patients with Acute Coronary Syndrome

While STEMI needs opening of the occluded artery as quickly as possible; preferably mechanically. The timing of intervention in NSTEMI is not clear.

In STEMI, the coronary artery is blocked 100% by an occlusive thrombus which needs to be opened either pharmacologically or mechanically as (primary Angioplasty) quickly as possible- giving rise to the well-known adage-time is muscle. The time of intervention for NSTE-ACS varies from immediate early (within 24 hours) or delayed (after 24 hours). The European guidelines recommend angiography within 24 hours for high-risk patients. In a large meta-analysis including 8 trials (5,324 patients), Alexander Jobs et. al. looked into the data to find whether early invasive strategy leads to a better outcome or not. The median follow-up was 180 days. The result shows that overall there was no significant reduction of mortality in the early invasive group compared to the delayed invasive group (HR 0.81, 95% (10.65 - 1.03; P= 0.0879).

The subgroup analysis turned out to be interesting. Four subgroup of high-risk patients tended to benefit by early intervention- they were (1) those with high concentration of cardiac biomarkers, (HR -.76), (2) diabetics (HR 0.67), (3) GRACE risk score of more than 140 points (HR 0.70), and (4) patients aged more than 75 years (HR 0.65).

Overall the data shows the lack of benefit in rushing with early intervention. The high-risk subset of biomarker positive, diabetic, high GRACE score, and elders might benefit from early intervention; however, the strength of evidence could be considered not very robust.

Currently European and American guidelines recommend angiography within 24 hours of hospitalisation for patients with non-ST elevation myocardial infarction (NSTEM). Key to these recommendations was the TIMACS trial (Timing of Intervention in Acute Coronary Syndromes) which found that invasive angiography within 24 hours of admission was associated with a reduced rate of recurrent ischemia at 6 months when compared with angiography > 36 hours after admission [1]. Additionally, a reduced rate of the composite primary endpoint (death, myocardial infarction (MI), and stroke) was noted among patients with a GRACE score > 140 receiving early angiography. Further support came from the RIDDLE-NSTEMI trial, which found that early angiography (median time 1.4 hours) following NSTEMI was associated with reduced mortality/ recurrent MI at both 30 days and 1 years when compared with a delayed strategy (median time 61 hours)

[2]/ Meta-analyses have provided additional support for these recommendations. [3.4]. Of note, Jobs et al. analsysed data from eight studies (including TIMACS and RIDDLE-NSTEMI) and found reduced 6-month mortality among NSTEMI patients treated with an early invasive strategy [4].

The recent VERDICT (Very EaRly Vs Deferred Invasive evaluation using Computerized

Tomography) trial provided evidence of the potential benefits of even earlier intervention in high-risk patients. Patients without life- threatening features were randomised to receive angiography within 12 hours or between 48 and 72 hours. Among the early intervention group, patients with a GRACE score > 140 were found to have a reduced rate for the primary composite endpoint (all-cause death, nonfatal recurrent MI, admission for refractory myocardial ischemic, or heart failure) at 4 years [5]. However, there are limitations in the design of the VERDICT

trial that potentially reduce its applicability to clinical practice. Firstly, early angiography was delivered with a median door-to- catheter (DTC) time of 44.7 hours (IQR 3.- 12.2), compared to a delayed strategy with a median DTC time of 61.6 hours (IQR 39.4 - 87.8). This represents a substantial treatment delay that high-risk patients typically would would not experience in routine clinical practice. Secondly, DTC times between 12 and 24 hours were not considered despite a significant proportion of patients in clinical practice likely experiencing a delay of this length.

The sheer volume of NSTEMI admission makes the timely delivery of angiography a significant challenge for clinicians and the latest evidence from the VERDICT trial could be interpreted as supporting an even more challenging angiography target in high-risk NSTEMI.

In a matched cohort of NSTEMI patients without life- threatening features, patients receiving invasive angiography within 12 hours had similar one-year cardiovascular outcomes to those treated between 12 and 24 hours. This finding was independent of GRACE score, with high-risk patients (GRACE score > 140) having similar outcomes in both the 12 h and 12 - 24h groups.

Relevance to Routine Clinical Practice: The VERDICT trial was key to the conception of this study. It demonstrated that angiography within 12 hours was only associated with improved long-term outcomes among non-ST elevation acute coronary syndrome (NSTE-ACS) patients with a GRACE score > 140 [5]. However, direct comparison of these results with those of the VERDICT trial should be limited due to an important difference between the delayed intervention groups. In the VERDICT trial, early angiography was compared with delayed angiography conducted between 48 and 72 hours (median DTC time 61.6 hours, IQR 39.4-87.8) In routine clinical practice, high-risk NSTE-ACS patients typically do not experience such long delays, with current guidelines recommending angiography within 24 hours [9, 10]. Thus, this

key finding from the VERDICT trial should not come as a surprise. It is not uncommon for patients hospitalised with NSTEMI to experience delays prior to angiography. In this study, admission out-of-hours was the factor most strongly associated with delays of greater than 12 hours. These delays do not have a significant association with one-year cardio- vascular outcomes, provided that angiography is performed within the guideline- recommended 24 hours timeframe. Support for these findings come from the TIMACS trial which noted no significant difference in 6 month outcomes between patients treated within 6 hours, 6 to 12 hours of 12 - 24 hours.

Benefits of early versus Delayed Angiography: The theoretical benefit of early angiography is the early identification of significant lesions facilitating early revascularisation and salvage of ischemic myocardium. Additionally, early angiography can promote early discharge. Patients in the 12 - 24 hr group had significantly longer hospital stays likely reflecting the delay in receiving angiography. On the other hand, delayed angiography following NSTEMI may provide adequate time for optimal medical treatment in order to decrease thrombus burden, improve plaque stability, and reduce subsequent stent thrombosis risk. The presence of coronary thrombus at the time of angiography is known to worsen outcome following ACS. Furthermore, in vitro models have shown that $P2Y_{12}$ agents can disrupt and even reverse thrombus stability. Longer pretreatment with P2Y12 agents is also associated with improved coronary perfusion before PCI. The proportion of

patients with coronary thrombus may be significantly higher in the early intervention group. Thus, it could be hypothesised that angiography deferred to between 12 and 24 hours may provide time for the beneficial effects of medical therapy to be seen.

Acute coronary syndromes: interventions- Further debate continues .....

Acute coronary syndromes (ACS) usually occur on the basis of coronary atherosclerosis. The treatment of coronary artherosclerosis largely depends on the symptoms of the disease. Besides reduction of risk factors, current treatment of ischaemic heart disease consists of medical treatment with or without such interventional strategies as coronary angioplasty and coronary artery bypass grafting. In stable coronary artery disease, interventional therapy is indicated only when change in lifestyle and medical treatment have failed. Single-vessel coronary artery disease and easily accessible multivessel disease are usually treated with percutaneous transluminal coronary angioplasty. For extensive multivessel disease or failed angioplasty, coronary artery bypass grafting is preferred. In the 1970s and 1980s randomised comparisons of coronary artery bypass surgery with medical treatment of stable coronary artery disease did not show any benefit of surgery over drug treatment, apart from in cases of triple-vessel disease with impaired left-ventricular function (19, 20). Randomised comparisons of coronary angioplasty with medical treatment in stable, mildly symptomatic coronary disease did not show a benefit in survival either, although symptoms were better controlled with interventional therapy (21, 22). Randomised studies that directly compared coronary surgery with coronary angioplasty have been done in Europe and the USA and did not show a survival benefit for one therapy over the other although surgery provided a superior freedom of angina at similar cost of coronary angioplasty, which has to be repeated in many patients (23). Both the interventional and medical strategies to control symptomatic stable coronary artery disease have been improved substantially during the decades in which the trials were conducted. Arterial grafting in coronary surgery and the widespread use of stents have contributed to a better invasive strategy. The introduction of antiplatelet therapy, Blockers, inhibitors of angiotensin- converting enzyme (ACE) and statins has enlarged the arsenal of effective drugs therapy.

So have these achievements in invasive therapy improved the management of ACS ?

Rationale for Invasive therapy-

The prognosis of ACS (unstable angina pectoris and non-Q or non-ST elevation myocardial infarction) is worse than for stable coronary artery disease (23, 24). In hospital death and (re)infarction usually amount to 5-10%. Also, in the first month after the acute episode of ACS, death and (recurrent) infarction occur in another 5-10% of patients despite optimum anti- ischaemic and anti-thrombotic therapy (aspirin and heparin). Angiograms in patients with ACS usually indicate the presence of coronary artery disease. However, this may vary from moderate single-vessel disease to sevcere triple-vessel disease or stenosis of the left main coronary artery. From earlier observations, when coronary artery surgery was the sole revascularisation procedure, it became clear that patients with triple-vessel coronary disease did worse over time than patients with moderate or single-vessel coronary artery(19, 25) disease. Therefore, strategies of early revascularisation have been developed for the management of patients with ACS. The strategy consists of early angiography and subsequent triage for invasive therapy. The purpsoe of this strategy is to reduce the risk of recurrent myocardial ischaemia, infarction, and coronary death within the hazardous first month after the acute episode.

Observational data

With systematic early invasive strategy, the risks of revascularisation procedures in ACS should be taken into account. Early coronary surgery in patients admitted with unstable angina and non-ST elevation myocardial infarction has been deemed unsafe for a long time. However, with the use of better cardio protective drugs and

cardioplegic techniques, the safety of early coronary surgery (25, 27) in ACS has become acceptable. Emergent coronary angiplasty (28, 32) for ACS was developed during the 1980s and proved safe. Early invasive therapy may carry procedural risks but the long-term outlook for patients undergoing it may be improved, as shown by the long-term results of larger studies. The surgical studies date from the 1980s when percuaneous intervention was not yet available as an alternative. Therefore, they may give an optimistic view of coronary surgery. No study addresses the differential risk of an acute, an early, and a deferred procedure separately. The relative benefits of a systematic early invasive strategy had to be compared with an early conservative strategy in which invasive diagnosis and management is based only on recurrent clinical signs and symptoms of myocardial ischaemia (selective invasive strategy). Properly randmised and adequately sized trials to evaluate these strategies were not been published until the 1990s.

Studies on invasive therapy in ACS that reported acceptable efficacy and safety data were uncontrolled and mostly included patients who were selected patients who were selected for invasaive therapy. Decisions to perform invasive therapy for ACS are probably more common in hospitals with catheterisation facilities than in hospitals without such facilities. The absence of a catherisation laboratory may stimulate the strategy of "watchful waiting" in patients admitted with ACS. Until recently, it was unclear whether the latter approach may harm patients or protect them against the risk of early invasive therapy. In the largest registry ever of patients admitted with ACS, the presence or absence of catheterisation facilities has been extensively studied. In the OASIS registry, which was started from a large randomised trial that compared hirudin with heparin in ACS, the presence of a catheterisation laboratory in the hospital where patients with ACS were initially admitted doubled the use of invasive procedures but did not lead to an improvement of 6 month prognosis. On the contrary, the incidence of death, myocardial infarction, and especially stroke increased (33). Although early angiography improves risk assessment, it also leads to overuse of invasive procedures that may be harmful to the patient. Interestingly, in the low- risk patients in the OASIS-2 registry, the outlook of patients who were initially admitted to units with catheterisation facilities was slightly improved, whereas the high-risk patients did significantly worse when initially admitted to units where a catheterisation laboratory was present.

Randomised trials of early invasive versus early conservative strategies-

During the 1970s and 1980s, two trials had been done to compare coronary surgery with medical therapy in patients admitted with unstable angina pectoris. In those days, early management consisted of medical therapy, and coronary bypass surgery was done days after the patient had been stablised (25, 34). Neither study contained sufficient patients to be conclusive and the first, the National Cooperative Study (34) was not randomised. Furthermore, they were carried out when percutaneous intervention was not available, and thus are not applicable to modern cardiology.

With the introduction of percutatneous re-vascularisation, earlier triage of patients had become possible. In the TIMI-IIIB trial (35) 1473 patients were randomised at admission to an early invasive strategy (coronary angiography within 18-48 h after randomisation followed by a revascularisation procedure when possible) or to an early conservative strategy (patients underwent coronary angiography only when recent myocardial ischaemia was detected by ECG, Holter ST-monitoring, a positive thallium exercise test, readmission for angina, or severe residual angina with a positive exercise test during follow-up). Mortality or (recurrent) myocardial infarction at 6 weeks occurred in 7.2% of patients randomised to an invasive strategy and in 7.8% of patients randomised to a conservative strategy (RR 0.92, p=0.69); the corresponding rates at 1 year were 10.8% versus 12.2% (RR 0.89, p=0.42(. A marked crossover to an invasive approach was observed in 65% at 6 weeks and 73% at 1 year in the patients randomised to medical therapy.

In the VANQWISH (Veterans Affairs Non-Q Wave Infarction Strategies in Hospital) study (36), 916 patients with evolving non-ST elevation myocardial infarction were randomised to an early invasive or to a medical strategy. In these high-risk patients, 1 year death and reinfarction were 24% in the surgical group- versus 19% in the medical group

(RR 1.29, p=0.05). The excess morality in the invasive group (13% Vs 8% medically) was almost exclusively due to a high preoperative mortality in patients randomised to the invasive to the invasive strategy, in whom it was decided to perform early coronary surgery. Angioplasty in the patients in the invasive group proved to be safe (no procedural mortality). The crossover rate in this trial was 20% at 30 days.

in March, 1999, the preliminary outcome of the FRISC-2 trial was presented (37). In this trial an early systematic invasive strategy was compared with a selecive invasive therapy in 2457 patients admitted with ACS in the Scandinavian countries. Patients were randmomised within 2 days after admission to an early invasive strategy, which comprised coronary angiography within 48 h after randomisation followed by a revascularisation procedure when possible, or to a selective invasive strategy, in which patients underwent coronary angiography only when recurrent myocardial ischaemia was detected clinically or by exercise ECG, or when a (re)infarction occurred. Mortality or (recurrent) myocardial infarction at 6 months were seen in 9.5% of patients randomised to the systematic invasive strategy and in 12.0% of patients randomised to the selective invasive strategy (RR 0.79, p=0..045). A substantial corssover of 48% was observed in the patients randomised to the conservative group. Procedural mortality was low in this study (1.2% in the systematic invasive group Vs. 0.4% in the selective invasive group). It should be stated that in the first week of hospital admission many patients were on B-blockers and all were on subcutaneous low- molecular-weight heparin. Half of the patients were randomly assigned to low-molecular- weight heparin subcutaneously for another 90 days.

The main outcomes of the randomised trials are different and cannot lead to firm conclusions. It should be noted that there are notable baseline-risk differences between the three main trials: the baseline risk was lowest in the FRISC-

2 patients (least smoking, hypertension, and previous infarction) and highest in the VNQWISH patients.

The results of the randomised trials of a systematic invasive versus a selective invasive therapy of ACS accord with the observational data of the large OASIS registry (33). This applies both to the high-risk patients, in whom a routine invasive strategy of this approach may be harmful (for example, in VANQWISH), and to low-risk patients, in whom the results of this approach may be equivocal (TIMI-IIIB), or even beneficial (FRISC 2). Apparently, the strategy of "watchful waiting" is also efficacious in large unselected populations of patients admitted with ACS, which probably did not represent the patients in the randomised trials.

Risk stratification-

The benefit of a systematic invasive strategy, if any, is marginal in the longer term and only reached statistical significance in the largest trial FRISC-2, despite the high crossover rates. Crossover to invasive therapy in unstable angina has increased substantially over the years. Patients with an evolving non-ST segment elevation myocardial infarction have a higher risk as addressed in the VANQUWISH trial. here, it seems that an early systematic invasive strategy may be harmful, although this effect was not observed post hoc in the non-Q wave infarction subset in TMIM-IIIB (35). Although more studies are needed, it seems that the higher the baselines-risk, the higher the risk of a systematic invasive strategy compared with routine conservative therapy. Baselines biochemical markers, such as troponin I or T and C-reactive protein, may be of help in assessing risk and may help in the subsequent decision to use a medical or an invasive strategy.

Limitation of clinical trials-

Ever since the 1980s both invasive and

conservative strategies in the management of patients with ischemic heart disease have dramatically improved. Coronary angioplasty has been introduced as an alternative to coronary artery bypass surgery in many cases of symptomatic ischemic heart disease

(23). Nowadays, coronary artery surgery is almost exclusively done in patients with left main coronary artery stenosis; triple-

vessel coronary artery disease, with diminished ventricular function; and other cases of multiple-vessel coronary artery disease where angioplasty is not an option. The use of arterial grafts has improved the long-term outcome of coronary artery bypass surgery(38). Also coronary angioplasty has been strongly improved by the use of better balloon technology, the introduction of better stents, and better antiplatelet therapy (ticlopidin) (39) and glycoprotein IIB/IIIA receptor antagonists (31, 40, 31). On the other hand, the use of coronary angiography in the risk stratification of patients with unstable angina has become an increasingly common practice in institutions where a catheterisation laboratory is available (33). This trend may lead to the "oculostenotic reflex" resulting in overuse of coronary procedures, with possible harm to the patient.

The pharmacological approach to patients with symptomatic ischaemic heart disease has also changed dramatically. The use of aspirin and B-blockers had been common practice since the middle of the 1980s. The addition of ACE inhabitors to the usual treatment of heart failure and in patients with large myocardial infarction has improved prognosis. Secondary prevention with statins has changed the prognosis in a variety of patients with (a) symptomatic coronary artery disease. Both the improvement of invasive and pharmacological therapy of patients with inchaemic heart disease constantly challenge the so far rather neutral outcome of trials that compare an early invasive with an early conservative strategy in patients with ACS.

Future directions-

From the above discussion it may be clear that the scenario of treatment of unstable coronary artery disease is dynamic. Several large scale trials are underway that compare the role of early intervention therapy with a conservative strategy in patients who present with acute coronary syndrome. In the UK, RITA-3 is comparing an early invasive strategy with an early conservative approach in patients admitted with acs and treated with low-molecular-weight heparin. The TACTICS-TIMI-18 trial evaluates the place of an early invasive therapy versus modern early conservative strategy consisting of treatment with intravenous unfractionated heparin systematically combined with an intravenous glycoprotein IIb/ IIIa receptor antagonist (43). These two large trials may or may not challenge the current idea that an early conservative strategy ("watchful waiting") is preferable in patients with ACS in selected cases.

Benefit of Early Invasive Therapy in Acute Coronary Syndromes - hence early coronary angio-

Although early invasive therapy is recommended for non-ST (44) segment elevation acute coronary syndromes (NSTE-ACS), the use of this approach remains suboptimal among eligible patients (450. This strategy reduces composite cardiac outcome, largely by decreasing recurrent unstable angina and the need for subsequent rehospitalization and revascularization)46). Meta-analyses have reported that early invasive therapy increase mortality, and myocardial infarction during the index hospitalization (47), although a modest reduction in mortality may emerge later (47, 49). Moreover, the most recent trial on this topic documented a 50% increased risk for myocardial infarction (p = 0.005), with similar mortality 1 year after hospitalization for the NSTE-ACS (p=0.97) (50). Because additional studies and prolonged follow-up of earlier trials have now been reported, an updated meta-analysis to determine the magnitude of benefit of early invasive therapy on individual outcomes of mortality, myocardial infarction, and recurrent unstable angina is presented here.

Analysis of 7 contemporary randomized trials in over 8,000 NSTE-ACS patients treated in the era of potent antiplatelet therapy and coronary stents shows that early invasive therapy decreases mortality by 25% at a mean of 2 years of follow-up, compared with a more conservative approach. To save 1 life, 652 patients need to be treated with early invasive therapy. Early invasive therapy also decreases nonfatal myocardial infarction by 17% and recurrent unstable angina requiring rehospitalization by 31%. To prevent 1 myocardial infarction, 66 patients need to be treated, and to prevent 1 future episode of rehospitalization for unstable angina, 11 patients need to be treated with this approach.

Trials that performed very early invasive therapy (median of 9.3 h) did not show an improvement in long-term survial compared with trials that performed later angiography (median o 39.4 h). The ISAR-COOL trial was the only trial in whcih both study arms underwent invasive therapy, and this study found that very early angiography (median of 2.4 h) was superior to delayed angiography (median of 86 h), however, it is also possible that delaying invasive therapy for nearly 4 days with continuous glycoprotein 11b/111a inhitition could have been harmful (64).

Although later angiography in our analysis was associated with improved survival, we would caution against purpose-fully delaying invasive therapy because these trials were also those that revascularized a large proportion of early invasive patients relative to conservatively treated patients. These findings suggest that revascularization may be the key determinant and not the timeliness of invasive therapy in improving late clinical outcomes. The goal in the management of NSTE-ACS should be to perform early invasive therapy within 48 h. This view if also supported by recent insight from the CRUSADE registry, in which a delay of invasive therapy of 46 h was not associated with increased adverse events, compared with a delay of only 23 h (65).

The ICTUS trial documented a high incidence of post-procedural myocardial infarction, although this study used the lowest threshold for defining (creatine kinase- MB fraction more than the upper limit of normal) and the highest frequency of sampling (every 6 h after PCI for 24 h) for these event (50). Although this definition is consistent with the current consensus document of the joint European Society of Cardiology/ American College of Cardiology (66), it is in contradistinction to the other trials, which generally only sampled blood once after PCI and defined a postprocedural myocardial infarction as a creatine kinase-MB > 1.5 to 5 times the upper limit of normal. It is possible that the other trials in this analysis would have also documented the same finding had they used a similar threshold and frequency for detecting such events. The significance of increased postprocedural events has been controversial (67, 68), although an analysis of over 14,000 NSTE- ACS patients showed that spontaneous myocardial infarction is associated with a 6% to 8% higher absolute mortality compared with postprocedural myocardial infarction

(69). The FRISC-II trial also showed that over the long term, the benefit of revascularization seems to out-weight any early harmful effects. In this trial, mortality and myocardial infarction were both significantly reduced at 1 year from early invasive therapy despite a small excess in early myocardial infarctions (57).

The results of the ICTUS trial may have moved some practioners to a state of uncertainty in regard to the optimal treatment of NSTE-ACS (50). In fact, an accompanying editorial to this trial suggested that the current American College of Cardiology/ American Heart Association and European Society of Cardiology guidelines may need to be challenged (70). This position should be tempered by the current meta-nalysis, which provides solid evidence that early invasive therapy results in a long-term survival advantage without early harm.

A strength of this study is that it reflects current practice. Analysis of non contemporary trials performed before the era of potent antiplatelet therapies and coronary stents showed that early invasive therapy was associated with harm

(48). Glycoprotein IIb/IIIa inhibitors and stents enhance the safety of PCI by decreasing major adverse cardiac events, including myocardial infarction and death (71, 72). Additionally, a meta-regression identified alycoprotein IIb/IIIa inhibitors and stents to be the most significant predictros of event-free survival among invasively treated NSTE-ACS patients. Other concerns exist with noncontemporary trials such as VANQWISH (Veternas Affairs Non-Q Wave Infarction Stretegies In Hospital), in which the use of heparin, beta-blockers, angiotensin- converting- enzyme inhibitors, and lipid- lowering therapies were encouraged, but not required, and in TIMI IIIb, in which half of the participants received tissue plasminogen activator, although fibrinolytic agents are now contraindicated in this population (44). Accordingly, for a meta- analysis to be relevant and guide management decisions, the studies that are included for analysis should reflect current practice (75).

The optimized medical management that treated conservatively needs to be emphasized. By discharge, 94% of conservatively treated patients were taking a statin, and 49% were taking clopidogrel. Both of these therapies have been shown to reduce composite cardiac outcomes, including mortality, in the management of NSTE-ACS (76-79). Although the current body of evidence clearly supports early invasive therapy in the management of NSTE-ACS, future research is needed to more precisely determine the optimal timing of this approach,; the appropriate concomitant adjuvant therapy that is required, and whether additional risk stratification is needed before angiography is performed.

In summary, early invasive therapy in the management of NSTE-ACS provides a durable survival advantage without increasing early adverse events. This approach also reduces nonfatal myocardial infarction and recurrent unstable angina requiring rehospitalization.

References-

1. S.R. Mehta, C.B. Granger, W.E. Boden et al., "Early versus delayed invasive intervention in acute coronary syndromes" New England Journal of Medicine Vo. 360, no. 21, pp. 2165-2175, 2009.

2. A. Milosevic, Z. Vasiljevic-Pokrajcic, D. Milasinovic et al., "Immediate versus delayed invasive intervention for non- STEMI patients," JACC: Cardiovascular Interventions, Vo. 9, no.6, pp. 541- 549, 2016.

3. E.P. Navarese, P.A. Gurbel, F. Andreotti et al., "Optimal timing of coronary invasive strategy in non-ST- segment elevation acute coronary syndromes," Annals of Internal Medicine, vol. 158, no.,4, p. 261, 2013.

4. A. Jobs, S.R. Mehta, G. Montalescot et al., "Optimal timing of an invasive strategy in patients with non-ST- elevation acute coronary syndrome: a meta-analysis of randomised trials," The Lancet, vol. 390, pp. 737-746, 2017.

5. K.F. Kofoed, H. Kelbaek, P.R. Hansen et al., "Early versus standard care invasive examination and treatment of patients with non-St- segment elevation acute coronary syndrome: the VERDICT (very Early vs deferred invasive evaluation using computerized Tomography)- randomized controlled trial," Circulation, vol. 138, no. 24, 2018.

6. R. Auer, B. Gencer, L. Raber et al., "Quality of care after acute coronary syndromes in a prospective cohort with reasons for non-prescription of recommended medications," PLoS One, vo. 9, no. 3, Article ID e93147, 2018.

7. K. Thygesen, J.S. Alpert, A.S. Jaffe et al., "Third universal definition of myocardial infarction," European, Heart Journal, vo. 33, no. 33, pp. 2551-2567, 2012.

8. S. Buuren and K. Groothuis-Oudshoorn, "Mice: multivariate imputation by chained equations in R," Journal of Statistical Software, vol. 45, no.3, pp. 1-67, 2011.

9. M. Roffi, C. Patrono, J.P. Collet et al., "2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation," European Heart Journal, vo. 37, no.3, pp. 267-315, 2016.

10. E.A. Amsterdam, N.K. Wenger, R.G. Brindis et al, "2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes," Circulation, vo. 130, no. 25, pp. e344- e426, 2014.

11. C. Melta Hansen, T.Y. Wang, A.Y. Chen et al., "Contemporary patterns of early coronary angiography use in patients with non-ST-segment elevation myocardial infarction in the United States," JACC: Cardiovascular Interventions, vo. 11, no.4, pp. 369-380, 2018.

12. G.P. Martin, T. Kinnaird, M. Sperrin et al., "Effect of weekend admission on process of care and clinical outcomes for the management of acute coronary syndromes: a retrospective analysis of three UK centres," BMJ Open, vo.. 7, Article ID e016866, 2017.

13. P. Sorajja, B.J. Bersh, D.a. Cox et al., "Impact of delay to angioplasty in patients with acute coronary syndromes under-going invasive management," Journal of the American College of Cardiology, vol. 55, no. 14, pp. 1416-1424, 2010.

14. M. Singh, G.S. Reeder, E.M. Ohman et a., Does the presence of thrombus seen on a coronary angiogram affect the outcome after percutaneous coronary angioplasty ? an angiographic trials pool data experience," Journal of the American College of Cardiology, vo. 38, no.3, pp. 624-630, 2001.

15. H.E. Speich, V. Bhal, K.H. Houser et al., "Signaling via $P2Y_{12}$ may be critical for early stablization of platelet aggregates," Journal of Cardiovascular Pharmacology, vo. 63, no.6, pp. 520-527 , 2014.

16. N. Spinthakis, M. Farag, Y.X. Gue, M. Srinivasan, D.M. Wellsted,and D.A. Gorog, "Effect of P2Y, inhibitors on thrombus stability and endorgenous fibrinolysis," Thrombosis Research, vo. 173, pp. 102-108, 2019.

17. A. Bellemain- Appaix, C. Begue, D.I. Bhatt et. al., The efficacy of early versus delayed $P2Y_{12}$ inhibition in percutaneous coronary intervention for ST-elevation myocardial infarction: a systematic review and meta-analysis," EuroIntervention, vo. 14, no.1, pp. 78- 85, 2018.

18. R. Giugliano, E. Braunwald., "Non-ST segment elevation ACS", Braunnauld's Heart Disease, 12th edition, pp. 716- 719, 2022

19. Alderman EL, Bourassa MG, Cohen LS, et al. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990; 82: 1629-46.

20. European Coronary Surgery Study Group. Long-term results of a prospective randomised study of coronary artery bypass surgery for stable angina pectoris. Lancet 1982' 2: 1173-80.

21. Veterans Affairs ACME Investigators, A comparison of angioplasty with medical therapy in single-vessel coronary artery disease. N Engl. I. Med 1992, 325:10-16.

22. RTTA-2 trial participants. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RTA-2) trial. Lancet 1997; 350: 461-68.

23. Simoons ML. Myocardial revascularization-bypass surgery or angioplasty. N Engl I. Med 1996: 335: 275-77.

24. Braunwald E, Jones RH, Mark DB, et al. Diagnosing and managing unstable angina. Circulation 1994, 90:613-22.

25. Parisi AF, Khuri S, Deupree RH, et al. Medical compared with surgical management of unstable angina: 5-year mortality and morbidity in the Veterans Administration Study. Circulation 1989; 80: 1176-89.

26. Rahimtoola SH, Nunley D, Grunkemeier G, Tepley J, Lambert L, Starr A. Ten-year survival after coronary bypass surgery for unstable angina. N. Engl. I Med 1983. 308: 676-81.

27. McKormick JR, Schick EG, McCabe CH, et al, Determinants of operative mortality and long-term surival in patients with unstable angina. I Thorac Cardiovasc Sing 1985: 89: 683-88

28. De Feyter PJ, Serruys PW, Van den Brand M, et al. Emergency coronary angioplasty for refractory unstable angina. N Engl. J Med 1985; 313: 342-46.

29. Plokker HWM, Ernst SMG, Bal ET, et al. Percutaneous transluminal coronary angioplasty in patients with unstable angina refractory to medical therapy. Cath Cardion asc Dign 1998; 15: 15-18.

30. Morrison DA, Saks J, Gover F, Hammermeister KE, Effectiveness of percutaneous transluminal coronary angiplasty for patients with medically refractory rest angina pectoris and high-risk of adverse outcome with coronary artery bypass grafting Am I Cardiol 1995; 75: 237-40.

31. Topol EJ, Ferguson JJ, Weisman HF, et al. Long-term protection from myocardial ischemic events in a randomized trial of brief intergrin B_3 blokade with percutaneous intervention. JAMA 1997;278: 479-84.

32. Marzochhi A, Pionvaccari G, Marrozzini C, et al. Results of coronary stenting for unstable versus stable angina pectoris. Am J. Cardiol 1997; 79: 1314-18.

33. Yusuf S, Flather M, Pogue J, et al. Variations in invasive cardiac procedures and outcomes in patients with suspected unstable angina or myocardial infarction without initial ST elevation. Lancet 1998-352: 507-14.

34. Hultgren HN, pfeifer JF, Anegell WW, Lipton MJ, Bilisoly J. Unstable angina: comparison of medical and surgical management. Am I Cardiol 1977; 39: 734-40.

35. TIMI-IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-St elevation myocardial infarction: results of the TIMI-IIIB trial. Circulation 1994; 89: 1545-56.

36. Boden WE, O'Rourke RA, Crawford MH, et al. Outcomes in patients with acute non-Q wave myocardial infarction randomly assigned to an invasive as compared to a conservative management strategy. N Engl I Med. 1998; 338: 1785-92.

37. Wallentin L. FRISC-2 trial. Presented at the 48th Annual Scientific Session Amercian College of Cardiology, New Orleans, March, 1999.

38. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-mammary-artery grafts: effects on survival over a 15 year period. N. Engl I Med 1996; 334: 216-21.

39. Schomig A, neumann FJ, Kastran A, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents. N Engl J. Med 1997; 334: 1084-89.

40. EPILOG Investigators. Platelet glycorprotein IIB/IIIa receptor blockade with abciximab with low-dose heparin during percutaneous coronary revascularization. N Engl I Med 1997; 336: 1689-96.

41. EPISTENT Investigators, Randomized placebo-controlled and baloons angioplasty-controlled trial to assss safety of coronary stenting with use of plastelet glycoprotein IIb/IIIa receptor blackade. Lancet 1998; 352: 87-92.

42. Serruys PW, Van Hout B, Bonnier H, et al. Rndomised comparison of implantation of heparin-coated stents with balloons angioplasty in selected patients with coronary artery disease (BENESTENT-II). Lancet; 1998; 352: 673-81.

43. Cannon CP, Weintraub WS, Demopolous I.A., et al. Invasive versus conservative strategies in unstable angina and non-Q wave myocardial infarction followng treatment with tirofiban: rationale and study design of the international TACTICS-TIMI 18 trial. Am I Cardiol 1998; 82: 731-36.

44. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA guideline update for the management of patients with unstable angina and non-St-segment elevation myocardial infarction-2002. summary article: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients. With Unstable Angina). Circulation 2002; 106: 1893-900.

45. Bhatt DL, Roe MT, Peterson D, et al. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes; results from the crusade Quality Improvement Initiative. JAMA 2004; 292: 2096-104.

46. Fragimin and Fast Revsacularisation During Instability in coronary Artery Disease Investigators, Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999; 354:708-15.47. Mehta SR, Cannon C, Fox KA, et al. Routine vs selective inasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. JAMA 2005; 293:2908-17.

48. Bavry AA, Kumbhani DJ, Quiroz R, Ramchandani SR, Kenchaiah S, Antman EM. Invasive therapy along with glycoprotein IIb/IIIa inhibitors and intracoronary stents improves survival in non-ST- segment elevation acute syndromes: a meta-analysis and review of the literature. Am J Cardiol 2004; 93:830-5.

49. Batt DL. To cath or not to cath: that is no longer the question. JAMA 2005; 293: 2935-7.

50. de Winter RJ, Windhause |F, Cornel JH, et al. early invasive versus selectively invasive management for acute coronary syndromes. N Engl J Med 2005; 353: 1095-104.

51. TIMI IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non Q-wave myocardial infarction. Results of the TIMI IIIB Trial. Thrombolysis in Myocardial Ischemia. Circulation 1994; 89: 1545-56.

52. McCullough PA, O'Neill WW, Grahm M, et al. A time-to-treatment analysis in the Medicine versus Angiography in Thrombolytic Exclusion (MATE) trial J. Interv Cardiol 2001; 14: 415-22.

53. Boden WE, O'Rourke RA, Craford MH, et al. Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared iwth a conservative management strategy. Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial Investigators. N. Engl J Med 1998; 338: 1785-92.

54. SWIFT (Should We Intervene Following Thrombolysis) Trial Study treatment after thrombolysis with anistreplase in acute myocardial infarction BMJ 1991; 302: 533-60.

55. Madsen JK, Grande P, Saunamaki K, et al. Danish multicenter randomized study of of invasive versus conservative treatment in

patients with inducible ischemia after thrombolysis in acute myocardial infarction (DNAMI). Danish Trial in Acute Myocardial Infarction. Circulation 1997; 96: 748-55.

56. Pfisteter M, Buser P, Osswald S, et al. Outcome of elderly patients with chronic symptomatic coronary artery diseae with an invasive vs. optimized medical treatment strategy: on-year results of the randomized time TRIAL, JAMA, 2003; 289: 1117-23.

57. Wallentin L, Lagerqvist B, Husted S. Kontny F, Stable E, Swahn E. Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disase: the FRISC II invasive randomised trial. FRISC II Investigators. Fast Revascularisation During Instability in Coronary Artery Disease. Lancet 2000; 256: 9-16.

48. Lagerqvist B, Huted S, Kontny F, et al. A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease two-year follow-up of the FRISC-II invasive study. J Am Coll Cardiol 2002; 40: 1902-14.

59. Michalis LK, Stroumbis CS, Pappas K, et al. Treatment of refractory unstable angina in geographically isolated area without cardiac sugery. Invasive versus conservative strategy (GRUCS study). Eur Heart J. 200-; 21: 1954-9.

60. Cannon CP, Weintraub WS, Demopoluous LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor triofiban, N. Engl J Med. 2001; 344: 14879-87

61. Speacek R, Widimsky P, Straka Z, et al. Value of first day coronary angiograph/ angioplsty in evolving non-ST segment elevation myocardial infarction: an open multicenter randomized trial. The VINO Study. Eur Heart j. 2002; 23: 230-8.

62. Fox KA, Poole-Wilson PA, henderson RA et al. Interventional versus conservative treatment for patients with unstable angina or non-ST- segment elevation mycardial infarction: the British Heart Foundation RITA 3 randomised trial, 'Randomized Intervention Trial of Unstable Angina. Lancer 2002; 360: 343.51.

63. Fox KA, Poole-Wilson P, Clayton TC, et al. 5-year outcome of an interventional strategy in non-St segment elevation acute coronary syndrome: the British heart Foundation RITA 3 randomised trial. Lancet 2004; 366: 914-20.

64. Neumann FJ, Kastrati, A, Pogatsa-Murray G, et al. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomizaed controlled trial. JAMA 2003, 290: 1593-9.

65. Ryan JW, Peterson ED, Chen AY, et al. Optimal timing of intervention in non-ST-segment elevation acute coronary syndromes: insights from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) Registry, Circulation 2005; 122: 3049-57.

66. Alpert JS, Thygesen K, Antman E, Bassand JP, Myocardial infarction redefined- a consensus document of The Joint European Society on Cardiology/ American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardio 2000; 36: 39-69.

67. Roe MT, Mahaffey KW, Kilarti R, et al Creatine Kinase- MB elevation after percutaneous coronary intervention predicts adverse outcomes in patients with acute coronary syndromes, Eur Heart J 2004: 25: 313-21.

68. Bhatt DL, Topol EJ. Does creatinine Kinase-MB elevation after percutaneous coronary intervention predict outcomes in 2005?

Periprocedural cardiac enzyme elevation predicts adverse outcomes. Circulation 2005; 112: 209-15.

69. Akherhuis KM, Alexander JH, Tardiff BE, et al. Minor myocardial damage and prognosis: are spontaneous and percutaneous coronary intervention- related events different? Circulation 2002; 105: 554-6.

70. Boden WE. Acute coronary syndromes without ST-segment- elevation- what is the role of early intervention? N. Engl J Med 2005; 353: 1159-61.

71. Zhu MM, Feit A, Chadow H, Alam M, Kwan T, Clark LT. Primary stent implanation compared with primary balloon angioplasty for acute myocardial infarction: a meta-nalysis of randomized clinical trials. Am J Cardiol 2001; 88: 297-301.

72. Boersma E, Harrington RA, Moliterno DJ, et al. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;' 359: 189-98.

73. Karvouni E, Katristis DG, Ioannidis JP, Intravenous glycoprotein IIb/IIIa receptor antagonists reduce mortality after percutaneous coronary interventions. J Am Coll Cardiol 2003; 41: 26-32.

74. Biondi-Zocai GG, Abbate A, Agotoni , et al. Long-term benefits of an early invasive management in acute coronary syndromes depend on intracoronary stenting and aggressive antiplateler treatment: a metaregression. Am Heart J 2005; 149: 504-11.

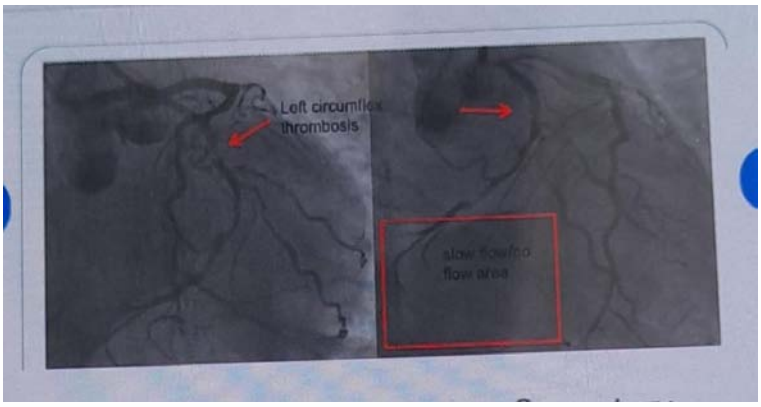
75. Bavry AA, Kumbhani DJ. Routine vs. selective invasive strategies in acute coronary syndromes. JAMA 2005; 294: 2844-5.

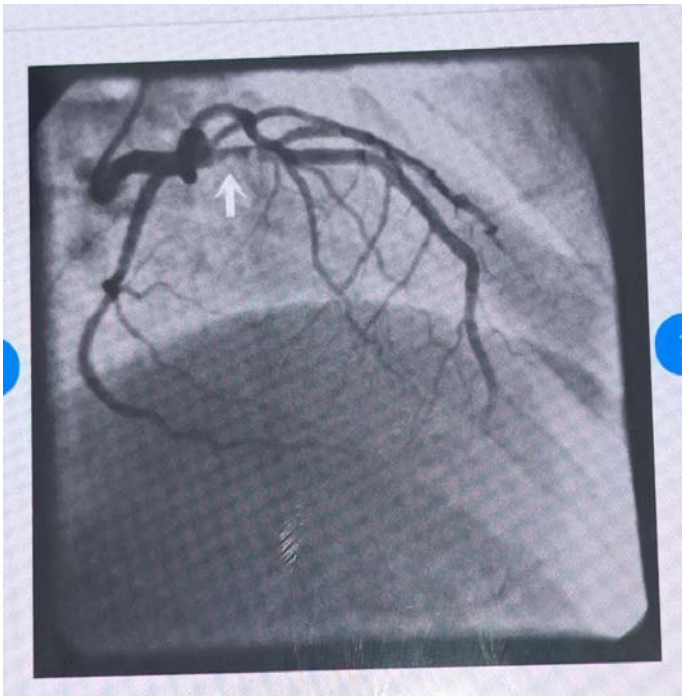
76. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N. Engl. J. Med. 2004; 350: 1495-504.

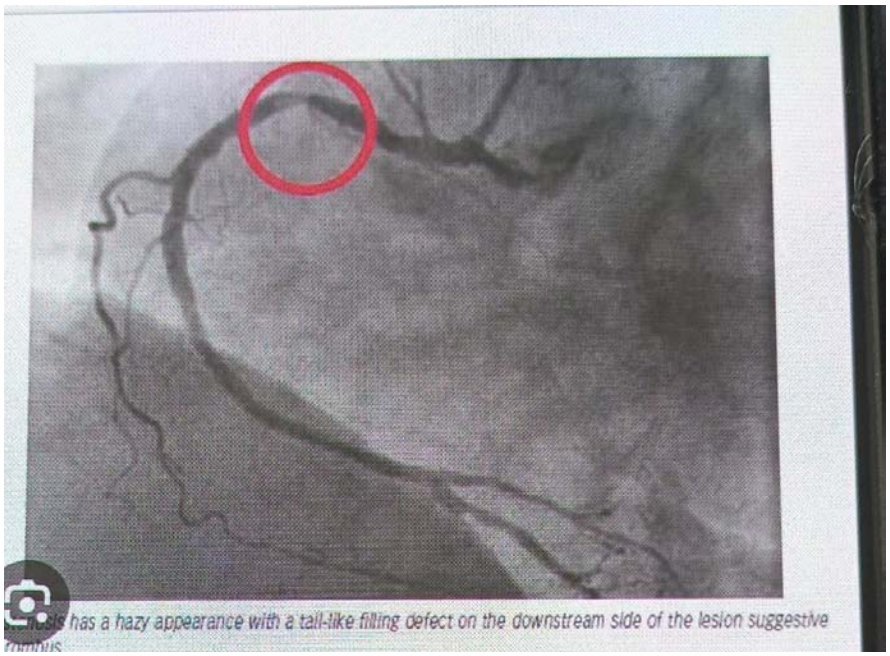
77. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl. J Med 2001; 345: 494-502.

78. Bavry AA, Mood G. Borek PP, Kumbhani DJ, Bhatt DL. Benefit of early statin therapy during acute coronary syndromes: a meta-analysis, J Am Coll Cardiol 2005; 57 Suppl A:205A.

79. Helton TJ, Bavry AA, Kumbhani DJ, Bhatt DL Quantifying the risk and benefit of additing clopidogrel to aspirin in coronary disease. Circulation 2005; 112. II-2093.


Left circumflex
thrombosis
slow flow/no
flow area




has a hazy appearance with a tail-like filling defect on the downstream side of the lesion suggestive

Role of CT Coronary Angiography and Cardiac MRI in Coronary Artery Disease

Dr. Deepak Bulla
MD DNB DMRD EDIR (Europe) FRCR (UK)
Consultant Radiologist, Vijaya Diagnostic Center
No: 3-6-16 & 17, Street No.19, Himayatnagar, Hyderabad, Telangana, INDIA 500029
Email: deepak0107@yahoo.com

INTRODUCTION:

Coronary artery disease is a leading cause of mortality globally. A large number of this burden falls on low- and middle-income countries accounting for nearly 7 million deaths annually. Coronary artery disease is characterized by presence of atherosclerosis in coronary arteries. Coronary Heart Disease (CHD) / Ischaemic Heart Disease (IHD) includes the diagnosis of Stable angina, Acute Coronary Syndrome (ACS) and silent myocardial ischemia. Atherosclerosis of coronary arteries begins as early as second decade of life. Coronary artery disease occurrence and progression is multifactorial. The most common risk factors are, and not limited to a strong family history, sedentary lifestyle, metabolic syndrome, diabetes, smoking and obesity.

Computed tomography coronary angiography (CTCA) and cardiac magnetic resonance imaging (CMRI) play a crucial role in screening individuals for coronary artery disease, quantifying the severity of coronary artery disease, plaque characterization, identifying the effects of coronary artery disease on myocardium, evaluating the viability and perfusion of myocardium, evaluating the ventricular function, in post-treatment follow up of coronary artery disease patients by evaluating the patency of cardiac stents, coronary bypass grafts and in evaluating the effectiveness of revascularization treatment.

The updated 2016 NICE (The National institute for health and care excellence) guidelines are notable for suggesting the use of CTCA as the first line investigation in all patients with typical or atypical anginal symptoms.

This article aims to discuss the procedure, common indications and benefits of coronary CT angiography (CTCA) and cardiac MRI (CMRI) along with few radiological images.

CT CORONARY ANGIOGRAM (CTCA)

MOST COMMON INDICATIONS

- For detection and assessment of severity of coronary artery disease.
- For detection of anomalous coronary arteries.
- For preoperative workup of patients planned for trans catheter aortic valve implantation procedure (TAVI).
- For evaluation of coronary artery stent patency.
- For evaluation of bypass graft patency.
- For evaluation of distal vessel patency in chronic total occlusions and ostial occlusions of coronary arteries where the invasive coronary angiogram (ICA) findings could be unclear.

PROCEDURE

With the advent of ultrafast new generation CT scanners, CT coronary angiogram is increasingly being used as a reliable alternative for invasive coronary angiogram. Several meta analysis studies reveal the sensitivity of CT coronary angiogram in detecting coronary artery disease to be above 95% and specificity to be approximately 86%, compared to the gold standard invasive coronary angiogram.

Minimum technical requirements for a coronary CT angiogram are the following:

- 64 rows of detectors in CT scanner.
- Detector element with a width of d" 0.625 mm.
- Detector coverage of 4 cm.
- Option for cardiac CT and ECG gated triggering.

The patient needs to be fasting and should have normal renal function parameters. A stable and low heart rate of around 60-65 bpm is an ideal prerequisite for a good quality CT angiogram study. Premedication with beta-blockers to achieve a desired heart rate may be required in select few patients. However, with the advent of newer CT scanners which can acquire images in a single heartbeat, premedication with beta-blockers is seldom required. Sublingual nitroglycerin is administered just before the scan to achieve optimal coronary vasodilatation.

The initial step of examination is acquisition of a CT coronary calcium score. It is worth noting that a CT coronary calcium score estimation alone can be used as a good screening tool for detection of coronary artery disease in patients with low to intermediate risk categories, according to The Framingham Coronary Heart Disease Risk Scoring system.

Following this, a tailored quantity of intravenous iodinated non-ionic contrast is given and the images are acquired in the arterial phase of study. Images can be acquired either with prospective or retrospective ECG gating.

The acquired images are then post processed and necessary multiplanar reformatted, volume rendered and maximum intensity projection images can be derived to optimally evaluate coronary arteries.

CORONARY ARTERY DISEASE - REPORTING AND DATA SYSTEM (CAD RADS 2.0).

CAD RADS 2.0 was developed to standardize the reporting of coronary CT angiograms, to improve communication and to guide therapy. The updated version 2.0 was released in year 2022. The table below illustrates CAD RADS 2.0: (Table 1)

Table 1 - CAD RADS categories:

Score	Stenosis	Interpretation	Further investigation
0	0%	Absence of CAD	None
1	1-24%	Minimal non-obstructive CAD	None
2	25-49%	Mild non-obstructive CAD	None
3	50-69%	Moderate stenosis	Consider functional assessment
4A	70-99% single or double vessel	Severe stenosis	Consider ICA or functional assessment
4B	Left main > 50% or3 vessel e" 70%	Severe stenosis	ICA
5	100%	Total coronary occlusion	Consider ICA and viability assessment
CAD RADSN	Non-diagnostic study	Obstructive CAD cannot be excluded	Additional evaluation needed

ICA – Invasive coronary angiography

Source: An expert consensus document of SCCT, ACR, ACC & NASCI. DOI: 10.1148/ryct.220183

CT CORONARY ANGIOGRAPHY IN EVALUATION OF CORONARY ARTERY DISEASE

In addition to diagnosis of coronary artery disease and estimating the severity of disease in different coronary arteries, CT coronary angiogram is also able to characterize plaques and identify high risk plaques which are often associated with plaque rupture and myocardial infarction. A heavily calcified plaque would require different treatment strategy compared to a non-calcified plaque.

CT coronary angiogram has a high negative predictive value in excluding an obstructive coronary artery disease. It is often useful in excluding coronary artery disease in patients with a positive treadmill test.

CT angiogram findings of a high- risk plaque in coronary artery are - presence of a low attenuating plaque, positive remodeling of the vessel, spotty calcification of vessel walls and presence of a 'Napkin ring sign'.

CT coronary angiogram provides useful information in chronic total occlusion of coronary arteries with information about the distal vessels.

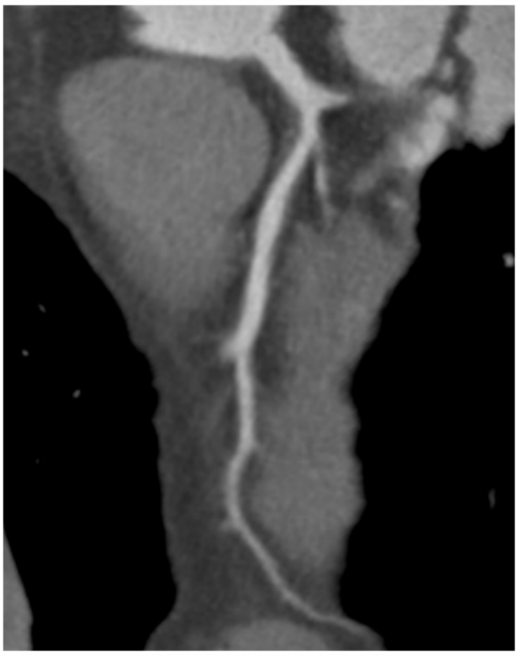


Figure 1: Curved multiplanar reformation CT coronary angiogram image showing mild luminal stenosis in proximal Left anterior descending artery.

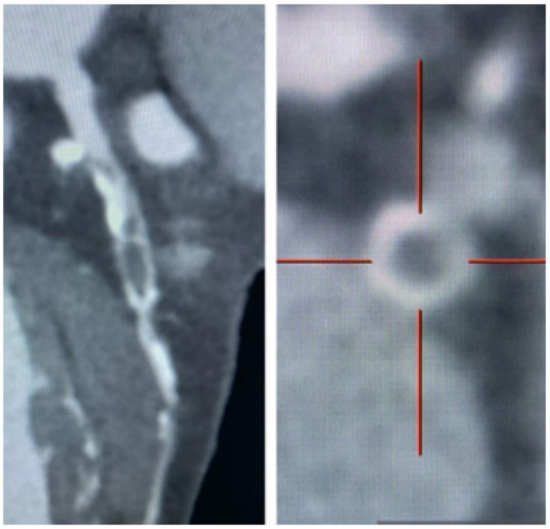


Figure 2: Curved multiplanar reformation and axial CT coronary angiogram image showing 'napkin ring sign' of a high-risk plaque in coronary artery which is prone for rupture.

CT CORONARY ANGIOGRAPHY IN EVALUATION OF CORONARY ARTERY STENTS AND BYPASS GRAFTS

CT coronary angiogram provides a reliable alternative to invasive caronary angiography in evaluating coronary artery stents and bypass graft patency. CTCA can detect early changes of intimal hyperplasia within the coronary stent and can reliably grade severity of instent restenosis. CTCA provides wholesome view of the bypass grafts with important information of vessels distal to the anastomosis. It is useful in identifying acute graft occlusions and chronic stenosis of grafts. It can identify different complications related to coronary artery bypass grafting and percutaneous transluminal coronary angioplasty (PTCA) procedure. (Figure 3, 4, 5)

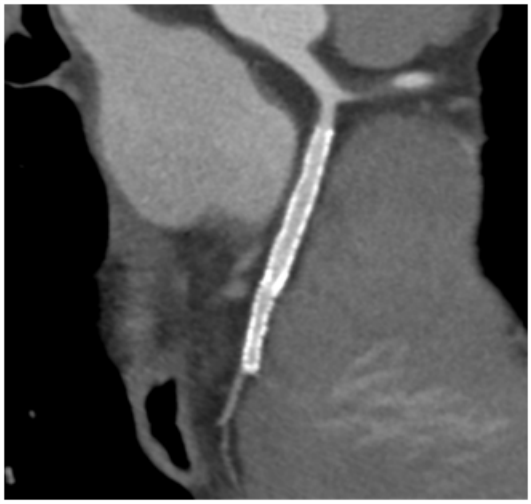


Figure 3: Curved multiplanar reformation CT coronary angiogram image showing good details of coronary stent lumen.

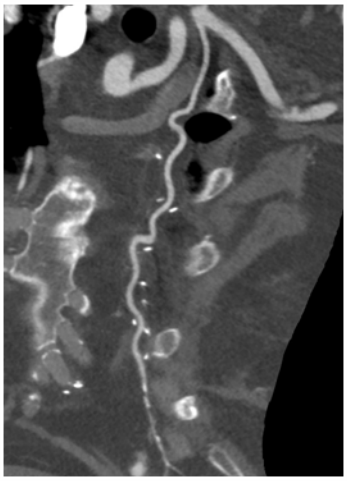


Figure 4: Curved multiplanar reformation CT coronary angiogram image showing good details of a Bypass graft lumen.

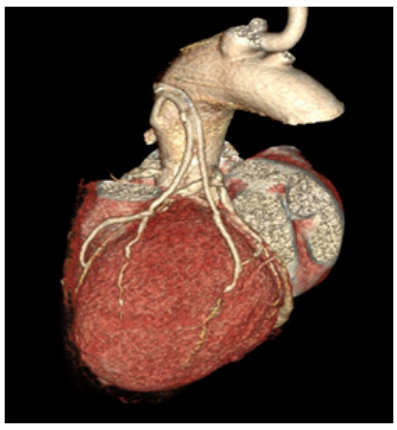


Figure 5: Volume rendering technique (VRT) CT coronary angiogram image showing good overview of bypass grafts.

CT FRACTIONAL FLOW RESERVE (CT FFR)

Although not widely available, CT FFR - a computer-based technology that produces functional information using computational fluid dynamics in determining functional significance of an atherosclerotic plaque. A value of less than 0.7-0.8 is indicative of a hemodynamically significant obstructive plaque.

CTCA IN MISCELLANEOUS CONDITIONS

CTCA can accurately diagnose incidental or unsuspecting conditions like coronary artery dissection, anomalous origin of coronary arteries, coronary artery pseudoaneurysm, vasculitis, coronary arteries fistula, extrinsic coronary artery compression and arteriovenous malformations.

As the lung parenchyma surrounding heart is visible in CTCA, it is often possible to detect incidental findings in lung parenchyma and subdiaphragmatic region.

ROLE OF CARDIAC MRI IN CORONARY ARTERY DISEASE

PROCEDURE

Magnetic resonance imaging is dependent on magnetic properties of spinning hydrogen nuclei or protons found in the water and fat molecules within the body. There is no radiation involved in cardiac MRI. The duration of a cardiac MRI study varies between 30 minutes to an hour. Presence of aneurysmal clips, cardiac pacemakers, implantable cardioverter defibrillator and cochlear implants are contraindications for cardiac MRI.

Multiple static and cine pulse sequences are used in cardiac magnetic resonance imaging (CMRI) during a cardiac cycle. Myocardial stress imaging with adenosine and dobutamine stress wall motion analysis are performed in certain clinical scenarios. Intravenous gadolinium-based contrast agent is administered, following which early and late post-contrast images are obtained. Flow studies are performed for valvular functional analysis.

ASSESSMENT OF MYOCARDIAL VIABILITY

Cardiac MRI helps to differentiate between viable, dysfunctional and non-viable myocardium.

The late post-contrast images are especially useful in detecting non-viable myocardium. Presence of late Gadolinium enhancement is an evidence of disrupted cell membrane and presence of myocardial scar tissue. It is based on principle of delayed clearance of Gadolinium in extracellular tissues of scarred and infarcted myocardium. The pattern of late Gadolinium enhancement is distinct in ischaemic heart disease and follows a transmural on subendocardial pattern of enhancement in specific arterial territories of myocardium. This helps to distinguish between ischaemic and non-ischaemic myocardial pathologies.

MRI also quantitatively estimates the burden of non-viable myocardium and provides useful information to identify patients who would benefit from revascularisation procedures.

Non viable myocardium in cardiac MRI is thinned and has an end diastolic wall thickness of < 6 mm, shows hypokinesis and late Gadolinium enhancement.

Below table demonstrates different physiological states of myocardium along with corresponding contractility and myocardial perfusion. (Table 2) (Fig 2)

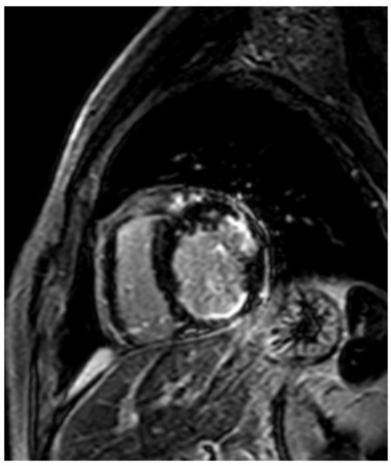


Figure 6: Cardiac MRI late gadolinium post contrast images demonstrate subendocardial (curved arrow) and transmural (straight arrow) infarcts in LV myocardium.

ASSESSMENT OF GLOBAL AND REGIONAL VENTRICULAR FUNCTION

Cardiac MRI accurately determines the ventricular function, myocardial mass and ventricular volumes. Parameters obtained in cardiac MRI are accurate and reproducible. This makes it superior to echocardiography in assessing ventricular function. These parameters are important in guiding treatment options in different clinical scenarios.

Regional wall motion abnormalities of ventricular myocardium can be accurately detected in cardiac MRI.

Myocardial contractile reserve can be estimated by Dobutamine stress study and myocardial perfusion can be estimated with Adenosine stress cardiac MRI.

Cardiac MRI is a good alternative to single photon emission computed tomography (SPECT) and positron emission tomography (PET) for evaluation of myocardial perfusion and function.

Table 2: Different physiological states of myocardium:

Physiological state of myocardium	Contractility	Myocardial perfusion
Viable	Normal	Normal
Stunned	Reduced	Transiently decreased followed by recovery
Hibernating	Reduced	Reduced
Non-viable	Absent	Absent

CARDIAC MRI IN DETECTING COMPLICATIONS OF ISCHEMIC HEART DISEASE

Cardiac MRI plays an important role in assessment of complications of ischaemic heart disease. It is useful in detecting ventricular thrombus, mitral valvular regurgitation, myocardial rupture and ventricular aneurysms.

Microvascular obstruction (MVO) can be detected within an infarcted myocardium using early and late post contrast images.

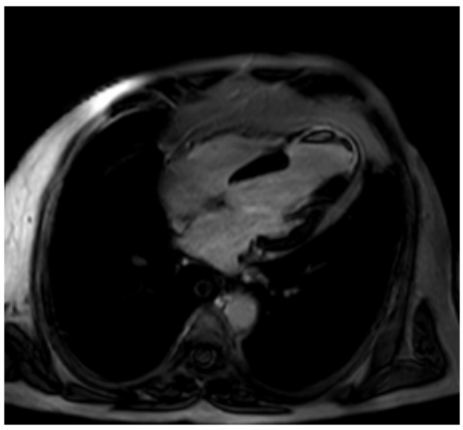


Figure 7: Cardiac MRI late gadolinium post contrast image demonstrates a subendocardial infarct with thrombus, seen as a filling defect (straight arrow).

ADVANCES IN CARIAC MRI

Parametric imaging of myocardium is increasingly being used and helps in tissue characterisation and differentiation of various infiltrative myocardial pathologies. It consists of T1 mapping, T2 mapping, T2* mapping and extracellular volume (ECV) fraction quantification. Although its main utility is in Infiltrative cardiomyopathy, it can be used in patients with chronic renal failure and CAD in whom intravenous Gadolinium is contraindicated. It provides information about myocardial fibrosis and inflammation.

Cardiac MRI ventricular strain imaging can help in early detection of ventricular dysfunction before decline of ventricular ejection fraction.

SUMMARY

Coronary CT angiography and cardiac MRI play a vital role in evaluation of patients with coronary artery disease and provide crucial inflammation in guiding treatment and in post-treatment follow up. With continuing research and advancement in technology, these two imaging modalities are likely to make a bigger impact in diagnosis and treatment of coronary artery disease.

REFERENCES:

- Moss AJ, Williams MC, Newby DE, Nicol ED. The updated NICE Guidelines: Cardiac CT as the First-Line Test for Coronary Artery Disease. Curr Cardiovasc Imaging Rep 2017;10:15.
- Postgrad Med J 2010;86:532e540. doi:10.1136/pgmj.2009.093856.
- Journal of Epidemiology and Global Health Vol. 11(2); June (2021), pp. 169–177 DOI: https://doi.org/10.2991/jegh.k.201217.001; ISSN 2210-6006; eISSN 2210-6014 https://doi.org/10.1148/rg.210174.
- Myocardial Strain Evaluation with Cardiovascular MRI: Physics, Principles, and Clinical Applications: Prabhakar Shantha Rajiah et al. https://doi.org/10.1148/rg.210174.
- Messroghli, D.R., Moon, J.C., Ferreira, V.M. et al. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). J Cardiovasc Magn Reson 19, 75 (2017). https://doi.org/10.1186/s12968-017-0389-8.

Percutaneous Coronary Interventions in ACS

Dr Rajeev Menon
Director & Head, Dept., of Cardiology
AIG Hospitals, Hyderabad
Dr. Chenna Keshava
Consultant Cardiologist, AIG Hospitals, Hyderabad

INTRODUCTION: DEFINITION OF ACS:

The spectrum of ACS includes ST-segment elevation myocardial infarction (STEMI) and the non–ST elevation acute coronary syndromes (NSTE-ACS). The latter consist of non–ST elevation myocardial infarction (NSTEMI) and unstable angina (UA) (Fig.1), which have indistinguishable clinical presentations at the initial evaluation and are differentiated by the presence of elevated cardiac enzymes (Especially Troponins) in the former.

Several features help to differentiate ACS from chronic stable angina (now rechristened as Chronic coronary syndrome), including

1. Any new onset angina
2. Sudden onset of symptoms at rest (or with minimal exertion) that last at least 10 minutes unless treated promptly
3. Patients with chronic stable angina who experience increase in frequency, duration or intensity or in whom pain occurs with lesser exertion.
4. Post prandial angina
5. Post procedure angina.

The 12- lead electrocardiogram (ECG) and markers of myocardial necrosis are essential tools in distinguishing between the three types of ACS mentioned previously.

Patients with typical symptoms without persistent (>20 minutes) ST-segment elevation in at least two contiguous electrocardiographic leads, but with elevation of myocardial biomarkers (>99% of the normal range), are classified as having NSTEMI.

Patients with typical symptoms and serial negative markers of myocardial necrosis are classified as having UA, which carries a better prognosis.

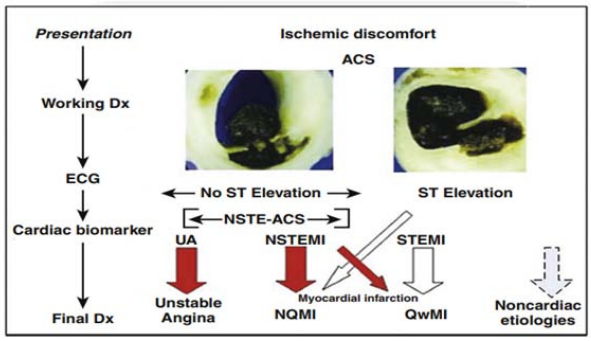


FIG-1:The clinical, pathologic, electrocardiographic, and biomarker correlates in ACS and approach to management. Flow reduction may be related to a completely occlusive thrombus or subtotally occlusive thrombus. Most patients with ST elevation (thick white arrow in bottom panel) develop Q wave myocardial infarction (QwMI), and a few (thin white arrow) develop non–Q wave myocardial infarction (NQMI). Those without ST elevation have either UA or NSTEMI (thick red arrows), a distinction based on cardiac biomarkers. Most patients presenting with NSTEMI develop NQMI; a few may develop QwMI. C

Percutaneous Coronary Intervention (PCI) Overview

Introduction

The first balloon angioplasty in humans was performed by Dr. Andreas Gruentzig in 1977 in Zurich, Switzerland, when he passed a prototype, fixed-wire balloon catheter across a severe lesion in the left anterior descending artery (LAD).[1]

Coronary stents, introduced in the 1990s, dramatically improved upon angioplasty's efficacy and reduced periprocedural complications. Bare-metal stents gave way to drug-eluting stents that addressed the problem of in-stent restenosis, and the diversity of lesions treatable with percutaneous coronary intervention (PCI) has increased exponentially over the past two to three decades. In addition, to these and other technical innovations on the procedural side, there have also been significant improvements in peri- and post-procedural medications, widespread availability of mechanical circulatory devices for very high-risk patients, as well as systematic adoption of care-delivery pathways. All of these have led to improvements in outcomes post-PCI in a synergistic fashion and enabled operators to tackle even the most complex and high-risk patients and lesions successfully

Explanation of PCI

In coronary angioplasty procedure catheters are introduced percutaneously under local anesthesia. However, since angioplasty involves selective cannulation of coronary arteries with guidewires and balloon catheters , temporary occlusion of antegrade coronary arterial flow, as well as manipulation of the culprit lesion by balloon inflation, as well as stent deployment, the procedure is significantly more complicated and entails approximately 1 0-fold higher risk (i. e., 1% versus 0.1 %) as compared with a diagnostic catheterization.[2] However, the risks of coronary angioplasty vary widely with the baseline clinical condition of the patient, the characteristics of the lesion to be treated, and the techniques used

REPERFUSION STRATEGIES in STEMI (Primary vs other Reperfusion strategies)

Selection of reperfusion strategy (Primary PCI Vs Thrombolysis):

Primary PCI strongly preferred, especially for patients with cardiogenic shock, heart failure, late presentation, or contraindications to fibrinolysis. For patients with symptoms of >12 hours, fibrinolytic therapy is not indicated, but emergent PCI may be considered, particularly for patients with evidence of ongoing ischemia or those at high risk of death.

Treat with fibrinolysis if PCI unavailable within **120 minutes of first medical contact,** symptoms <12 hours, and no contraindications

Primary Percutaneous Coronary Intervention:

Twenty-three randomized clinical trials[3] compared primary angioplasty in myocardial infarction (PAMI) with fibrinolytic therapy and demonstrated that PAMI was better than fibrinolysis in reducing the incidence of short-term and long-term adverse outcomes, including death. It was found that patients undergoing PAMI, increases in the door-to-balloon time (especially by >2 hours) were associated with higher mortality rates. Selection of either fibrinolysis or PAMI as the appropriate reperfusion strategy should depend on the clinical scenario.

Primary PCI is generally preferable if it is rapidly available because it yields better outcome than fibrinolysis. The effectiveness of both fibrinolytic therapy and PAMI diminishes with the passage of time. Thus, PCI is generally preferred for patients who arrive at the hospital late after the onset of symptoms (>3 hours).

Facilitated PCI:.

Facilitated PCI is routine PCI after Fibrinolytic Treatment, this approach involves fibrinolysis followed by early and mandatory PCI. This procedure tries to improve patency by fibrinolysis before performing PCI. Potential advantages of this approach include earlier time to reperfusion, smaller infarct size, better patient stability, lower infarct artery thrombus burden, and greater procedural success rate.

However, higher mortality was seen with this approach mostly due to stent thrombosis rather than bleeding complications. Firstly, the prothrombotic circumstance caused by short application of fibrinolytic agents may have limited the benefit of PCI. Secondly, fibrinolytic agent would soften the fresh thrombus and divide them into small pieces. Thirdly, the differences in time

of reperfusion may affect first 2 hours after the onset of infarction, and the time interval can hardly be met in many of the included studies which enrolled patients with less than 12 hours, 6 hours or 3 hours of symptom onset. Therefore, the time-dependency of PCI-mediated salvage may be considerably attenuated.[4]

Rescue Percutaneous Coronary Intervention:

In this approach, those patients who suffer failed thrombolysis are treated with emergency PCI to salvage jeopardized myocardium. Failed thrombolysis usually manifests as persistent ischemic symptoms, hemodynamic instability and failure to achieve 50–70% resolution of maximal ST segment elevation at 90 minutes after initiation of infusion. This approach was proved to be more effective than repeat thrombolysis. However was inferior to Primary PCI.

Pharmacoinvasive PCI:

A strategy of combining fibrinolysis followed by transfer for early PCI has been shown to be an effective reperfusion strategy for STEMI patients presenting to non-PCI hospitals compared with fibrinolysis alone.

In contrast to facilitated PCI, this approach includes PCI which follows fibrinolysis after some delay so that early prothrombotic phase would get resolved preventing the increased incidence of stent thrombosis. This strategy aims at reduction of mortality seen with facilitated PCI.

Pharmacoinvasive strategy consists of administration of fibrinolysis at a non-PCI centre followed by immediate transfer to a PCI-capable hospital for routine early catheterization performed within 2–24 hours of start of fibrinolytic therapy, regardless of whether thrombolysis results in successful reperfusion or not. Thus, the time to PCI is longer than with facilitated PCI.[5]

In the recent past, several clinical trials and patient registries using pharmaco invasive strategy [GRACIA-2 [6] (Grupo de Análisis de la Cardiopatía Isquémica Aguda) TRANSFER-AMI[7] (Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction), FAST-MI (French Registry of Acute ST-elevation or Non-ST-elevation Myocardial Infarction),[8] WEST[9]] have demonstrated mortality that is comparable to that documented with primary PCI. These trials reinforced that pharmacologic regimen rapidly delivered, coupled with routine coronary intervention within 24 hours of initial treatment, may not be different from timely expert PCI.

STREAM Study [10] ,evaluated whether a fibrinolytic-therapy approach consisting of prehospital or early fibrinolysis with contemporary anti platelet and anticoagulant therapy, coupled with timely coronary angiography, provides a clinical outcome similar to that with primary PCI in patients with STEMI who present early after symptom onset. In this trial, 1,892 patients with STEMI who presented within 3 hours after symptom onset were randomly assigned to undergo either primary PCI or fibrinolytic therapy with bolus tenecteplase clopidogrel, and enoxaparin before transport to a PCI-capable hospital. If fibrinolysis failed, emergency angiography was performed otherwise; it was performed after 6–24 hours. Emergency angiography was required in 36.3% patients whereas the remainder of patients underwent angiography at a median of 17 hours after randomization. Thus, early prehospital fibrinolysis along with antithrombotics coupled with timely coronary angiography resulted in effective reperfusion in patients who presented within 3 hours after symptom onset. However, increased risk of intracranial bleeding was a concern with early fibrinolytic therapy.[10]

STREAM-2[11] (Strategic Reperfusion in Elderly Patients Early After Myocardial Infarction) was an investigator-initiated, open-label, randomized, multicenter study. Patients e"60 years of age with e"2 mm ST-segment elevation in 2 contiguous leads, unable to undergo primary PCI within 1 hour, were randomly assigned (2:1) to half-dose tenecteplase followed by coronary angiography and PCI (if indicated) 6 to 24 hours after randomization, or to primary PCI. Efficacy end points of primary interest were ST resolution and

the 30-day composite of death, shock, heart failure, or reinfarction. Safety assessments included stroke and non-intracranial bleeding.

In this study with Half dose of tenecteplase in a pharmaco-invasive strategy in this early-presenting, older STEMI population was associated with electrocardiographic changes that were at least comparable to those after primary PCI. Similar clinical efficacy and angiographic end points occurred in both treatment groups. The risk of intracranial hemorrhage was higher with half-dose tenecteplase than with primary PCI. If timely PCI is unavailable, this pharmaco-invasive strategy is a reasonable alternative, provided that contraindications to fibrinolysis are observed and excess anticoagulation is avoided.[11]

Summarising, primary PCI is the best reperfusion strategy in STEMI. Pharmacoinvasive therapy has proven to be as effective as primary PCI. All other strategies such as facilitated PCI and rescue PCI are inferior.

FIG-5 Selection of non–ST-segment elevation acute coronary syndrome treatment strategy and timing according to initial risk stratification. (Adapted from Collet J-P, et al. 2020 ESC Guideline for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2020; 42(14):1289–1367.

PREPOROCEDURE CONSIDERATIONS:

REPERFUSION STRATEGIES IN NSTEMI/UA

In patients with Unstable angina/NSTEMI, the management decision starts with risk assessment. The following figure 3 summarises the indications for PCI after risk assessment.

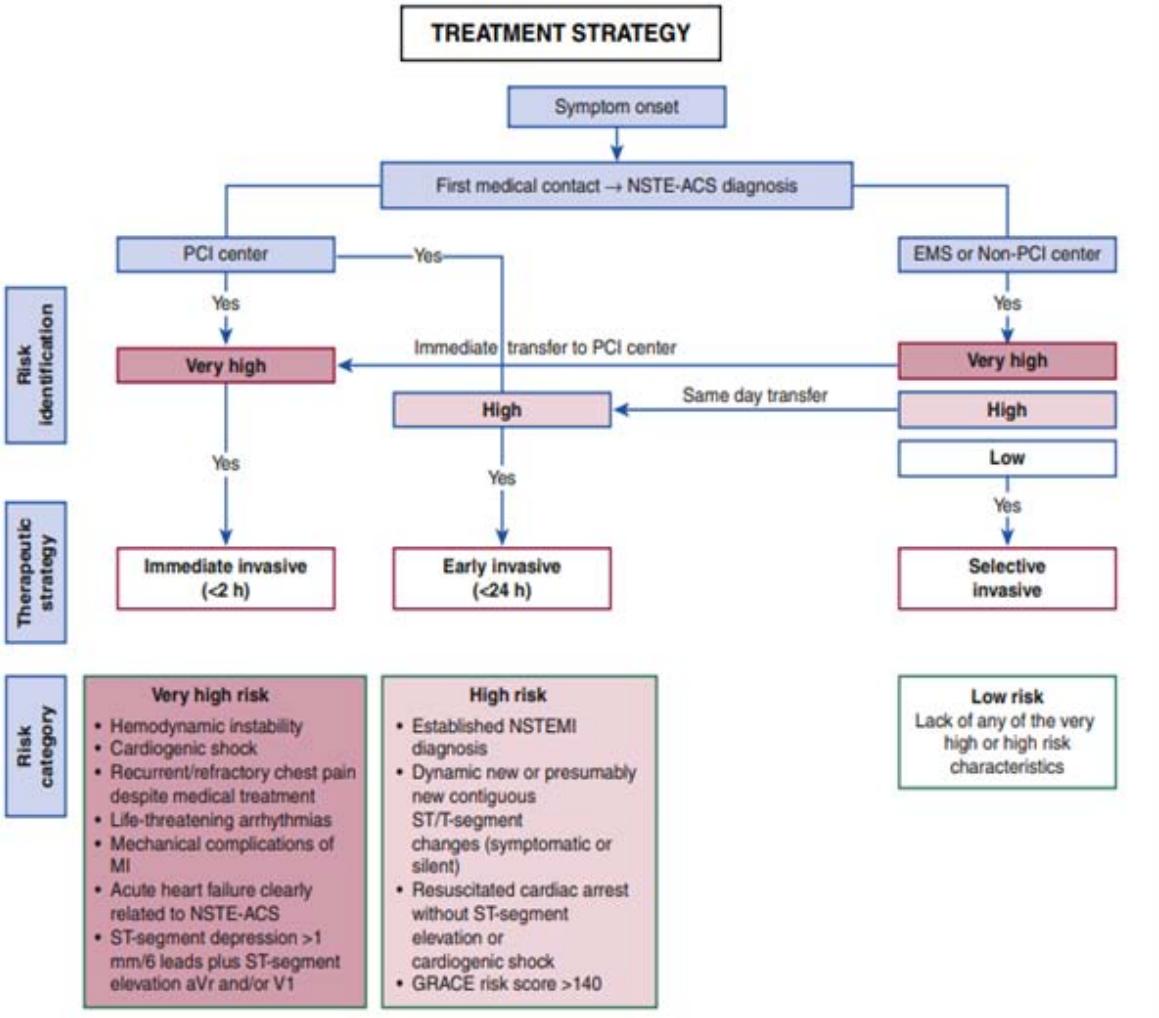


Figure 2 summarises the approach to reperfusion in patients with STEMI

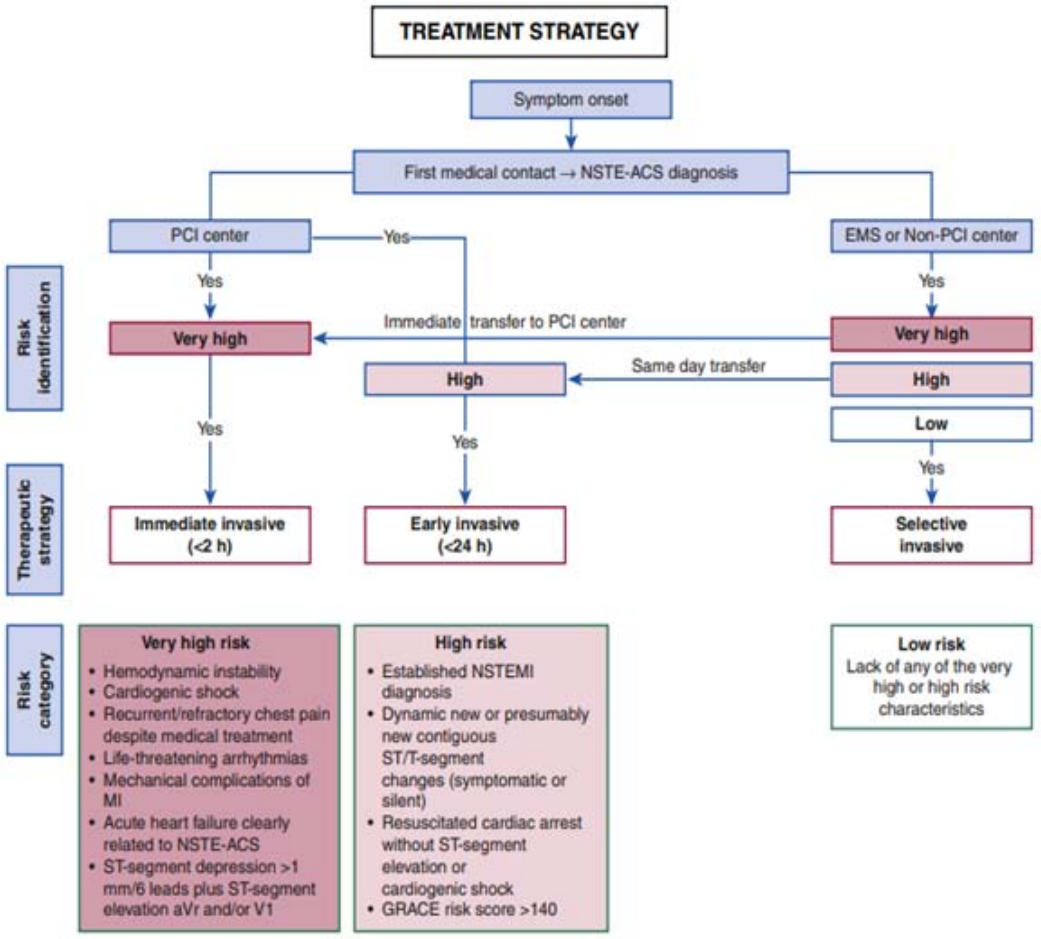


Figure 3 : FIG-5 Selection of non–ST-segment elevation acute coronary syndrome treatment strategy and timing according to initial risk stratification. (Adapted from Collet J-P, et al. 2020 ESC Guideline for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2020; 42(14):1289–1367.

Pre-Procedure Considerations

Access site selection (radial vs. femoral)

Possible access sites for coronary angiography are the femoral artery and the radial artery. Although the radial access approach is associated with fewer vascular and bleeding complications, femoral access is still commonly used because, it allows for larger diameter equipment that could be necessary in case of PCI. In addition, accessing from the femoral artery usually grants an easier advancement of the catheter to the aortic root due to the lack of tortuosity in the descending aorta.

Radial access should always be considered first, before resorting to the femoral approach, as it has shown mortality benefit in primary PCI.[12]

Femoral is preferred over radial access in case of patient is in cardiogenic shock, feeble peripheral pulse and requiring IABP support.

Choice of anticoagulants and antiplatelet agents

A. Give oral antiplatelet therapy (in addition to aspirin) to all patients:

1. **Patients treated with fibrinolytic therapy:** Give clopidogrel loading dose 300 mg if age 75 years or less; if age over 75 years, give loading dose of 75 mg.
2. **Patients treated with no reperfusion therapy:** Give ticagrelor loading dose 180 mg.
3. **Patients treated with primary PCI:** Give

ticagrelor loading dose of 180 mg or prasugrel loading dose of 60 mg (if no contraindications: prior stroke or TIA, or relative contraindications for prasugrel such as those age 75 years or older, weight less than 60 kg). For patients at high risk of bleeding or those for whom prasugrel or ticagrelor cannot be used, give clopidogrel 600 mg

B. Give anticoagulant therapy to all patients:

1. **For patients treated with primary PCI,** prefer UFH to bivalirudin. This recommendation assumes that patients will receive a potent oral antiplatelet agent (ticagrelor or prasugrel), which is preferred to clopidogrel.

- **Dosing of UFH:** An initial IV bolus of **50 to 70 units/kg** up to a maximum of 5000 units. Additional heparin may be given in the catheterization laboratory based on the results of ACT monitoring.
- **Dosing of bivalirudin:** Initial bolus of **0.75 mg/kg IV followed by IV infusion of 1.75 mg/kg per hour**; can be discontinued after PCI.

2. **For patients treated with fibrinolysis,** prefer enoxaparin for patients not at high bleeding risk or fondaparinux for those at high bleeding risk. For those patients in whom PCI is possible or likely after fibrinolytic therapy, UFH is reasonable

- **Dosing of enoxaparin**
- Patients <75 years: Loading dose of 30 mg IV bolus followed by 1 mg/kg subcutaneously every 12 hours; maximum of 100 mg for the first 2 subcutaneous doses. The first subcutaneous dose should be administered with the IV bolus.

o Dose adjustment for renal impairment (CrCl <30 mL/minute): Loading dose of 30 mg IV followed by 1 mg/kg subcutaneously every 24 hours. The first subcutaneous dose should be administered with the IV bolus.

- Patients e"75 years: No IV loading dose. Administer 0.75 mg/kg subcutaneously every 12 hours; maximum of 75 mg for the first 2 doses.

o Dose adjustment for renal impairment (CrCl <30 mL/minute): No IV loading dose. Administer 1 mg/kg subcutaneously every 24 hours.

- Supplemental IV bolus dose for patients who will receive PCI after >1 dose of therapeutic enoxaparin: 0.3 mg/kg if last enoxaparin dose was given 8 to 12 hours earlier; no supplemental IV dose if last enoxaparin dose was within 8 hours; use UFH if last enoxaparin dose was more than 12 hours ago.

§ **Dosing of UFH:** IV bolus of 60 to 100 units/kg to a maximum of 4000 units, followed by an IV infusion of 12 units/kg per hour (maximum 1000 units per hour) adjusted to achieve a goal aPTT of approximately 50 to 70 seconds (1.5 to 2 times control).

- **Dosing of fondaparinux:** 2.5 mg intravenously, followed by 2.5 mg subcutaneously every 24 hours. This drug should be avoided in CrCl <30 mL/minute.

3. **For patients not receiving reperfusion therapy,** we can use enoxaparin or UFH.

Procedure Steps

1. Access site preparation:

Both radial and femoral sites are prepared for access. Cleaning and draping of access site is done. After that radial or femoral access is attained and 5fr sheaths are used for coronary angiogram, 6 Fr sheaths are used for PCI.

2. Angiography and lesion assessment

For radial angiography 5fr Terumo Optitorque is used, for femoral approach, the diagnostic catheters most commonly used are the Judkins and the Amplatz catheters. Judkins catheters can be used both for the femoral and for the right/left radial approach.

After coronary angiogram, lesion assessment is done. The degree of the stenosis can be evaluated by comparing the minimum diameter of the vessel at the level of the lesion to the diameter of the adjacent segment upstream of the stenosis.

Stenoses are defined as minimal if the narrowing is visually less than 50%, moderate between 50% and 70%, and severe with diameter reduction 70% or more.[13] Evaluation of stenosis is most commonly estimated visually by the interventional cardiologist reading the angiogram.

3. Guidewire insertion and lesion crossing

0.014 x 180 or 0.014 x 190 cm guide wires are inserted into the vessel, for which the stenting is planned and care must be taken while crossing the lesion to avoid wire related dissections and thrombus formation, which leads to complete occlusion of vessel. If the vessel is already completely occluded, care must be taken to avoid vessel dissection as well as perforation.

4. Balloon angioplasty and stent deployment

After crossing the lesion, balloon angioplasty and appropriate stent deployment is done. Now a days most of the stents used are drug eluting stents.

5. Post-PCI angiography and optimization

After stent deployment, angiography is done to check the stent under expansion and post dilatation is done if necessary with non-compliant balloon for optimization. If imaging (IVUS,OCT) is used better results are attained.

Adjunctive Therapies

Glycoprotein IIb/IIIa inhibitors

The GP IIb/IIIa receptor is an integrin, a heterodimer consisting of noncovalently associated á and â subunits, which mediate the final common pathway of platelet aggregation. In specific, the GP IIb/IIIa receptor consists of the áIIb and â3 subunits. By competing with fibrinogen and vWF for GP IIb/IIIa binding, GP IIb/IIIa antagonists interfere with platelet cross-linking and platelet-derived thrombus formation . Because the GP IIb/IIIa receptor represents the final common pathway leading to platelet aggregation, these agents are very effective in inhibiting platelets

Three parenteral GP IIb/IIIa antagonists have been approved for clinical use: abciximab, eptifibatide, and tirofiban.

Timing of Glycoprotein IIb/IIIa Administration:

In summary, these agents are now not routinely used. They are indicated only in specific situations with residual thrombus burden, sub optimal result, residual dissection and no flow/slow flow. Pre

Table: 3 Characteristics of the Glycoprotein IIb/IIIa Inhibitors

	Abciximab	Eptifibatide	Tirofiban
Molecule	Fab 7E3	Synthetic peptide	Nonpeptide mimetic
Molecular weight	~50,000	~800	~500
Stoichiometry (drug to GP IIb/IIIa)	~1.5:1	≫100:1	≫100:1
Binding	Noncompetitive	Competitive	Competitive
Half-life	Plasma: 10–15 h Biologic: 12–24 h	Plasma: 2–2.5 h Biologic = plasma	Plasma: 2–2.5 h Biologic = plasma
PCI dosing	Bolus: 0.25 mg/kg (10–60 min) Infusion: 0.125 μg/kg/min (12 h)	Bolus: 180 μg/kg (10 min) + 180 μg/kg Infusion: 2 μg/kg/min (24–48 h)	Bolus: 25 μg/kg (30 min) Infusion: 0.10 μg/kg/min (48 h)
Renal adjustment	No	Bolus: 180 μg/kg Infusion: 1 μg/kg/min (24–48 h)	Bolus: 12.5 μg/kg (30 min) Infusion: 0.10 μg/kg/min (48 h)

Fab, Fragment antigen binding; *GP*, glycoprotein; *PCI*, percutaneous coronary intervention.

hospital administration was not found to be better than on table administration and intracoronary administration was not superior to IV administration.[14,15,16,17,18,19]

Thrombus aspiration

There are two main types of thrombectomy/ aspiration devices for coronary lesions, mainly for primary PCI during STEMI: simple catheter aspiration (such as Export and Pronto catheters), and mechanical aspiration (such as AngioJet and X-Sizer) . Initial trials showed promise, but later trials indicated no improvement in clinical outcomes with an increased rates of stroke.

Based on this evidence, routine aspiration thrombectomy was downgraded to a class III recommendation in the 2015 ACC/AHA STEMI guidelines.[20]

Distal protection devices

Presently there is no role for dital protection devices in primary PCI. [21,22,23]

Complications and Management

Percutaneous coronary intervention (PCI) is associated with rare but serious complications. Most of the complications are generic to all diagnostic coronary angiography procedures, and some are specific to coronary intervention. Events like death, myocardial infarction (MI), and bleeding occur at higher rates for interventional procedures since there is prolonged procedural time, complexity, and the use of anticoagulation.

Femoral Access Complications

1. **Pseudo-Aneurysm**

   Small pseudoaneurysms (<2 cm) often close spontaneously within 1 month. In larger pseudoaneurysms, or in small ones that fail to close, active treatment is necessary. The two most common treatment methods are ultrasound-guided compression or thrombin injection.

2. **Arteriovenous Fistula**

   This is recognized on physical examination by a palpable thrill or an audible continuous bruit. Unlike pseudoaneurysms, conservative treatment with watchful waiting is the most common treatment modality (90%). One-third of persistent AV fistulae will close during the first 12 months. Most persistent AV fistulae are asymptomatic and do not require repair. Rarely, they can be symptomatic (moderate pain) and, in large patient series, about 10% of AV fistulae will ultimately require surgical repair.

3. **Bleeding**

   The last and most dangerous complication of groin access is major femoral bleeding. Large femoral hematomas have an incidence of 2.8% compared to a 0.3% incidence of retroperitoneal bleeds. A retroperitoneal hematoma or a significant femoral hematoma (>5 cm) often requires blood transfusions and prolonged hospitalization. More significant bleeds can require surgery, and significant bleeding in relation to PCI has been shown to correlate with mortality. The bleeding complication of most concern is a retroperitoneal hematoma because large amounts of blood can fill the pelvic cavity, and shock can develop rapidly. If a retroperitoneal bleed is suspected , volume (crystalloid solutions) should be given and blood should be ordered immediately for transfusion as soon as available.

A vascular surgeon should also be consulted immediately. If the patient remains hemodynamically unstable despite volume resuscitation, surgery or endovascular repair (covered stent placement) may be needed; this occurs in approximately 16% of patients. However, the majority (84%) of cases can undergo a conservative "watchful waiting" strategy because the hematoma usually stabilizes from tamponade of the initial site of extravasation.

A computed tomography (CT) scan will be confirmative of the clinical diagnosis and should be ordered early to diagnose retroperitoneal hematoma and identify site of bleed. Most

retroperitoneal hematomas are caused by bleeding from the external iliac artery above the inguinal ligament or inferior epigastric artery. Rarely, bleeding below the inguinal ligament can track between tissue planes and extend into a retroperitoneal accumulation. Bleeding might also rarely extend to the scrotum through extension along the spermatic cord. Most cases of scrotal hematoma can also be managed conservatively with elevation and ice. However, rarely, large tense scrotal hematomas can cause significant pain and may compromise the viability of the scrotal skin and/or testicle, which would require urgent surgical exploration

Complications of Radial Access

1. **Radial Artery Occlusion (2%–10%):**

   The radial artery may not be found to be patent following radial catheterization procedures; however, in most instances, the consequence of this complication is felt to be quite benign. Giving adequate heparin, using vasodilators and attaining hemostasis without occluding the artery helps in preventing occlusion.

2. **Radial Artery Spasm (12%–22%)**

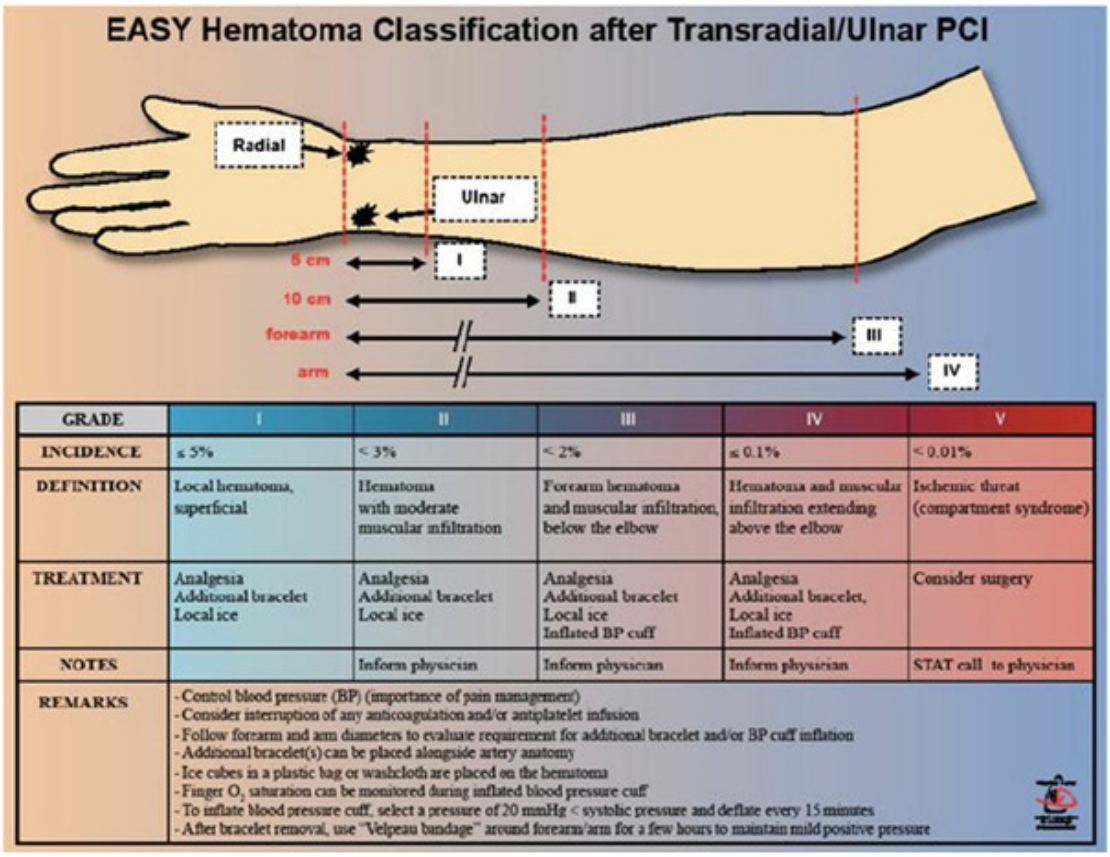
   Spasm of the vessel can occur and is frequently due to significant alpha1 adenoreceptors within the medial layer of the vessel; it is overcome and minimized by the use of vasodilators (e.g., intra-arterial verapamil and/or nitroglycerin). Occasionally, it has been reported that a severe spasm entraps the catheter or long sheath so that it cannot be withdrawn. This diffuse and severe spasm has been managed by increased sedation, sometimes requiring a local nerve block or induction of general anesthesia. Care should be taken to never "force" the withdrawal of a catheter or sheath when resistance has been met because radial artery evulsion has also been reported.

3. **Forearm Bleeding, Hematoma, and Compartment Syndrome**

   Bleeding within the forearm can arise if a perforation occurs anywhere within the course of the radial artery . This can occur particularly with the use of hydrophilic guidewires (as opposed to non-hydrophilic J-tipped wires) that can advance into small side branches without much appreciated resistance felt by the operator. Furthermore, navigating anatomic variants such as a radial recurrent loop also increases the risk of perforation. . Prevention can be achieved by avoiding hydrophilic straight guidewires for the most part. Bleeding must be recognized in the event of a hematoma or pain within the forearm after the procedure. If the sheath is still in place, angiography can demonstrate extravasation of contrast and thus the location of the bleed. Compression, often achieved with an ACE bandage wrapped around the entire forearm, and avoidance of further anticoagulation are often enough to avoid further complication. However bleeding into the forearm can result in increased pressure within the fascial planes and resultant compartment syndrome. This would be the most serious complication from radial artery catheterization because it threatens the entire hand and must be recognized and treated emergently. Measurement of interfascial pressure with a manometer confirms the diagnosis, and fasciotomy with hematoma evacuation remains the only treatment available. Fortunately, this is a very rare occurrence. Following figure 5 is the treatment algorithm for management of forearm hematomas.

Contrast Media Complications

Intravascular radiographic contrast media (RCM) can be associated with anaphylactoid reactions and acute renal failure. Fortunately, anaphylactoid reactions are rare, occurring in only 0.23% of procedures.



GRADE	I	II	III	IV	V
INCIDENCE	≤ 5%	< 3%	< 2%	≤ 0.1%	< 0.01%
DEFINITION	Local hematoma, superficial	Hematoma with moderate muscular infiltration	Forearm hematoma and muscular infiltration, below the elbow	Hematoma and muscular infiltration extending above the elbow	Ischemic threat (compartment syndrome)
TREATMENT	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice Inflated BP cuff	Analgesia Additional bracelet, Local ice Inflated BP cuff	Consider surgery
NOTES		Inform physician	Inform physician	Inform physician	STAT call to physician
REMARKS	- Control blood pressure (BP) (importance of pain management) - Consider interruption of any anticoagulation and/or antiplatelet infusion - Follow forearm and arm diameters to evaluate requirement for additional bracelet and/or BP cuff inflation - Additional bracelet(s) can be placed alongside artery anatomy - Ice cubes in a plastic bag or washcloth are placed on the hematoma - Finger O_2 saturation can be monitored during inflated blood pressure cuff - To inflate blood pressure cuff, select a pressure of 20 mmHg < systolic pressure and deflate every 15 minutes - After bracelet removal, use "Velpeau bandage" around forearm/arm for a few hours to maintain mild positive pressure				

Fig. 5 Proposed upper extremity hematoma classification system from the EASY trial. (Reproduced with permission from: Bertrand OF. Acute forearm muscle swelling post transradial catheterization and compartment syndrome: prevention is better than treatment! Catheter Cardio Inte 2010;75:366 – 8)

Contrast-Induced Nephropathy (CIN)

Intravascular contrast media also can put the patient at risk for acute renal failure following PCI. This contrast-induced nephropathy (CIN) is likely caused by acute tubular necrosis. Mehran et al. developed a validated risk scoring system in order to predict the likelihood of developing CIN (see Fig. 6).

The use of iso-osmolar contrast agents, sodium bicarbonate intravenous fluids, or N-acetylcysteine (600–1200 mg PO bid × 4 doses) are also purported to be effective, but the supporting data for each are weak. All other potential therapies, including diuretics, mannitol, dopamine, fenoldopam, or theophylline, have not been consistently proved to work for preventing CIN and should not be used.

Medication regimen after PCI

Anticoagulation is stopped after PCI in ACS unless there is another indication to continue anticoagulation.

DAPT should be continued up to minimum of 12 months,which was summariesd in the fig 7

SUMMARY:

ACS continues to be a major cause of mortality and morbidity related to heart diseases. Percutaneous coronary intervention done at the proper time saves many lives. Understanding how to treat and when to refer a patient with ACS goes a long way in mitigating the risks of ACS.

Table 4 The Mehran risk score for the prediction of CIN[9]

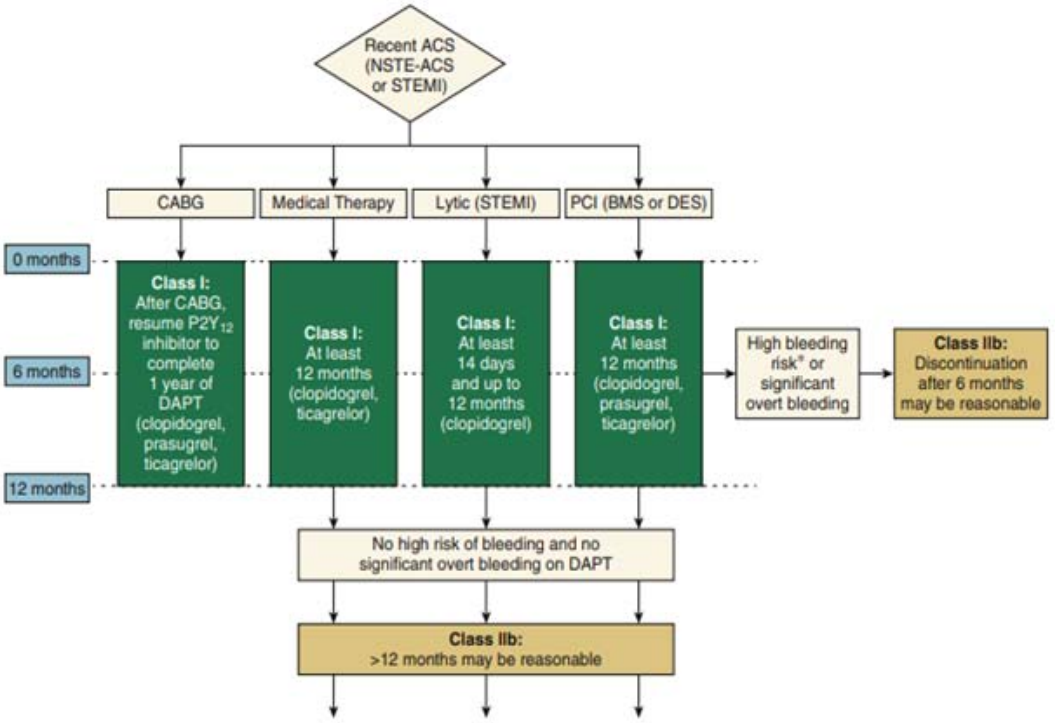
Mehran score periprocedural CIN risk factor	Score
Hypotension (SBP <80 mm Hg or >1 h of inotropic support)	5
Intra-arterial balloon pump therapy	5
Chronic heart failure, (NYHA III/IV or recent pulmonary oedema)	5
Age >75 years	4
Diabetes mellitus	3
Anaemia (male: HCT<0.39, female: HCT<0.36)	3
Estimated glomerular filtration rate <20 mL/min	6
Estimated glomerular filtration rate 20–40 mL/min	4
Estimated glomerular filtration rate 40–60 mL/min	2
Contrast media volume	1 per cc

Score	<5	6–10	11–16	>16
CIN risk	Low 7.5%	Moderate 14%	High 26.1%	Very high 57.3%
Dialysis risk	0.04%	0.12%	1.09%	12.6%

CIN, contrast-induced nephropathy; HCT, haematocrit; NYHA, New York Heart Failure Association; SBP, systolic blood pressure.

Mehran et al. *JACC* 2004;44:1393-1399.

Fig 6 : CIN is typically defined as a relative increase in serum creatinine of greater than 25% or an absolute increase of greater than 0.5 mg/dL. While it is not uncommon to develop transient increases in serum creatinine, it is rare to need temporary dialysis and even rarer to need permanent dialysis following CIN. The time course of CIN demonstrates an increase in creatinine starting in 12–24 hours for most patients, but it may take as long as 48–96 hours to peak. Most cases show a return to baseline creatinine by days 3–5 but can take up to 7–10 days. Serum creatinine should be routinely obtained at 48–72 hours following contrast administration in a high-risk patient. In high-risk patients, CIN prevention consists of two principles: adequate hydration and limitation of the volume of contrast administered.



Treatment algorithm for the duration of P2Y12 inhibitor therapy in patients with recent acute coronary syndrome (NSTE-ACS or STEMI). Arrows at the bottom of the figure denote that the optimal duration of prolonged DAPT is not established. Aspirin therapy is almost always continued indefinitely in patients with coronary artery disease. *High bleeding risk denotes those who have or develop a high risk of bleeding (e.g., treatment with oral anticoagulant therapy) or are at increased risk of severe bleeding complication (e.g., major intracranial surgery). BMS, Bare-metal stent; CABG, coronary artery bypass graft surgery; DAPT, dual-antiplatelet therapy; DES, drug-eluting stent; lytic, fibrinolytic therapy; NSTE-ACS, non–ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction. (From Levine GN, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016;68(10):1082–1115.)

References

1. Gruntzig A. Transluminal dilatation of coronary-artery stenosis. Lancet. 1978;1:263

2. Levine GN, Kern MJ, Berger PB, et a!.; American Heart Association Diagnostic and Interventional Catheterization Committee and Council on Clinical Cardiology Management of patients undergoing percutaneous coronary revascularization. Ann Intern Med 2003;139:123-136

3. . Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review of 23 randomised trials. Lancet. 2003;361:13-20.

4. Ellis SG, Tendera M, de Belder MA, et al. Facilitated PCI in patients with STelevation myocardial infarction. N Engl J Med. 2008;358:2205-17.

5. Hanna EB, Hennebry TA, Abu-Fadel MS. Combined reperfusion strategies in ST-segment elevation MI: Rationale and current role. Cleve Clin J Med. 2010;77(9):629-38.

6. Ferna'ndez-Avile's F, Alonso JJ, Pena A, et al. Primary angioplasty vs. early routine post fibrinolysis angioplasty for acute myocardial infarction with ST segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. Eur Heart J. 2007;28:949-60.

7. Cantor WJ, Fitchett D, Borgundvaag B, et al. Routine Early Angioplasty after Fibrinolysis for Acute Myocardial Infarction. N Engl J Med. 2009;360:2705-18.

8. Danchin N, Coste R, Ferrières J, et al. Comparison of Thrombolysis Followed by Broad Use of Percutaneous Intervention with Primary Percutaneous Coronary Intervention for ST-Segment Elevation Acute Myocardial Infarction: Data from the French Coronary Registry on Acute ST-Elevation (FAST-MI). Circulation. 2008;118:268-76.

9. Armstrong PW. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after STelevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. Eur Heart J. 2006;2711:530-8

10. Armstrong PW, Gershlick AH, Goldstein P, et al. Fibrinolysis or primary PCI in Cardiological ST-segment elevation myocardial infarction. N Engl J Med. 2013;368:1379-87.

11. Van de Werf F, Ristiæ AD, Averkov OV, Arias-Mendoza A, Lambert Y, Kerr Saraiva JF, Sepulveda P, Rosell-Ortiz F, French JK, Musiæ LB, Vandenberghe K, Bogaerts K, Westerhout CM, Pagès A, Danays T, Bainey KR, Sinnaeve P, Goldstein P, Welsh RC, Armstrong PW; STREAM-2 Investigators. STREAM-2: Half-

Dose Tenecteplase or Primary Percutaneous Coronary Intervention in Older Patients With ST-Segment-Elevation Myocardial Infarction: A Randomized, Open-Label Trial. Circulation. 2023 Aug 29;148(9):753-764. doi: 10.1161/CIRCULATIONAHA.123.064521. Epub 2023 Jul 13. PMID: 37439219

12. Yusuf Sÿþ, Cairns Jÿþ, et al; RIVAL Trial Group. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. ÿþ *Lancet*. 2011;377(9775):1409-1420. doi:10.1016/S0140-6736(11)60404-2

13. Bhatt DL. Cardiovascular Intervention: A Companion to Braunwald's Heart Disease. 1st ed. 2015

14. Giugliano RP, White JA, Bode C, et al. Early versus delayed, provisional eptifibatide in acute coronary syndromes. N Engl J Med. 2009;360:2176–2190.

15. De Luca G, Suryapranata H, Stone GW, et al. Abciximab as adjunctive therapy to reperfusion in acute ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. JAMA. 2005;293:1759–1765.

16. Mehilli J, Kastrati A, Schulz S, et al. Abciximab in patients with acute ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention after clopidogrel loading: a randomized double-blind trial. Circulation. 2009;119:1933–1940.

17. Ellis SG, Tendera M, de Belder MA, et al. Facilitated PCI in patients with ST-elevation myocardial infarction. N Engl J Med. 2008;358:2205–2217.

18. Shimada YJ, Nakra NC, Fox JT, et al. Meta-analysis of prospective randomized controlled trials comparing intracoronary versus intravenous abciximab in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Am J Cardiol. 2012;109(5):624–628.

19. Thiele H, Wöhrle J, Hambrecht R, et al. Intracoronary versus intravenous bolus abciximab during primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction: a randomised trial. Lancet. 2012;379(9819):923–931.

20. Jolly SS, Cairns JA, Yusuf S, et al. Randomized trial of primary PCI with or without routine manual thrombectomy. N Engl J Med. 2015;372:1389–1398.

21. . Baim DS, Wahr D, George B, et al. Saphenous vein graft angioplasty free of emboli randomized trial I. Randomized trial of a distal embolic protection device during percutaneous intervention of saphenous vein aorto-coronary bypass grafts. Circulation. 2002;105(11):1285–1290.

22. Stone GW, Webb J, Cox DA, et al. Distal microcirculatory protection during percutaneous coronary intervention in acute ST-segment elevation myocardial infarction: a randomized controlled trial. JAMA. 2005;293(9):1063–1072.

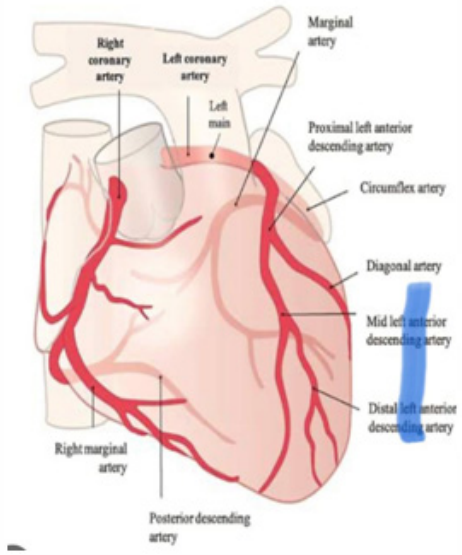
23. Kelbaek H, Terkelsen CJ, Helqvist S, et al. Randomized comparison of distal protection versus conventional treatment in primary percutaneous coronary intervention: the drug elution and distal protection in ST-elevation myocardial infarction (DEDICATION) trial. J Am Coll Cardiol. 2008;51(9):899–905.

Surgical Management of Ischemic Heart Disease Patient

Prof (Dr) Santanu Dutta
Professor, Department of Cardio-thoracic & Vascular Surgery
Institute of Post Graduate Medical Education & Research , Centre of Excellence,Kolkata – 700020
E-mail: dr.santanudutta14@gmaill.com

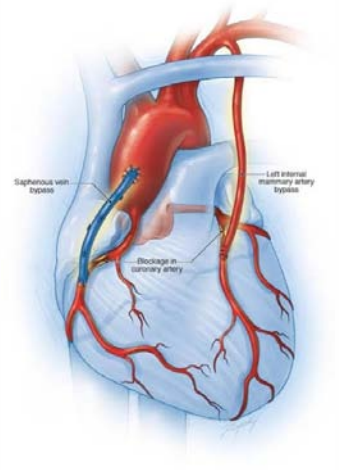
Introduction

- Coronary circulation- It is the circulation of blood in the blood vessels of the heart muscle (myocardium).
- The heart muscle needs oxygen-rich blood to function, coronary arteries supply blood to the heart muscle.
- The coronary arteries wrap around the outside of the heart.
- Since the coronary arteries deliver blood to the heart muscle,
- Any disorder or disease of the coronary arteries can have serious implications by reducing the flow of oxygen and nutrients to the heart muscle.
- This can lead to ischemia and fibrosis of heart muscle and possibly sudden death of the patient.



Coronary Artery Bypass Grafting (CABG)

- It involves the bypass of a blockage in one or more of the coronary arteries using conduits like the saphenous veins(RSVG), Internal mammary artery(LIMA;RIMA), radial artery or Gastroepiploic artery.
- It is done on Cardio Pulmonary Bypass or Off CPB (OP-CABG).



INDICATIONS (AHA Class I and IIA) (Table 1)

Procedure (OP-CABG)

- In supine position under general anesthesia.
- Chest is opened via median sternotomy.
- Conduits are harvested.

LIMA

- After median sternotomy, the parietal pleura and pericardium are depressed gently.
- The course of the internal thoracic artery is identified from its origin near the first rib

Table 1

COR	LOE	Clinical or Anatomic Setting
I	A	One or more significant (>70%) coronary artery stenoses amenable to revascularization and unacceptable angina despite best medical therapy *(consider PCI as alternative)*
I	B	Unprotected left main disease (>50%)
I	B	Triple-vessel disease with or without proximal LAD artery disease
I	B	Survivors of sudden cardiac death with ischemia-mediated ventricular tachycardia
I	B	Double-vessel disease with proximal LAD artery disease
I	B	Emergency CABG after failed PCI in presence of ongoing ischemia or threatened occlusion with substantial myocardium at risk (without impaired coagulation and without a previous sternotomy); surgical repair of a postinfarction mechanical complication (i.e., septal or free wall rupture)
I	B	Emergency CABG in patients with cardiogenic shock, suitable for CABG irrespective of time interval from MI to onset of shock and time from MI to CABG.
I	C	Patients undergoing noncoronary cardiac surgery with left main disease (>50%) or any other CAD (>70%)
I	C	Heart team approach recommended for unprotected left main disease or complex CAD
IIa	B	CABG over PCI in patients with complex triple-vessel CAD (i.e., SYNTAX > 22)
IIa	B	Double-vessel disease without proximal LAD disease with extensive ischemia
IIa	B	Single-vessel proximal LAD disease with LITA for long-term benefit
IIa	B	CAD with left ventricular ejection fraction 35% to 50%
IIa	B	Hybrid (LITA to LAD artery CABG + PCI for non-LAD arteries) for limitation for CABG (unsuitable conduits) or unfavorable LAD artery for PCI

CABG, Coronary artery bypass grafting; *CAD,* coronary artery disease; *COR,* class of recommendation; *LAD,* left anterior descending; *LITA,* left internal thoracic artery; *LOE,* level of evidence; *MI,* myocardial infarction; *PCI,* percutaneous coronary intervention.
Derived from 2011 AHA/ACC guidelines for CABG.[43]

to its termination beyond its bifurcation in the rectus sheath.

- A Favaloro retractor provides excellent exposure.
- The internal thoracic artery is usually harvested as a pedicle with extensive use of electrocautery for chest wall hemostasis but not pedicle hemostasis.
- The internal thoracic artery is usually harvested as a pedicle with extensive use of electrocautery for chest wall hemostasis but not pedicle hemostasis.
- Because the internal thoracic artery is a delicate structure, any undue stretching, clamping, or misplaced metal clips results in permanent vascular injury and therefore unsatisfactory short- and long-term results.
- Excessive traction during mobilization should be avoided as it can lead to dissection of the vessel wall.
- When the patient's condition is unstable, it may be preferable to harvest the internal thoracic artery while the patient is on cardiopulmonary bypass.
- Before the distal end of the internal thoracic artery is divided, its correct length must be ascertained.
- The internal thoracic pedicle should lie very comfortably on the heart when it is full and the lungs are fully inflated.
- Similarly, it should not be redundant because too long a pedicle may curl or kink into the substernal area, increasing the risk of injury at reoperation.

Radial artery

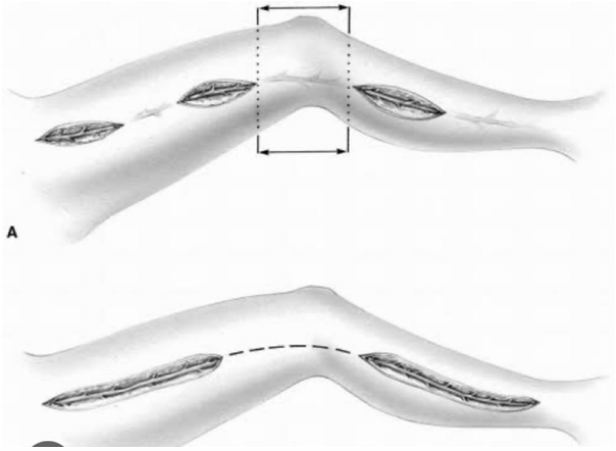
- Usually, the nondominant arm is identified preoperatively for radial artery harvest.
- Intravenous catheters and venipunctures are avoided in this arm.
- Allen test is performed using a Doppler probe to ensure adequate ulnar artery filling of the palmar arch.
- The distal portion of the radial artery tends to calcify. Unless the extra length is needed, the most distal segment of the artery should not be harvested and left *in situ.*
- The superficial radial nerve provides cutaneous innervation to the radial aspect of the thumb and dorsum of the hand. It follows the middle third of the radial artery and is prone to injury.
- Similarly, excessive lateral retraction of the brachioradialis muscle may lead to injury to

this nerve and resultant numbness of the thumb.

- The dissection of the radial artery begins distally by dividing the fascia and then proceeding proximally between the belly of the brachioradialis and flexor carpiradialis muscles.
- A vessel loop is then passed around the radial artery to facilitate exposure. The artery is dissected along with the two venae comitantes, double clipping and sharply dividing all the branches.
- When the radial artery is completely mobilized, the radial recurrent artery is identified proximally and the superficial palmar artery is seen distally. These two large branches define the limits of the dissection and should be preserved.
- The radial artery is divided distally and proximally and placed in a solution of heparinized blood and papaverine.
- The distal limit of the skin incision should be 3 cm above the wrist joint to decrease postoperative discomfort.
- The distal end of the radial artery is dissected free of the accompanying veins and surrounding tissue. An oblique opening is created, which can be enlarged to match the coronary artery opening by making a short longitudinal incision at the heel.

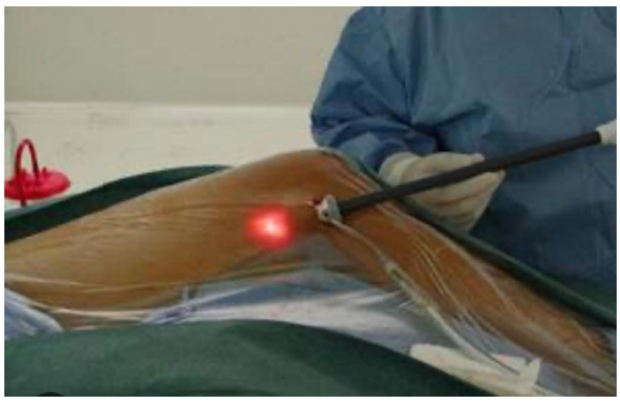
Great Saphenous vein Harvest

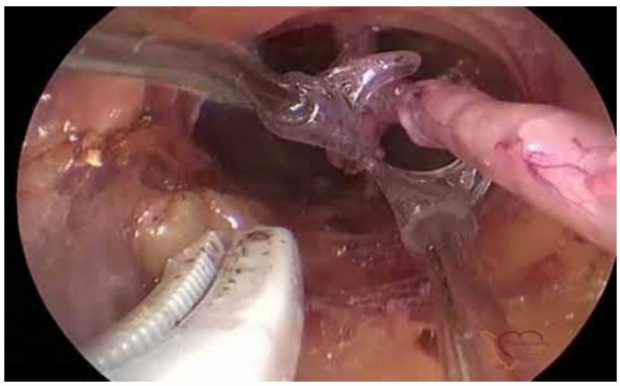
- After preoperative examination of both legs using color doppler, with the patient erect, and with ultrasonic imaging when indicated, the right or left greater saphenous vein is chosen for removal.
- Presence of superficial varicosities does not indicate an unusable saphenous vein. However, wound healing may be poor in such extremities.
- If possible, a leg without varicosities is chosen; multiple large varicosities in the saphenous vein render it unsuitable.
- For removal of the greater saphenous vein, the leg is abducted and the knee flexed about 45 degrees and supported.
- If the vein from the lower leg is to be used, the initial skin incision is made just anterior to the medial malleolus. If the upper portion of the vein will be used, the initial skin incision is made in the groin.
- A continuous incision or multiple small incisions over the length of the vein may be used.
- Care is taken to preserve the saphenous nerve.



- Whenever possible, a single long segment (usually 50-65 cm) of the greater saphenous vein is removed. About 12 to 15 cm may be needed for diagonal branches of the LAD, about 20 to 24 cm for marginal Cx branches, and about 18 to 22 cm for the RCA and its branches.
- So long as the external diameter of the vein is greater than about 3.0 to 3.5 mm, vein width is probably not an important consideration
- When the usable vein has been exposed and its length measured, the proximal (femoral) end is isolated and divided between ligatures. A vascular clamp is placed on the vein to mark what will become the *distal* end of the graft.

- Branches should be ligated or clipped flush with the saphenous vein to avoid creating diverticula, which can be the nidus for thrombus formation.
- Alternatively, the greater saphenous vein can be removed endoscopically. Using small transverse or vertical incisions, a lighted dissector is introduced into the wounds. A plane of dissection anterior to the vein is established with a balloon-tipped dilator or other device and the dissector used to isolate the vein and its branches.

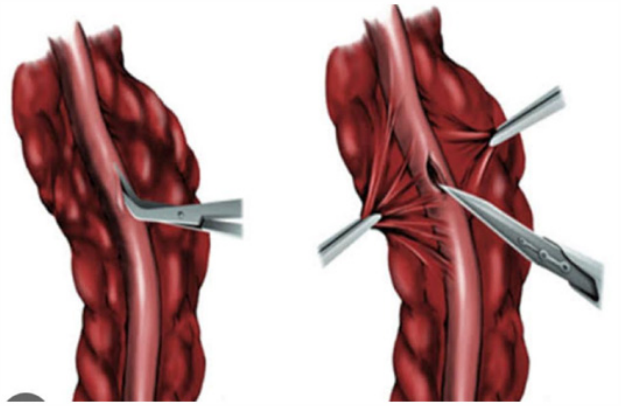




- The branches are clipped and divided with a cautery, and after ligating its proximal and distal ends, the vein is removed. Time required to remove veins with this technique is somewhat longer than with the conventional method, but a lower prevalence of leg wound complications and leg discomfort have been observed.
- When the wanted vessels are harvested , the patient is given heparin to prevent the blood from clotting.
- One end of each graft is sewn on to the coronary arteries beyond the blockages and the other end (in cases of reversed venous graft)is attached to the aorta.

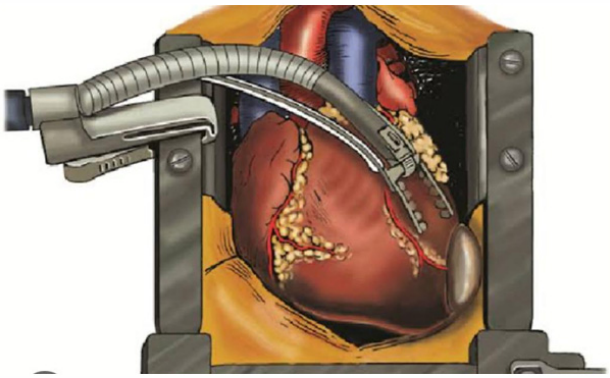
General Principles of Arteriotomy

- An appropriate site for arteriotomy is selected. This site should be, as much as possible, free of any gross disease. The epicardium overlying the coronary artery is incised and spread sideways.
- This allows better inspection of the coronary artery wall. After the exact site of arteriotomy has been established, a pointed no.11 blade is used to incise the anterior wall of the coronary artery.

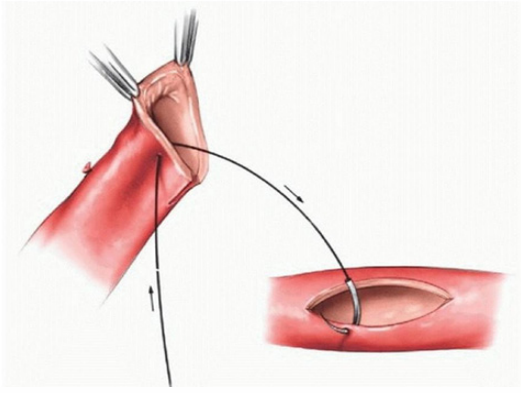


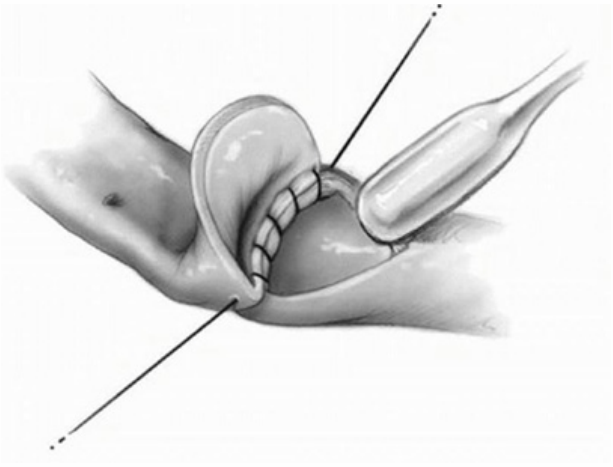
- The surgeon must memorize the precise anatomy of the coronary arteries as depicted in the angiogram so that the bypass graft is placed distal to the site of obstruction of the coronary artery.
- Care must be taken to perform the arteriotomy in the midline of the coronary artery. An oblique incision results in distortion of the artery at the heel or toe of the anastomosis.
- Special precautions must be taken not to damage the posterior wall of the coronary artery. This can happen if the angle of the blade is perpendicular to the vessel. The angle should always be approximately 45 degrees with respect to the coronary artery.
- A laparotomy pad is placed into the pericardium behind the heart and through strategic placement of deep pericardial sutures.

- This maneuver usually exposes the anterior surface of the heart quite well. The LAD, diagonal, and, with some minor adjustments, ramus intermedius coronary arteries can be viewed with ease.
- There are several devices that can locally immobilize the target coronary artery during off-pump surgery.
- The Acrobat System utilizes both suction and compression to stabilize the target vessel.
- The Octopus System obtains stabilization by applying high-pressure suction to the surrounding tissue through multiple suction cups.



- The arteriotomy is enlarged to a length of 5 to 7 mm with Potts scissors.
- The distal end of the conduit must be tailored to have an oblique, hood-shaped lumen with a circumference at least 25% larger than that of the arteriotomy.
- The distal anastomosis is started with, 7-0 or 8-0 Prolene sutures.





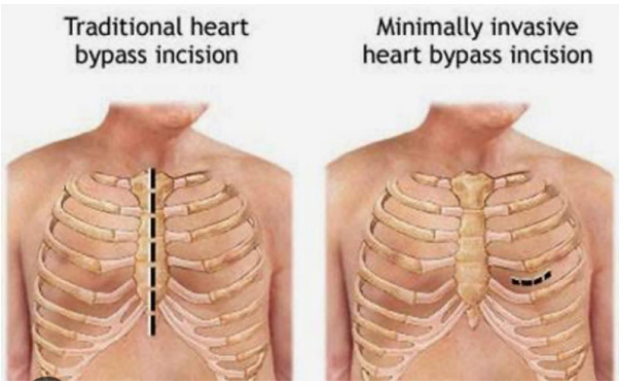
- A probe can be left in the lumen of the coronary artery to stop the flow of blood and allow accurate placement of stitches.
- Traditionally, the vein or the thoracic artery is held by the assistant surgeon with two atraumatic forceps. The forceps ideally should hold the adventitial tissue of the conduit.
- The epicardial tissue on each side of the coronary arteriotomy is very often incorporated into the suturing process to ensure a more secure anastomosis.
- The pedicle of the internal thoracic artery is tacked to the epicardium on each side of the anastomotic site with simple 6-0 Prolene sutures. This prevents the pedicle from twisting on itself and therefore obstructing flow through the vessel.
- The proximal anastomoses are performed with a side-biting clamp applied to the aorta.
- The circumference of the vein graft must be at least 20% larger than the aortic opening; otherwise, the vein stretches out flat and compromises the lumen.
- Placement of proximal anastomoses should be on the normal aortic wall. Calcific sites should be avoided.
- With a no. 11 blade, a 3- to 4-mm slit-like incision is made at a precise site for each proximal anastomosis. The opening is dilated slightly with the tip of a fine forceps.

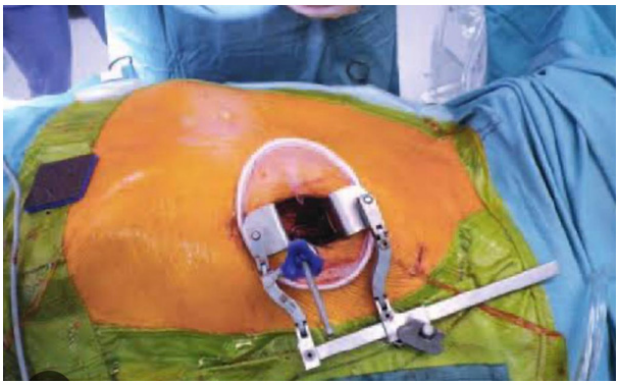
A disposable punch is introduced into the slit-like opening, and a circular part of the aortic wall, 4.0 to 4.8 mm in diameter, is removed.

- The proximal anastomosis is done with a 5-0 or 6-0 Prolene double-armed suture.
- Protamine given to reverse effect of heparin and haemostasias achieved.
- Chest tubes are placed in the mediastinal and pleural space if required to drain blood from around the heart and lungs.
- The sternum is wired together and the incisions are sutured closed.

Minimally invasive direct coronary artery bypass (MIDCAB)

- It is done with a small incision between the ribs in 4th or 5th ICS lateral to left sternal border.
- Both LIMA harvest and bypass anastomosis done via same incision.
- LIMA harvest can also be done using Robotics via 3 small ports in left anterior axillary line followed by anastomosis done through left 4th ICS.
- It is less painful with minimal blood loss.
- There is lower risk of complications.
- Short term hospital stays.
- Less wound site complications.





Complications of CABG

- Postoperative Bleeding
- Perioperative Myocardial Infarction (may be secondary to graft-related problems or native coronary artery problems)
- Neurologic deficit (due to cerebral emboli, hypoperfusion, or inflammation related to CPB).
- Postoperative Renal Dysfunction (risk factors include age older than 70 years, diabetes mellitus, chronic kidney disease, CHF, reoperation, prolonged CPB times,preoperative anaemia, perioperative transfusion)
- Postoperative atrial fibrillation (POAF) develops in 20% to 40% of patients undergoing CABG, with a peak incidence on the second and third postoperative days. It is usually transient and most patients return to sinus rhythm within 2 to 3 days of treatment.
- Sternal wound infections (more common in advanced age, male sex, COPD, obesity, diabetes mellitus, smoking history, steroid use, renal insufficiency, nonelective surgery, repeat operations, long operative times, re-exploration for bleeding patients)

Mechanical Complications of Myocardial Infarction

The mechanical complications of acute myocardial infarction have serious clinical implications and are generally associated with a poor prognosis.

Necrosis of the free ventricular wall may cause acute myocardial rupture.

Necrosis of the ventricular septum may result in an acute septal defect and sudden left-to-right shunt, leading to hemodynamic instability.

Necrosis of papillary muscles will result in papillary muscle dysfunction or rupture, causing severe mitral valve insufficiency.

ACUTE MYOCARDIAL RUPTURE

Through a rent in the ventricular endocardium, blood gradually leaks into the area of infarction and distends the necrotic tissue. This hematoma continues to expand and finally ruptures the myocardium.

The sudden onset of cardiogenic shock 3 to 4 days after acute myocardial infarction may herald the development of cardiac tamponade due to myocardial rupture.

Immediate surgical exploration through a standard median sternotomy should be undertaken. If the heart has actually overtly ruptured, only a salvage operation may be successful.

This entails prompt initiation of cardiopulmonary bypass.

The infarcted necrotic tissue is removed. An appropriate patch of Hemasheild or bovine pericardium is sewn to the healthy normal myocardium with a continuous suture of 3-0 Prolene buttressed with a strip of felt to cover the defect.

The suture line may have to be reinforcedwith additional sutures.

VENTRICULAR SEPTAL RUPTURE

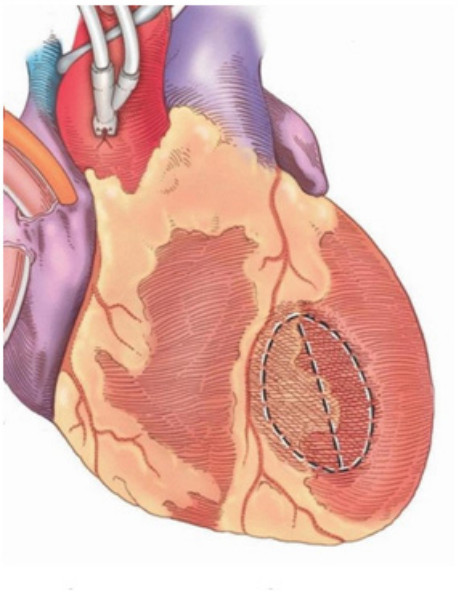
The ventricular septum receives blood from perforating branches of the left anterior descending artery as well as perforating branches of the posterior descending artery.

Despite this dual blood supply, there is frequently no septal collateral flow. Consequently, the interventricular septum remains quite vulnerable to ischemia and occasionally ruptures after myocardial infarction.

As with ventricular aneurysm, the antero-apical area is the most common site; it is involved in 65% of patients with ventricular septal rupture. The posterior segment of the septum is involved in 17% of the cases, and the middle segment in 13% of the cases; only 4% of the ruptures involve the inferior segment of the septum.

Because these patients tend to die of end-organ failure rather than heart failure, prompt temporary stabilization is achieved with the support of an intra-aortic balloon pump, ionotropic agents, and diuretics to maintain optimal tissue perfusion.

The septal defect is approached through an incision parallel to the course of the left anterior descending coronary artery in the centre of the left ventricular infarct.



The septal defect and the extent of surrounding necrotic friable tissue are identified.

With a continuous 3-0 Prolene suture, a generous patch of bovine pericardium is sewn to the left ventricular side of the septum, taking deep bites of normal, healthy muscular tissue as far away from the necrotic rim of the defect as possible.

The septal necrosis often extends to the ventriculotomy. The pericardial patch is then allowed to protrude outside the heart and be

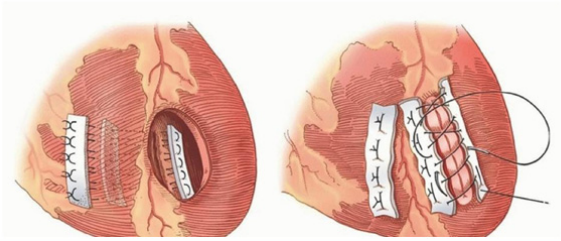
incorporated in the ventriculotomy closure.

The suture line on the septum is inspected and checked for any residual defects. It is reinforced with multiple interrupted sutures buttressed with felt pledgets. The patch is anchored to the anterior edge of the left ventricular wall with a felted suture.

The ventriculotomy is then closed with interrupted sutures of 3-0 Prolene with a layer of Teflon felt strip on both sides of the septum and anterior wall of the right ventricle.

The knots are then tied, and the ventriculotomy is closed.

This is reinforced with a continuous suture of 3-0 Prolene.



If the apex of the heart has infarcted and is necrotic, it is amputated.

The viable tissue is then reapproximated in a sandwich manner by means of four strips of Teflon felt, one on each side of the septum and one each on the right and left exterior ventricular walls, with a series of interrupted horizontal mattress sutures.

The approach to a rupture of the posteroinferior aspect of the septum through the infarcted inferior left ventricular wall is more challenging.

Often the posteromedial papillary muscle is also involved in the necrotic process, and concomitant mitral valve replacement may become necessary.

Coronary bypass grafting is performed judiciously on all by passable vessels to ensure full revascularization of the remaining myocardium.

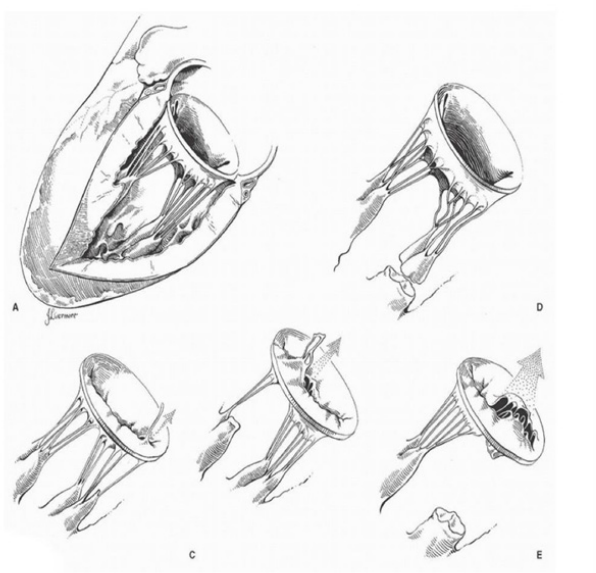
PAPILLARY MUSCLE RUPTURE

The anterolateral papillary muscle has a rich blood supply from both the left anterior descending and left circumflex coronary arteries.

In 90% of hearts, the right coronary artery is dominant and supplies the posteromedial papillary muscle. In the remaining 10%, its blood supply is provided by branches of the left coronary artery system.

Therefore, infarction of the posterior wall of the left ventricle frequently results in necrosis of the posteromedial papillary muscle. A papillary muscle rupture usually occurs during the first week after infarction or later with reinfarction.

Because both leaflets of the mitral valve are attached to each papillary muscle by chordae tendineae, complete disruption of either one, usually the posteromedial papillary muscle, results in gross mitral insufficiency, acute pulmonary edema, and death unless surgical intervention is prompt.



A: Spatial relationships of the anatomic components of the mitral valve apparatus. **B:** Rupture of chordae tendineae. **C:** Partial rupture of the head of the papillary muscle. **D:** Complete tear of the papillary muscle giving rise to gross valvular insufficiency **(E).**

Occasionally, a ruptured papillary muscle can be reimplanted, but it may be hazardous if the reimplantation site is necrotic.

Mitral valve replacement is the procedure of choice in most patients and can be performed with relative safety.

Coronary artery bypass grafting to by passable vessels is highly desirable to revascularize the viable myocardium as completely as possible.

SURGICAL VENTRICULAR RESTORATION

Following myocardial infarction, a discrete scar develops, resulting in an akinetic or dyskinetic segment.

The goal of surgery to reconstruct the left ventricle is to achieve a normal-sized cavity and to convert the more spherical shape to a more conical pattern.

Cardiopulmonary bypass is initiated in the standard manner. When the heart is still and vented empty, the extent of the old infarct is evaluated.

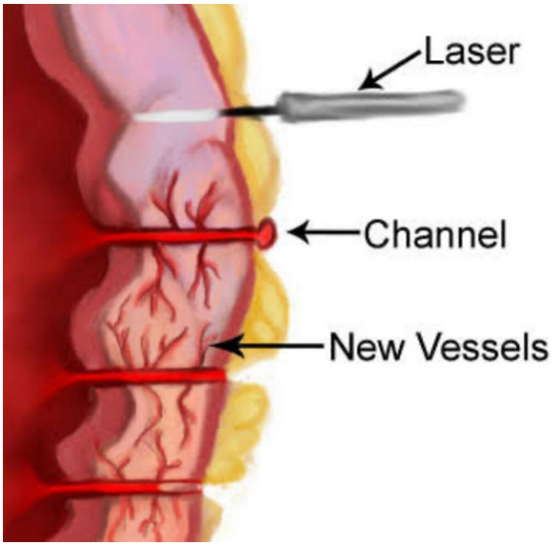
The scar segment of the left ventricular wall, devoid of myocardium, tends to be sucked in by the vent suction.

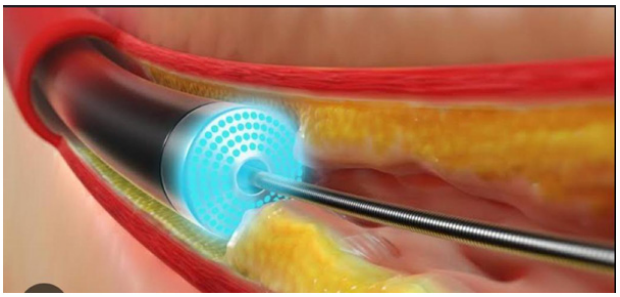
The heart is carefully dissected free from the pericardium. Traction sutures are placed in the scar tissue, and an incision is made through it.

The opening is then enlarged, and some excess scar tissue may be excised to provide easy access for removal of blood clots from within the left ventricle and/or aneurysm wall.

Transmyocardial Revascularization

- Laser ablation or photoablation is the process of removing material from a solid (or occasionally liquid) lipid accumulation surface by irradiating it with a laser beam.
- At low laser flux, the material is heated by the absorbed laser energy and evaporates or sublimates then remove blockage of artery.
- Carbon dioxide laser, holmium: YAG laser, and xenon chloride eximer laser have all been used to create channels into the left ventricular cavity. TMR with laser is used in patients with stable angina despite optimal medical therapy and with a region of myocardium that cannot be directly vascularized.
- However, it is typically performed after bypass grafting is completed, while the patient is still on cardiopulmonary bypass. The viable ischemic area is exposed.
- The laser is fired to create between 15 and 20 channels 1 cm apart, covering the ischemic but not directly the revascularized area.
- The carbon dioxide laser should be synchronized to the patient's electrocardiogram so that the pulse is delivered on the R wave, to minimize the likelihood of arrhythmia.
- After cardiopulmonary bypass is discontinued and protamine is administered, most channels readily seal at the epicardial surface with gentle digital pressure.
- Occasionally, a figure-of-eight 6-0 Prolene suture may be required for haemostasis.





Freedom from Cardiac Events Post CABG

- Sergeant and coworkers found that the freedom rate from return of angina was 94%, 82%, 61%, and 38% at 1, 5, 10, and 15 years.

- Freedom from MI was 97%, 94%, 86%, 73%, and 56% at 30 days, 5, 10, 15, and 20 years.
- In the BARI trial, freedom from angina was 84% at 5 and 10 years.
- The freedom from coronary reintervention was 80% at 10 years.
- In the Arterial Revascularization Therapies Study (ARTS) randomized trial, the rates of MI and reintervention at 5 years were 6.4% and 8.8%, respectively.
- Patients with diabetes mellitus (smaller number) had worse outcomes: their 5-year rates of MI and reintervention were 7.3% and 10.4% compared with 6.3% and 8.4% in patients without diabetes.
- Quality of life after CABG markedly improves in most patients and may correspond to that of a matched control population.

References

1. Hillis LD, Smith PK, Anderson JL, et al: 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 124:2610–2642, 2011.
2. Abbas Ardehali, Jonathan M. Chen, Siavosh Khonsari; Khonsarias Cardiac Surgery_Safeguards and pitfalls in operative technique; Fifth edition 2016; Chapter 9 Page 156-158.
3. DeRose JJ: Current state of integrated "hybrid" coronary revascularization. Semin Thorac Cardiovasc Surg 21(3):229–236, 2009.
4. Abbas Ardehali, Jonathan M. Chen, Siavosh Khonsari; Khonsarias Cardiac Surgery_Safeguards and pitfalls in operative technique; Fifth edition 2016; Chapter 10 Page 180.
5. Abbas Ardehali, Jonathan M. Chen, Siavosh Khonsari; Khonsarias Cardiac Surgery_Safeguards and pitfalls in operative technique; Fifth edition 2016; Chapter 10 Page 181-183.
6. Abbas Ardehali, Jonathan M. Chen, Siavosh Khonsari; Khonsarias Cardiac Surgery_Safeguards and pitfalls in operative technique; Fifth edition 2016; Chapter 10 Page 183-184.
7. Abbas Ardehali, Jonathan M. Chen, Siavosh Khonsari; Khonsarias Cardiac Surgery_Safeguards and pitfalls in operative technique; Fifth edition 2016; Chapter 10 Page 185-187.
8. Jatin Anand, Ashraf A. Sabe, William E. Cohn; SABISTON & SPENCER SURGERY OF THE CHEST; ninth edition; Volume 2 Chapter 89 Page 1599.
9. Mirhoseini M, Fisher JC, Cayton M: Myocardial revascularization by laser: a clinical report. Lasers Surg Med 3:241–245, 1983.
10. Horvath KA, Aranki SF, Cohn LH, et al: Sustained angina relief 5 years after transmyocardial laser revascularization with a CO(2) laser. Circulation 104:I81–I84, 2001.
11. Serruys PW, Morice MC, Kappetein AP, et al: Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 360:961–972, 2009.
12. Farkouh ME, Domanski M, Sleeper LA, et al: Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 367:2375–2384, 2012.
13. Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, et al. ACC/AHA Guidelines for Coronary Artery Bypass Graft Surgery: A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). American College of Cardiology/American Heart Association. J Am Coll Cardiol 1999;34:1262.
14. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346:1179.

Acute Coronary Syndrome (ACS): Understanding a Critical Cardiac Condition

Dr. Shubham Agarwal
Consultant and Interventional Cardiologist,
KVR Hospital, Kashipur, Uttarakhand

Acute Coronary Syndrome (ACS) is a term used to describe a range of cardiovascular conditions that occur due to a sudden decrease in blood flow to the heart muscle. It is typically caused by the blockage or narrowing of coronary arteries, the blood vessels that supply oxygen and nutrients to the heart. ACS is a medical emergency that requires immediate attention and intervention to prevent severe damage to the heart and potentially fatal outcomes.

Spectrum of ACS:

ACS encompasses a spectrum of conditions that vary in severity and clinical presentation. The three main types of ACS are:

1. **Unstable Angina:** Unstable angina is characterized by chest pain or discomfort that is new, occurs at rest, or becomes more frequent, severe, or prolonged than usual. Unlike other forms of angina, unstable angina does not follow a predictable pattern and may not be relieved by rest or medication.

2. **Non-ST-Segment Elevation Myocardial Infarction (NSTEMI):** NSTEMI occurs when there is a partial blockage of a coronary artery, leading to decreased blood flow to a portion of the heart muscle. This results in damage to the heart muscle, as evidenced by elevated cardiac biomarkers (such as troponin) in the blood. While ST-segment changes on an electrocardiogram (ECG) may be present, they are less pronounced compared to ST-segment elevation in STEMI.

3. **ST-Segment Elevation Myocardial Infarction (STEMI):** STEMI is the most severe form of ACS and occurs when a coronary artery is completely blocked, causing a significant portion of the heart muscle to be deprived of oxygen and nutrients. This leads to extensive tissue damage and results in a more pronounced elevation of the ST segment on an ECG. Immediate intervention is crucial to restore blood flow and prevent irreversible damage.

Causes of ACS:

The underlying cause of ACS is atherosclerosis, a process in which fatty deposits (plaques) build up on the inner walls of coronary arteries over time. These plaques can become unstable, leading to rupture or erosion. When this occurs, platelets in the blood form clots at the site of the rupture, which can partially or completely block blood flow through the artery. The lack of oxygen and nutrients reaching the heart muscle can cause chest pain (angina) and, in more severe cases, lead to heart muscle damage (myocardial infarction or heart attack).

Clinical Presentation:

The hallmark symptom of ACS is chest pain or discomfort, often described as a crushing or squeezing sensation. This pain can radiate to the left arm, neck, jaw, back, or stomach. Other symptoms include shortness of breath, sweating, nausea, vomiting, and lightheadedness. It's important to note that not everyone experiences chest pain, and symptoms can vary widely between individuals.

Diagnosis and Treatment:

The diagnosis of ACS involves a combination of clinical assessment, medical history, physical examination, electrocardiography (ECG), and cardiac biomarker measurements (such as troponin). These tests help healthcare professionals determine the type and severity of ACS and guide treatment decisions.

Treatment for ACS depends on the specific condition and its severity. Immediate interventions may include administering medications like aspirin, nitroglycerin, and antiplatelet drugs to reduce clot formation and improve blood flow. In more severe cases, procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) may be necessary to restore blood flow to the heart muscle.

Complications of Acute Coronary Syndrome: A Comprehensive Analysis

Introduction: Acute Coronary Syndrome (ACS) is a complex cardiovascular condition that can give rise to various complications, each with distinct mechanisms, clinical implications, and management strategies. Understanding these complications is essential for healthcare professionals to provide timely and effective care to ACS patients. Here are the different types of complications of ACS in detail:

Pathophysiology of ACS Complications:

Development of complications in ACS is rooted in the pathophysiological processes that underlie the condition itself. The primary etiology of ACS is **atherosclerosi**s, that is formation of lipid-rich plaques within the coronary arteries. These plaques can rupture, leading to the exposure of thrombogenic material such as collagen and tissue factor. The subsequent platelet aggregation and activation of the coagulation cascade result in the formation of intracoronary thrombi. The extent of vessel occlusion and the resultant ischemia determine the severity of ACS and its potential complications.

1. **Myocardial Infarction (MI):** MI is a central and severe complication of ACS. It occurs due to the prolonged ischemia of the heart muscle caused by the blockage of a coronary artery. MI can be categorized into two main types based on the extent of damage:

- **ST-Segment Elevation Myocardial Infarction (STEMI):** In STEMI, there is a complete occlusion of a coronary artery by a blood clot. This leads to rapid and extensive damage to the heart muscle. Immediate reperfusion therapy, such as percutaneous coronary intervention (PCI) or thrombolytic therapy, is crucial to restore blood flow and minimize tissue damage.
- **Non-ST-Segment Elevation Myocardial Infarction (NSTEMI):** In NSTEMI, there is partial occlusion of a coronary artery. Although less severe than STEMI, NSTEMI can still cause significant damage to the heart muscle. Treatment involves medications to stabilize the patient and prevent further complications.

2. **Arrhythmias:** ACS can disrupt the heart's electrical system, leading to various arrhythmias, which are abnormal heart rhythms. These include:

- **Ventricular Tachycardia (VT):** Rapid heartbeats originating in the ventricles. It can be life-threatening, potentially leading to cardiac arrest.
- **Ventricular Fibrillation (VF):** Chaotic, rapid electrical activity in the ventricles, leading to ineffective pumping and cardiac arrest. Immediate defibrillation is needed to restore normal rhythm.
- **Atrial Fibrillation (AF):** An irregular and often rapid heartbeat originating in the atria. AF increases the risk of stroke and requires management to control heart rate and prevent clot formation.

3. **Heart Failure:** Heart failure is a complication of ACS that arises due to the significant impairment of the heart's pumping ability. The weakened heart struggles to meet the body's demands, leading to fluid accumulation in the lungs and peripheral tissues. Management includes medications to improve cardiac function and alleviate symptoms.

4. **Cardiogenic Shock:** Cardiogenic shock is a life-threatening complication where the heart's pumping function is severely impaired, leading to inadequate blood supply to organs. It can occur following extensive MI and requires aggressive interventions, such as mechanical circulatory support and medications, to stabilize the patient's condition.

5. **Pericarditis:** Pericarditis is the inflammation of the pericardium, the sac surrounding the heart. It can occur as a result of ACS, leading to chest pain that worsens with breathing and is often accompanied by a characteristic friction rub on auscultation. Treatment involves anti-inflammatory medications to alleviate symptoms and prevent complications like cardiac tamponade.

6. **Mechanical Complications:** These complications result from structural damage to the heart due to ACS:

- **Ventricular Septal Rupture (VSR):** A tear in the septum between the ventricles, leading to shunting of blood between the chambers and hemodynamic instability.
- **Papillary Muscle Rupture:** Rupture of the papillary muscles, affecting the function of heart valves and causing acute mitral valve regurgitation and exacerbate heart failure.
- **Free Wall Rupture:** Rupture of the heart's free wall, leading to cardiac tamponade due to blood accumulating in the pericardial sac.

7. **Thromboembolism:** Intracoronary thrombi can embolize to other parts of the body, causing complications such as stroke or peripheral arterial embolism.

Conclusion: The complications of ACS span a wide range of cardiovascular emergencies, from myocardial infarction to arrhythmias, heart failure, and mechanical complications. Each complication requires specific diagnostic approaches and tailored management strategies. Early recognition and intervention are crucial in minimizing the impact of these complications on patients' health outcomes.

Clinical Manifestations and Diagnosis:

The clinical presentation of ACS complications can vary widely depending on the specific complication and its severity. While, certain common features are often observed. Chest pain or discomfort is a hallmark of ACS, but it might not be as prominent in some complications like arrhythmias or heart failure. Other symptoms can include shortness of breath, nausea, vomiting, diaphoresis, and fatigue.

The diagnosis of ACS complications involves a combination of clinical assessment, electrocardiography (ECG), cardiac biomarker measurement (such as troponin), and imaging studies like echocardiography and coronary angiography. These tools help differentiate between different complications and guide appropriate management strategies.

Management Strategies:

The management of ACS complications requires a multidisciplinary approach involving cardiologists, emergency physicians, nurses, and other healthcare providers. The specific strategies employed depend on the type and severity of the complication.

1. **Medical Therapy:** Pharmacological interventions play a crucial role in managing ACS complications. Antiplatelet agents, anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitors (ACE inhibitors), and statins are commonly prescribed to stabilize patients and prevent further complications.

2. **Revascularization:** For complications like MI and severe ischemia, revascularization procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) might be necessary to restore blood flow to the affected myocardial tissue.

3. **Arrhythmia Management:** Arrhythmias can be managed with medications, electrical cardioversion, or implantable devices like pacemakers and implantable cardioverter-defibrillators (ICDs).

4. **Heart Failure Management:** Heart failure resulting from ACS requires a combination of diuretics, ACE inhibitors, beta-blockers, and inotropic agents to improve cardiac function and reduce fluid overload.

5. **Surgical Interventions:** Surgical repair might be necessary for complications like ventricular septal rupture or papillary muscle rupture. Timely surgical intervention can prevent further deterioration.

Implications for Patient Outcomes:

The presence of complications significantly influences the prognosis and outcomes of ACS patients. Complications like MI can lead to irreversible damage to cardiac tissue, resulting in long-term functional impairment. Arrhythmias, if not managed promptly, can cause sudden cardiac death. Heart failure and cardiogenic shock are associated with high mortality rates. The timely recognition and appropriate management of complications are crucial for improving patient outcomes and reducing mortality.

Preventive Measures:

Preventing ACS complications begins with addressing the underlying risk factors for ACS. Lifestyle modifications such as adopting a healthy diet, engaging in regular physical activity, and avoiding smoking are essential. Managing conditions like hypertension, diabetes, and dyslipidemia also plays a pivotal role in reducing the risk of ACS and its complications.

Conclusion:

Acute Coronary Syndrome is a critical medical condition with potentially serious complications that can have profound impacts on patients' lives. From myocardial infarction to arrhythmias, heart failure, and more, these complications stem from the underlying pathophysiology of ACS. Timely diagnosis and appropriate management, involving a combination of medical therapy, revascularization, and surgical interventions, are paramount in improving patient outcomes. Preventive measures targeting modifiable risk factors can also significantly reduce the occurrence of ACS and its complications. As medical knowledge advances, a better understanding of these complications can lead to more effective strategies for both prevention and treatment, ultimately contributing to enhanced patient care.

Mechanical Complications:

We will explore the mechanical complications associated with ACS, their pathophysiology, clinical manifestations, diagnostic approaches, management strategies, and implications for patient care.

Mechanical complications of ACS can occur as a result of the profound ischemia, myocardial damage, and inflammation caused by the occlusion of coronary arteries. These complications can include:

1. **Myocardial Infarction (MI):** While MI is a well-known outcome of ACS, it is also considered a mechanical complication due to its impact on the myocardium's mechanical function. The sudden loss of blood supply leads to irreversible damage to myocardial tissue, affecting the heart's contractility and overall function.

2. **Ventricular Septal Rupture (VSR):** A rare but serious complication, VSR involves the rupture of the septum that separates the left and right ventricles. This rupture occurs due to the infarction of the septal wall, weakening its structure. Blood flows from the high-pressure left ventricle to the lower-

pressure right ventricle, leading to hemodynamic instability.

3. **Papillary Muscle Rupture:** The papillary muscles, which anchor the heart's atrioventricular valves (such as the mitral valve), can rupture due to ischemia. This leads to valve dysfunction and acute regurgitation, resulting in impaired cardiac output and potentially precipitating heart failure.

4. **Free Wall Rupture:** In severe cases of MI, the necrotic tissue of the heart's free wall can rupture, leading to cardiac tamponade. Blood accumulates in the pericardial sac, compressing the heart and impairing its ability to fill and pump effectively.

5. **Left Ventricular Aneurysm:** Following a transmural MI (one that affects the full thickness of the myocardium), a scarred area of weakened tissue can bulge out during contraction, forming an aneurysm. This aneurysm can alter the heart's geometry, potentially leading to arrhythmias, thrombus formation, and heart failure.

Pathophysiology and Clinical Manifestations:

The common thread in these mechanical complications is the disruption of the heart's normal structure and function due to the ischemic insult. The extent of damage to the myocardium and the specific location of the infarction determine the type of mechanical complication that may arise.

Clinical manifestations of mechanical complications can vary. Patients may experience worsening chest pain, dyspnea, palpitations, dizziness, and even syncope. Physical examination may reveal abnormal heart sounds, murmurs, and signs of heart failure.

Diagnostic Approaches:

Diagnosing mechanical complications of ACS involves a combination of clinical assessment, electrocardiography (ECG), echocardiography, cardiac biomarker measurements, and sometimes advanced imaging techniques such as cardiac magnetic resonance imaging (MRI). ECG changes, such as ST-segment elevation or depression, can offer insights into the location and severity of myocardial damage. Echocardiography helps visualize structural abnormalities and assess cardiac function.

Management Strategies:

The management of mechanical complications of ACS requires a multidisciplinary approach involving cardiologists, cardiac surgeons, and intensivists. Treatment strategies are tailored to the specific complication:

1. **Surgical Repair:** Surgical intervention is often necessary to address complications like VSR, papillary muscle rupture, and free wall rupture. Repairing the structural damage can restore normal cardiac function and prevent further deterioration.

2. **Medical Therapy:** Adjunctive medical therapies such as medications to reduce preload and afterload, diuretics, inotropes, and vasopressors may be used to stabilize patients with mechanical complications.

3. **Supportive Care:** Close monitoring, oxygen therapy, pain management, and treatment of heart failure symptoms are essential components of patient care.

Implications for Patient Outcomes:

The mechanical complications of ACS significantly influence patient outcomes. Early diagnosis and timely intervention are critical for preventing hemodynamic instability, improving cardiac function, and reducing mortality rates. The presence of these complications often necessitates longer hospital stays and more intensive medical management.

Conclusion:

Mechanical complications of ACS can lead to life-threatening situations and demand immediate recognition, accurate diagnosis, and prompt management. A comprehensive understanding of

the pathophysiology, clinical manifestations, diagnostic approaches, and treatment strategies is essential for healthcare professionals dealing with ACS patients. By addressing these complications with a multidisciplinary and patient-centered approach, we can enhance patient outcomes and minimize the impact of ACS on individuals' lives.

Chronic Complications of Acute Coronary Syndrome: Long-Term Impacts and Management

Acute Coronary Syndrome (ACS) is a critical cardiovascular condition marked by a sudden reduction in blood flow to the heart muscle. While the immediate consequences of ACS are well-recognized, its chronic complications can significantly affect patients' quality of life and long-term prognosis. This essay explores the chronic complications that may arise from ACS, delving into their pathophysiology, clinical manifestations, management approaches, and implications for patients.

Understanding Chronic Complications:

Chronic complications of ACS develop as a consequence of the initial ischemic insult and subsequent tissue damage. These complications often result from the scar tissue formed during the healing process after an ACS event. The most common chronic complications include:

1. **Chronic Heart Failure:** ACS-induced myocardial damage can lead to chronic heart failure, a condition in which the heart's pumping ability is compromised. The weakened heart struggles to meet the body's demands for oxygen and nutrients, leading to symptoms such as fatigue, shortness of breath, and fluid retention.

2. **Left Ventricular Remodeling:** Following ACS, structural changes occur in the heart's left ventricle as it attempts to compensate for the damaged tissue. The ventricle can become enlarged (dilated) and its shape can change, impacting cardiac function and increasing the risk of heart failure.

3. **Arrhythmias:** The scar tissue resulting from ACS can disrupt the heart's electrical conduction system, leading to the development of arrhythmias such as ventricular tachycardia and atrial fibrillation. These arrhythmias can cause palpitations, dizziness, and an increased risk of stroke.

4. **Chronic Ischemia and Angina:** In some cases, chronic ischemia, where blood flow to the heart is reduced over time, can develop after an ACS event. This can lead to chronic stable angina, characterized by recurrent chest pain or discomfort during physical activity or emotional stress.

Clinical Manifestations and Diagnosis:

The clinical manifestations of chronic complications depend on the specific complication and its severity. Patients with chronic heart failure may experience fatigue, shortness of breath, and fluid retention, while those with arrhythmias might report palpitations and dizziness. Chronic stable angina is characterized by recurrent chest pain during exertion.

Diagnosing chronic complications often involves a combination of clinical assessment, medical history, physical examination, electrocardiography, echocardiography, stress testing, and other imaging studies. These diagnostic tools help healthcare professionals determine the nature and extent of the chronic complications.

Management Strategies:

The management of chronic complications of ACS requires a comprehensive approach aimed at improving patients' symptoms, quality of life, and overall prognosis. Some strategies include:

1. **Heart Failure Management:** For chronic heart failure, a combination of medications, lifestyle modifications (such as dietary changes, exercise, and salt restriction), and, in severe cases, devices like implantable cardioverter-defibrillators (ICDs) or cardiac resynchronization therapy (CRT) devices can be employed.

2. **Arrhythmia Management:** The treatment of arrhythmias involves a combination of medications, lifestyle changes, and, if necessary, interventions such as catheter ablation or implantation of pacemakers or ICDs.

3. **Lifestyle Modifications:** Encouraging patients to adopt heart-healthy lifestyles, including a balanced diet, regular exercise, smoking cessation, and stress management, can help mitigate chronic complications and improve overall well-being.

Implications for Patients:

Chronic complications of ACS can significantly impact patients' lives. They may lead to reduced functional capacity, decreased quality of life, and an increased risk of hospitalizations. These complications also contribute to long-term morbidity and mortality rates, underscoring the importance of early detection, effective management, and ongoing monitoring.

Conclusion:

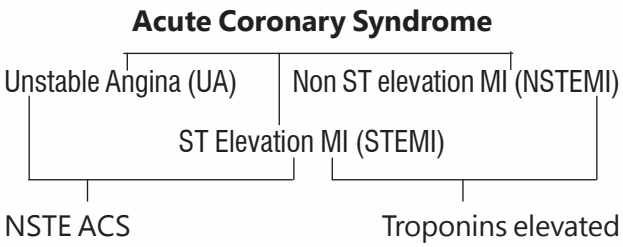
While the acute phase of ACS demands immediate attention, it is crucial not to overlook the potential chronic complications that can follow. Chronic heart failure, left ventricular remodeling, arrhythmias, and chronic stable angina can all arise from the initial ACS event, affecting patients' health and well-being over the long term. A comprehensive approach that includes medical interventions, lifestyle modifications, and ongoing patient education is essential in managing these chronic complications and improving patients' overall outcomes.

Recent Advances In Acute Coronary Syndrome

Dr. T. Govindan Unni
Professor, Department of Cardiology
Jubilee Mission Medical College & Research Institute
Thrissur, Kerala
Email: unni.govindan@gmail.com

Introduction:

Acute Coronary Syndrome (ACS) denotes a wide spectrum of diseases. At one end is unstable angina, where the ECG may be normal, troponins normal, echocardiogram normal and the only clue is provided by a good, well taken history. Unstable angina (UA) includes, recent onset angina, recent worsening of angina and rest pain lasting more than 20 minutes. Post myocardial infarction (MI) angina is also considered UA. The classic distinguishing feature of unstable angina is the absence of myocardial necrosis, as evidenced by a normal troponin value. At the other extreme is ST elevation myocardial infarction (STEMI), characterised by ST elevation in the ECG, total occlusion of a coronary artery in the majority and grave prognosis if not treated on time. In between is non-ST elevation MI (NSTEMI), where there can be any ECG changes other than ST elevation (or no changes) and rise in troponins. Patients with MI can present with chest pain or other angina equivalents, but cardiogenic shock (CS), acute left ventricular failure (LVF) or sudden cardiac death may also be the presenting feature. The distinguishing feature between UA and MI is rising troponins in the latter. The distinguishing feature between STEMI and NSTEMI is the presence of ST elevation in the former. Troponins and ECG changes are also important in risk stratification (1). UA and NSTEMI together is described as NSTE ACS.



Steps in the evaluation and management of ACS:

The 2023 European Society of Cardiology (ESC) guidelines (1) summarises the management of ACS into five steps. Step 1 is "think ACS". "A" stands for "Abnormal ECG", "C" stands for "Clinical context" and "S" stands for clinical "Stability". Abnormal ECG has to be interpreted taking into consideration the clinical context. Clinical stability assessed by clinical examination is the first and most important step in deciding the next course of action and is also an important prognostic sign. Step 2 is to consider invasive management as emergency in STEMI, immediate in very high risk NSTE ACS (less than 2 hours) and early (within 24 hours) in high risk NSTE ACS. Step 3 is anti-thrombotic and anti-coagulation therapy. Step 4 is revascularisation and step 5 is secondary prevention.

Clinical presentation:

Acute chest discomfort or its equivalents like tightness, heaviness, dyspnoea or burning sensation is the commonest classical presentation. Aided by a good history, physical examination and ECG, it should be possible to divide patients into cardiac, possibly cardiac and non-cardiac chest pain/discomfort. Within 10 minutes of arrival in the emergency department (ED), an ECG should be taken and properly interpreted. In suspicious cases with a normal ECG, it is important to take serial ECGs depending on the patient's symptoms. The prognosis is better if the patient seeks medical help earlier. One of the important contributors to the delay in presentation is the time taken from the onset of pain to getting medical help.

Shortening this time can be achieved by public education of the various presentations of ACS.

Importance of a proper physical examination is twofold. Non cardiac causes like pneumothorax, costochondritis, cholecystitis etc. can be excluded. Secondly, identification of signs of heart failure like a faint third heart sound, or mechanical complications like mitral regurgitation helps in risk stratification. It is essential to identify impending haemo-dynamic collapse. Indicators of high clinical risk include tachycardia, a narrow pulse pressure, hypotension, and signs of congestion (pulmonary oedema) or inadequate perfusion (cool extremities). Checking for absent pulses and identification of an aortic regurgitation murmur may be a clue to dissection of aorta.

Troponins:

Troponins are very sensitive and reasonably specific in detecting myocardial injury and hence considered gold standard in the diagnosis of MI. Other markers like CK MB are used only when troponins cannot be used. Rise or fall of high sensitivity troponins is the hall mark of MI. But in STEMI, the diagnosis and treatment are based on ECG changes and one should not wait for troponin results to initiate treatment. Troponins are also important prognostic markers. The initial troponin values may be normal, especially if the patient comes very early. Hence repeating troponins at 3 hours and even 6 hours may be required, if clinical suspicion is high. Troponin rise may not be always ACS. Troponin rise may be due to non-ischemic causes of myocardial injury like myocarditis, hypertensive crisis, stroke, arrhythmias, renal failure, septicaemia and a lot of other conditions. Hence the fourth universal definition of myocardial infarction specifies rise or fall of troponins accompanied by clinical evidence of ischaemia (symptoms, ECG changes, supportive ECG or other imaging findings, or evidence of coronary thrombus) to diagnose MI (2). In other words, while troponin rise is an important feature of MI, all troponin rise is not MI. The ESC suggests 0 h/1 h or 0 h/2 h algorithm for troponin measurement to rule out or rule in NSTEMI (3). Both the absolute value and the degree of rise are important. Zero hour is the time patient presents to the ED. One hour and two hours are calculated from the time patient presents to ED. If the zero-hour value is not available by one hour, the recommendation is to go ahead and take the one-hour sample. The same is true for the two-hour sample if one hour sample value is not ready. Even though point of care (POC) measurements gives faster results, they are not high sensitive troponin. The ESC algorithm should be used only with high sensitivity troponins which are measured in central labs. The cut off values of troponins vary with the manufacturer. In suspicious cases, a 3-hour sample or even six-hour sample may also be needed. A major determinant of the rise in troponin is the time of presentation from symptom onset. In a patient who comes very early (like less than one hour from symptom onset), more samples may be required to rule out or rule in MI compared to someone who comes later.

Acute coronary syndrome with persistent ST-segment elevation (STEMI):

2023 ESC guidelines (1) define STEMI as follows.

"ST-segment elevation (measured at the J-point) is considered suggestive of ongoing coronary artery acute occlusion in the following cases:

New ST elevation at the J-point in at least two contiguous leads:

- >2.5 mm in men 40 years, >2 mm in men > 40 years, or >1.5 mm in women regardless of age in leads V2–V3
- and/or >1 mm in the other leads (in the absence of left ventricular [LV] hypertrophy or left bundle branch block [LBBB])."

Before excluding STEMI, it is advisable to take right-sided chest leads, V3R and V4R to rule out right ventricular MI and posterior leads, V7 and V8 to rule out posterior wall MI. Another STEMI equivalent will be ST depression in all leads except aVR and V1, (where there is ST elevation). These ECG changes suggest very proximal disease like a left main disease or multivessel disease. It may not be difficult to assess ST segment elevation in

the presence of right bundle branch block (RBBB), but left bundle branch block (LBBB) pattern may affect ST segment elevation. An RV paced rhythm will also create confusion as it will look like an LBBB. A presumably new LBBB pattern is sometimes considered a STEMI equivalent.

The prime goal in these patients is coronary revascularisation at the earliest.

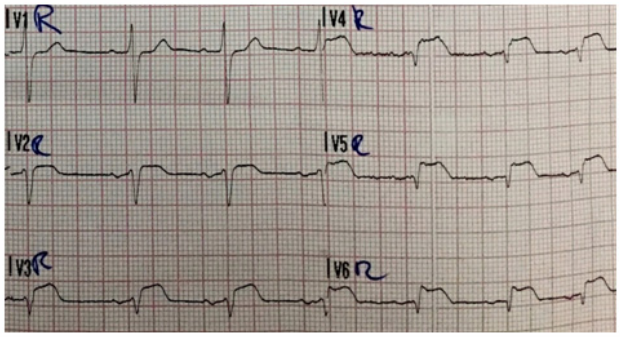


Fig:1. Right sided chest leads showing ST elevation in RVMI

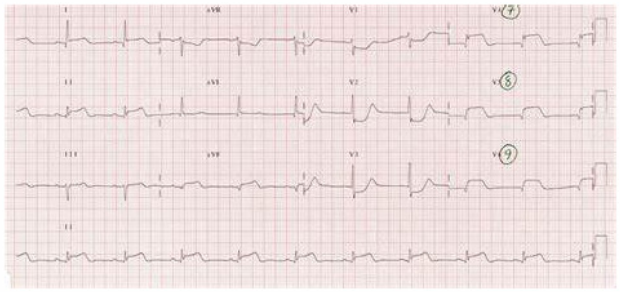


Fig:2. ST elevation in posterior leads V7, V8 and V9

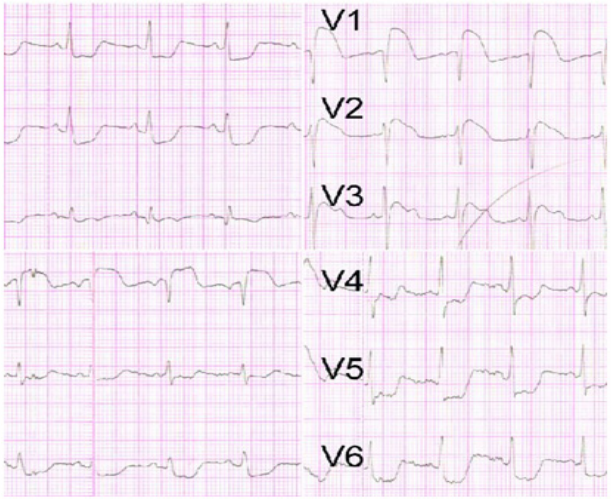


Fig:3. ST depression in all leads except aVR and V1 which shows ST elevation suggesting left main disease or multivessel disease

Acute coronary syndrome without persistent ST-segment elevation (non-ST elevation acute coronary syndrome):

In NSTE ACS, about one third will have normal ECG. ST depression and T inversion are the commonest findings. Two patterns of grave prognostic import are Wellen's sign and de Winter's sign, both suggesting proximal left anterior descending artery (LAD) disease. Wellens' syndrome is a phenomenon of T-wave inversions noted in the precordial leads of patients with unstable angina. These patients were originally described to have critical stenosis of the proximal LAD. If untreated, it progresses to anterior myocardial infarction in the majority of the cases. It is characterized by biphasic or deeply inverted T waves in V2-3, plus a history of recent chest pain now resolved. de Winter syndrome is a special equivalent of anterior ST-segment elevation myocardial infarction (STEMI) characterized by the absence of overt ST-elevation with upsloping ST-segment depression followed by tall symmetrical T-waves in the precordial leads, often associated with total occlusion of the proximal left anterior descending coronary artery.

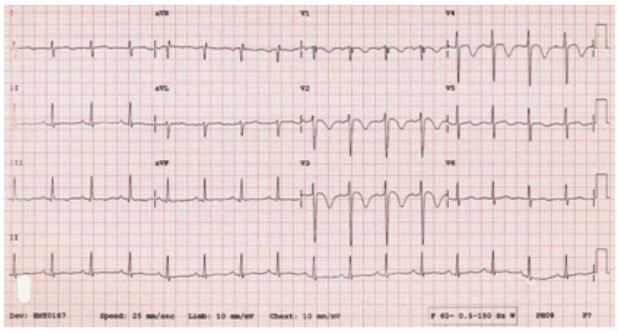


Fig:4. Wellen's syndrome

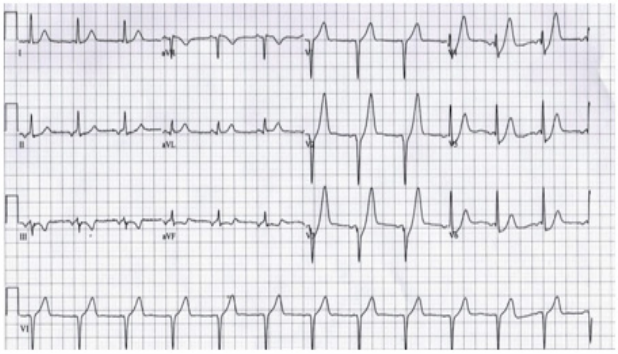


Fig:5. de Winters sign

Echocardiography:

Bedside echocardiography is very helpful in the ED. Identification of regional wall motion anomalies and LV function helps in diagnosis and prognostication. A large area of regional wall motion anomaly suggests a large amount of myocardium in jeopardy. The regional wall motion anomaly also gives an idea about the vessels involved. LV systolic dysfunction is another marker of poor prognosis. Other mechanical complications like ventricular septal rupture and mitral regurgitation can also be identified by echocardiogram. It also helps in identifying non coronary diseases like aortic dissection, severe aortic stenosis, hypertrophic cardiomyopathy etc.

Computed tomography (CT):

Routine CT is not recommended in the diagnosis of ACS. But in case of suspicion, CT will rule out three main life-threatening causes of chest pain namely ACS, pulmonary embolism and aortic dissection. When repeated ECGs and troponins are inconclusive, Coronary CT angiography (CCTA) may be of help in ruling out ACS. A normal CCTA has good negative predictive value and suggest a good prognosis.

Time to treatment:

Ventricular fibrillation and sudden cardiac death are frequent complications of STEMI. Hence early revascularisation is advised. There is ongoing muscle damage and hence delay in reperfusion translates into more myocardial death and worse long-term prognosis. Thus, time to treatment is of utmost importance in STEMI, where in the majority there is total occlusion of a vessel. Total ischemic time is the time from onset of symptoms to presentation to the first medical contact. This is an important determinant of the reperfusion strategy. The more the total ischemic time, the worse is the prognosis. Continuous clinical audit is advised to fasten the STEMI pathway and reduce the total ischemic time. The first delay is from the symptom onset to getting medical help. This delay can be reduced only by increasing public awareness about the need for getting early medical help.

The next delay is the system delay which is the time taken for reperfusion from the first medical contact. The system delay can be reduced by directing the patient straight to the catheterisation laboratory bye-passing the ED and non-PCI (percutaneous coronary intervention) capable hospitals. If the patient reaches a non-PCI capable hospital the "door-in, door-out time "is important. This is defined as the time taken from arrival of the patient at the non-PCI hospital to the time the patient is sent out in an ambulance to a PCI capable hospital. Ideally it should be less than 30 minutes.

All patients with suspected ACS should be admitted to a facility for continuous ECG monitoring and defibrillator to prevent death due to arrhythmias.

Initial pharmacotherapy:

Oxygen if there is hypoxemia (<90% saturation), nitrates to relieve pain either sublingually or intravenously and intravenous opioids, if required, form the initial pharmacotherapy. Contraindications for nitrates include, hypotension, bradycardia, RV infarction, severe aortic stenosis and use of phosphodiesterase 5 inhibitors during previous 48 hours. IV Beta Blockers have been tried in various randomised control trials (RCT). However, most were done in the era before invasive revascularisation. IV metoprolol may be considered at the time of presentation in STEMI patients prepared for primary PCI (PPCI) if there are no signs of acute LVF and BP is more than 120 mm Hg. (Class II a recommendation). It has been consistently associated with reduction in the incidence of VF and microvascular obstruction (4). IV beta blockers have not been tested in NSTEMI.

Selection of invasive strategy and reperfusion therapy:

Immediate reperfusion is the goal in STEMI. Primary PCI (PPCI) is the gold standard, but if that is not possible within 120 minutes, fibrinolysis is recommended. In very high risk NSTEMI, immediate invasive strategy (less than 2 hours) is recommended, while in high risk NSTEMI, early invasive strategy (less than 24 hours) is

recommended. Very high-risk features in NSTEMI include haemodynamic instability or cardiogenic shock, recurrent or ongoing chest pain refractory to medical treatment, acute heart failure presumed secondary to ongoing myocardial ischaemia, life-threatening arrhythmias or cardiac arrest after presentation, mechanical complications and recurrent dynamic ECG changes suggestive of ischaemia. High risk features in NSTEMI are confirmed diagnosis of NSTEMI based on ESC algorithms, GRACE risk score >140, transient ST-segment elevation and dynamic ST-segment or T wave changes (1).

Patients with STEMI presenting to a non-PCI capable hospital should be immediately transferred to a PCI capable hospital. If PPCI is not feasible within 120 minutes, these patients should be lysed. In patients presenting after 12 hours, lysis is not indicated and they should go for PCI. The value of PPCI after 12 hours is less well established compared to those who present before 12 hours. After 24 to 48 hours, routine revascularisation of totally occluded infarct related artery is not indicated in STEMI in an asymptomatic patient (7).

Fibrinolysis and pharmaco-invasive strategy in patients with ST-elevation myocardial infarction:

In patients presenting within 12 hours of symptom onset and where PPCI cannot be done in 120 minutes, fibrinolysis is an important reperfusion option for STEMI. When treated within six hours after symptom onset, 30 early deaths are prevented per 1000 patients (8). Pre hospital fibrinolysis is another attractive reperfusion option. There should be trained medical or allied health personnel who can interpret an ECG, or can transmit the ECG and get it remotely interpreted within 10 minutes. Pre hospital fibrinolysis should be started within 10 minutes of STEMI diagnosis and fibrin specific lytics (i.e., tenecteplase, alteplase, or reteplase) are preferred. When administered within 2 hours of symptom onset, pre hospital fibrinolysis reduced mortality by 17% compared to in-hospital fibrinolysis (9). In STEMI patients presenting within 3 hours of symptom onset, prehospital fibrinolysis followed by early PCI had similar outcome as transfer for primary PCI, if PPCI could not be done within one hour of FMC (10).

In patients with a failed fibrinolysis (ST-segment resolution <50% within 60–90 min of fibrinolytic administration) or in the presence of haemodynamic or electrical instability, worsening ischaemia, or persistent chest pain, rescue PCI should be done at the earliest (5). In these cases, re-administration of fibrinolytics is not useful. When the fibrinolysis is successful, invasive angiography should still be planned within 2 to 24 hours after the bolus injection (6). This strategy has been termed the pharmaco-invasive strategy. Compared to conventional fibrinolysis, benefits of pharmaco-invasive strategy are second only to PPCI (11).

Routine vs. selective invasive strategy in NSTEMI:

Invasive CAG prior to discharge is recommended in patients with NSTEMI (raised troponins) and in UA (normal troponins) if the clinical suspicion is high. In patients without very high- or high-risk features, a selective invasive strategy based on non-invasive tests like stress test or CCTA is advised.

Antithrombotic therapy (ATT):

Antithrombotic therapy is an important component in the treatment of ACS. The type, intensity and duration of ATT depends on various factors. The benefits of preventing thrombosis should be weighed against the risks of bleeding. Aspirin 300 mg loading dose followed by 75 to 100 mg as maintenance dose is the time-tested ATT. Dual anti platelet therapy (DAPT) with a second P2Y12 inhibitor is routinely recommended. Clopidogrel is the preferred drug during fibrinolysis. But after PCI, prasugrel and ticagrelor gets preference. Prasugrel is contra indicated in purely medically managed patients. Loading dose of clopidogrel is 300 to 600 mg before PCI and 300 mg at the time of fibrinolysis (no loading dose in those above 75 years). Loading dose of prasugrel is 60 mg and maintenance dose 10 mg. When body weight is less than 60 kg, 5mg maintenance dose is advised. Loading dose of

ticagrelor is 180 mg followed by maintenance dose of 90 mg twice daily. Pre-treatment (treatment before angiography and hence before anatomy is known) with P2 Y12 inhibitor is of questionable benefit (12). In STEMI, pretreatment with P2Y12 inhibitor may be considered (Class II b indication), but in NSTEMI, it is not recommended. When there is an anticipated delay of more than 24 hr for CAG, pretreatment may be considered in NSTEMI also (Class II b indication). DAPT should be maintained, routinely for 12 months post ACS. Shortening or extending this regime depends on bleeding risk and ischemic risk. In patients with high bleeding risk, deescalating from ticagrelor or prasugrel to clopidogrel can also be considered.

Early cessation of aspirin in high bleeding risk patients is a new concept. In the TWILIGHT trial cessation of aspirin after three months of PCI and continuation of ticagrelor resulted in less bleeding end points at the end of one year. There was no difference in the ischemic end points (13), though the trial was underpowered to detect the ischemic endpoints.

When patient requires an oral anti coagulation (OAC) for any reason, ESC 2023 guidelines (1) recommend triple therapy (DAPT plus OAC) for only a week after PCI. Then aspirin is discontinued and OAC and P2Y12 inhibitor, preferably clopidogrel, is continued for a year. After one year only OAC is required. Novel oral anti coagulants (NOACs) are preferred as OAC to vitamin K antagonists (VKA). In patients with high ischemic risk, triple therapy (aspirin, clopidogrel and NOAC) can be continued for one month after PCI (instead of one week). In patients with high bleeding risk, clopidogrel may be stopped after 6 months (instead of one year). In medically managed patients, there is no indication for triple therapy. Clopidogrel and NOAC for 6 months followed by NOAC alone is the recommendation.

Parenteral anticoagulation is recommended in all patients with ACS. Generally, they can be discontinued immediately after PCI. Unfractionated heparin is the standard of care in patients undergoing PPCI in STEMI. Alternatives include bivalirudin and LMWH. However, fondaparinux is not recommended in the invasive setting. Fondaparinux is recommended in NSTE ACS who does not undergo early angiography. In fibrinolysed patients, parenteral anticoagulation should be continued until revascularisation is done. In those not undergoing revascularisation, anticoagulation should be continued during the period of hospital stay. Enoxaparin is the anticoagulant of choice.

Myocardial infarction with non-obstructive coronary arteries (MINOCA):

Here the patient presents with symptoms suggestive of ACS, has a rise in troponin (suggesting myocardial infarction), but coronary angiogram shows no obstruction or only less than 50% obstruction in coronary arteries. Prevalence varies from 1% to 14% (13). Underlying causes are heterogenous and can be coronary or non-coronary, cardiac or noncardiac. The coronary causes include coronary embolism, coronary microvascular dysfunction, coronary spasm, coronary thrombosis, myocardial bridging, plaque rupture/erosion and spontaneous coronary artery dissection. The important non coronary cardiac causes are cardiac trauma, cardiomyopathy, cardiotoxins, myocarditis, strenuous exercise, Takotsubo cardiomyopathy and transplant rejection. The non cardiac causes are acute respiratory distress syndrome, allergic/ hypersensitivity reactions, end-stage renal failure, inflammation, pulmonary embolism, sepsis and stroke. MINOCA is a working diagnosis and it is essential that the underlying cause is identified for proper management. Cardiac magnetic resonance (CMR) combined with intra coronary optical coherence tomography (OCT) is the most useful strategy in finding the underlying cause of MINOCA. In about 87% of cases CMR with OCT was able to give the underlying diagnosis (14).

Complications:

Acute heart failure (HF) is one of the most dangerous complications of ACS. HF increases the risk of worsening renal failure and can increase the risk of in-hospital death. It is important to

identify pre-existing HF from de novo HF. Troponin rise may be secondary to pre-existing HF rather than ACS. Management of HF is similar to other types of HF. ACS complicated by HF, require immediate CAG and revascularisation. HF may lead to cardiogenic shock (CS).

Mechanical complications of ACS are also life threatening, unless properly dealt with. These complications usually are associated with STEMI and occurs during the first few days. In these days of timely PPCI, incidence of mechanical complications has come down considerably. Surgery is considered the treatment of choice. Severe mitral regurgitation secondary to papillary muscle dysfunction or rupture, ventricular septal rupture and free wall rupture are the commonest mechanical complications.

LV thrombus may be a precursor of systemic embolism and devastating stroke. 2 D Echocardiogram identifies most LV thrombus, but CMR is the best modality in identifying LV thrombus. Once identified, these patients require OAC at least for 6 months guided by repeated echocardiograms at frequent intervals.

Atrial fibrillation (AF) is one of the commonest complicating arrhythmias, while ventricular tachycardia (VT) and fibrillation (VF) may result in sudden cardiac death. If well tolerated, as in most cases, only oral anticoagulation is required for AF. If there is hemodynamic compromise, electrical cardioversion is needed. Rate control with beta blockers is also advised. Ischemia is the commonest trigger for VF and VT and hence early reperfusion is the treatment of choice. Beta blockers, amiodarone and lidocaine are the drugs recommended. VT and VF occurring in the first 48 hours is considered to have no long-term prognostic effect. Accelerated idioventricular rhythm secondary to reperfusion usually is benign and does not require any treatment.

Secondary prevention:

Secondary prevention is of utmost importance to reduce further events and improve quality of life. Smoking cessation, healthy diet, regular exercise, maintain body weight and psychosocial support form the basis of non-pharmacological treatment. Type and duration of antiplatelet therapy has already been discussed. All patients should get high intensity statin therapy, irrespective of baseline cholesterol levels. LDL cholesterol should be less than 55 mg/dl and there should be 50% reduction from baseline value. If these values are mot attained with high dose statins, Ezetimibe should be added. PCSK9 inhibitors can also be added to statins, though cost is an important constraint. Annual influenza vaccination is a class I recommendation. Blood pressure (BP) should be maintained below 130 mm systolic and 80 mm diastolic. HbA1C should be less than 7%. All patients with LV dysfunction should receive beta blockers (BB) and renin angiotensin aldosterone system (RAAS) blockers. In patients without LV dysfunction, the role of beta blockers is controversial. The general consensus is the benefits of BB decrease as the time from index MI increases. So, BB may be given for one year after MI, and possibly for 3 years. Beyond three years the benefits are unknown. RAAS blockers should be given to patients with LV dysfunction, DM, HTN, CKD and other high risk subsets. Mineralocorticoid receptor antagonists (MRA) are recommended after ACS in patients with LV dysfunction or diabetes mellitus. For diabetes management, in the presence of LV dysfunction, SGLT2 inhibitors are class I indication. GLP1 Receptor Agonists also have data to reduce MACE. Recent addition to the post ACS pharmacology is the anti-inflammatory drug colchicine (15).

Conclusion:

There have been significant improvements in the management of ACS during the last two decades. Even though the mortality has considerably come down, it is still significant. High sensitivity troponins have made the diagnostic algorithm simpler. Timely treatment is of utmost importance. More potent anti platelet regimes have reduced ischemic events at the cost of increasing bleeding events. New generation stents have reduced the incidence of stent thrombosis. Early revascularisation has reduced the incidence of

complications like acute LVF, CS and mechanical complications. Secondary prophylaxis to reduce further events consists of life style modification, statins and antiplatelets. Beta blockers and RAAS blockers also play an important role. Early diagnosis, timely treatment and long-term secondary prophylaxis forms the key to a healthy post ACS life.

References

1. Robert A. Byrne, Xavier Rossello, J.J. Coughlan, Emanuele Barbato, Colin Berry, Alaide Chieffo et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur. Heart J 2023;00: 1-107. https://doi.org/10.1093/eurheartj/ehad191

2. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Eur Heart J 2019;**40**:237–269. https://doi.org/10.1093/eurheartj/ehy462

3. Neumann JT, Twerenbold R, Ojeda F, Sörensen NA, Chapman AR, Shah ASV, et al. Application of high-sensitivity troponin in suspected myocardial infarction. N Engl J Med 2019;**380**:2529–2540. https://doi.org/10.1056/NEJMoa1803377

4. Ibanez B, Macaya C, Sánchez-Brunete V, Pizarro G, Fernández-Friera L, Mateos A, et al. Effect of early metoprolol on infarct size in ST-segment-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: the effect of metoprolol in cardioprotection during an acute myocardial infarction (METOCARD-CNIC) trial. Circulation 2013;**128**:1495–1503. https://doi.org/10.1161/circulationaha.113.003653

5. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, et al. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. N Engl JMed 2013;**368**:1379–1387. https://doi.org/10.1056/NEJMoa1301092

6. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med 2009;**360**:2705–2718. https://doi.org/10.1056/NEJMoa0808276

7. Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, et al. Coronary intervention for persistent occlusion after myocardial infarction. N Engl JMed 2006;**355**:2395–2407. https://doi.org/10.1056/NEJMoa066139

8. Fibrinolytic Therapy Trialists (FTT) Collaborative group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994;**343**:311–322. https://doi.org/10.1016/S0140-6736(94)91161-4

9. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. JAMA 2000;**283**:2686–2692. https://doi.org/10.1001/jama.283.20.2686

10. Sinnaeve PR, Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Lambert Y, et al. ST-segment-elevation myocardial infarction patients randomized to a pharmaco-invasive strategy or primary percutaneous coronary intervention: strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-year mortality follow-up. Circulation 2014;**130**:1139–1145. https://doi.org/10.1161/circulationaha.114.009570

11. Fazel R, Joseph TI, Sankardas MA, Pinto DS, Yeh RW, Kumbhani DJ, et al. Comparison of reperfusion strategies for ST-segment-elevation myocardial infarction: a multivariate network meta-analysis. J Am Heart Assoc 2020;**9**:e015186. https://doi.org/10.1161/jaha.119.015186

12. Koul S, Smith JG, Götberg M, Omerovic E, Alfredsson J, Venetsanos D, et al. No benefit of ticagrelor pretreatment compared with treatment during percutaneous coronary intervention in patients with ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Circ Cardiovasc Interv 2018;**11**:e005528. https://doi.org/10.1161/circinterventions.117.005528

13. Mehran R, Baber U, Sharma SK, Cohen DJ, Angiolillo DJ, Briguori C, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. N Engl J Med 2019; **381:** 1524–34.

14. Pasupathy S, Air T, Dreyer RP, Tavella R, Beltrame JF. Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries. Circulation 2015;**131**:861–870. https://doi.org/10.1161/circulationaha.114.011201

15. Pathik B, Raman B, Mohd Amin NH, Mahadavan D, Rajendran S, McGavigan AD, et al. Troponin-positive chest pain with unobstructed coronary arteries: incremental diagnostic value of cardiovascular magnetic resonance imaging. Eur Heart J Cardiovasc Imaging 2016;**17**:1146–1152. https://doi.org/10.1093/ehjci/jev289

16. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. N Engl J Med 2019;**381**:2497–2505. https://doi.org/10.1056/NEJMoa1912388

Acute Coronary Syndrome in Young Adults

Dr. Dilip Ratnani
Senior Interventional Cardiologist
Hod Cardiology-shri Shankarcharya Institute Of Medical Sciences
Email : dilipratnani@Yahoo.com
Mobile : 9826122379

Introduction

Coronary artery disease (CAD) mostly occurs in persons older than 45 years of age. In India, CAD manifests almost a decade earlier than in Western countries. India is currently in the fourth stage of epidemiological transitions where cardiovascular disease is the leading cause of mortality and morbidity. Acute coronary Syndrome in young adults is gradually increasing in India and is of major concern since the disease carries a significant morbidity, psychological effects, and financial constraints for the person and the family when it occurs at a young age. The causes of MI among patients aged less than 45 can be divided into four groups: (1) atheromatous coronary artery disease; (2) non-atheromatous coronary artery disease; (2) hyper-coagulable states; (4) MI related to substance misuse. There is a considerable overlap between all the groups.

Five MI types

- **Type 1 MI** is presented with acute atherothrombosis in an artery, which irrigates a certain part of myocardium.
- **Type 2 MI** are met when an imbalance of myocardial demanded oxygen occurs.
- **Type 3 MI** is described by cardiac death from suspected myocardial ischemia based on electrocardiogram changes in symptomatic patients, with no notification of elevated cTn levels until then.
- **Type 4** procedural MI is directly related to percutaneous coronary intervention and **Type 5** with coronary artery bypass grafting

Etiology

- *ATHERO THROMBOSIS due to Plaque rupture still remains the most common etiology of myocardial infarction in young in around 90% of cases ,in rest 10%cases it may be due to unique syndromes such as plaque erosion, coronary microvascular dysfunction, spontaneous coronary artery dissection, and coronary spasm related to drug abuse, coronary embolism*

Categories

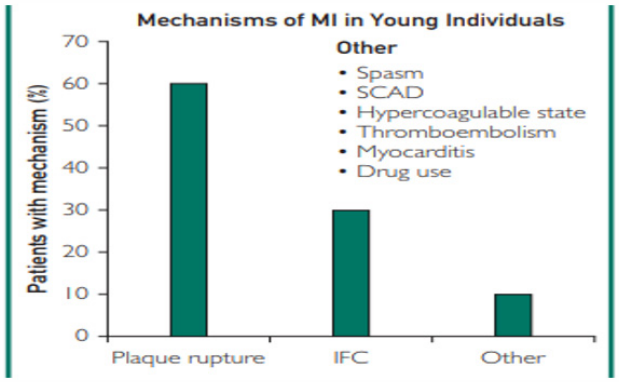
Myocardial infarction in young individuals can be grouped into 4 categories:

(1) MI related to Atheromatous coronary artery disease with traditional risk factors

(2) MI due to atheromatous coronary artery disease (CAD) but without critical coronary stenosis (MINOCA), coronary vasospasm, Microvascular dysfunction , MI with intact fibrous cap , MI due to SCAD (spontaneous coronary artery dissection), Myocarditis

(3) Hypercoagulable state & coronary embolism (CE),

(4) Use of recreational drugs such as cocaine, methamphetamine, and cannabis & Use of stimulants Androgenic anabolic steroids (AASs), Erythropoiesis-stimulating agents (ESAs)(rare in India)



as the etiology for myocardial infarction (MI) in young individuals. Only 10% to 11% of patients have a nonplaque etiology such as spontaneous coronary dissection (SCAD), coronary embolism, or coronary microvascular dysfunction. Among plaque-based mechanisms, an intact fibrous cap (IFC) or plaque erosion should be considered, especially in younger women without traditional cardiovascular risk factors (with the exception of smoking).

Acute MI in young (Indian perspective)

- Most common in male
- 89% due to Coronary Plaque Rupture
- Mostly Anterior wall MI (LAD artery involvement)
- Most common Risk factor is Smoking, Stress and Poor life style
- Delayed presentation; Mean time of presentation after symptom onset is around 16 hours
- Manifests decades earlier than western population
- Angiographic features include Single vessel disease with less than 2 lesions & predominant Thrombus with Eccentric atherosclerosis with inflammatory response
- Low HDL, High triglycerides, High Lp(a) levels are common
- In-hospital mortality is low with favourable outcome

Traditional Risk Factors for MI in Young & Old—— Comparison

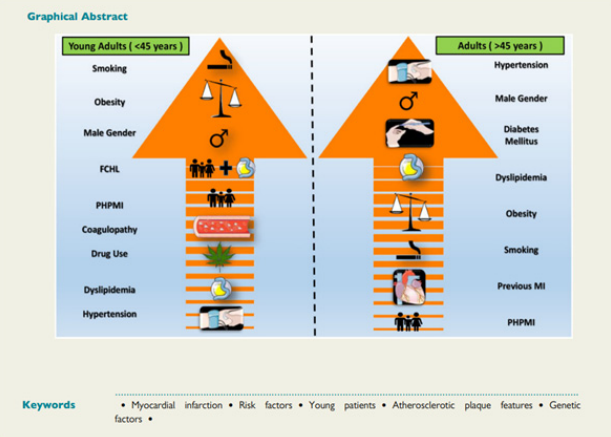
1. **Smoking** -A dose–effect response is associated with young MI incidence. Younger patients with MI were more likely to be smokers (80% vs. 57%) compared to the elderly
2. **Male Gender**; The patients of the young MI group were more likely to be male (80%). The dominance of men vs. women is frequently reported (80% vs. 71%)
3. **Diabetes Mellitus** DM is more common among elderly patients (10% vs. 37%)
4. **Obesity;** 80% of young patients with MI have a higher BMI. Compared to older MI age group (>45 years), patients in the younger group were more likely to be male and have a higher BMI (31 kg/m2 vs. 29 kg/m2)
5. **Homocysteine**; levels are increased in younger infarcted patients compared to the elderly (16.36 ± 7.8 mmol/L vs. 11.7 ± 5.6 mmol/L)
6. **Hypertension** ; More common among elderly patients (24% vs. 60
7. ***Dyslipidaemia*** *has a stronger correlation with MI incidence in the elderly compared to young individuals (43% vs. 36%)* Adolescents with a parental history of premature MI have increased lipoprotein-a [Lp(a)] levels. Likewise, a high level of Lp(a) has been described as an independent risk factor for MI in all age groups.
8. **FCHL**: Familial combined hyperlipidemia reduced the age onset of first MI by as much as 15 years. Approximately 10% of young MI patients present with elevated LDL-C levels. The EUROASPIRE IV cohort study of 7044 patients with MI, showed that 8.3% had probable FCHL, increasing to >15% in patients with premature event

9. **PHPMI;** Parenteral history of premature myocardial infarction Lp(a) levels are increased in healthy young patients with parental history of premature MI. PHPMI is reported in the vast majority of young MI cases (41–71%).

10. **Previous MI**; Incidence of previous MI is more common in the elderly (25% vs. 42%)

11. **Hereditary coagulopathies /Genetic Mutations**; Latest studies demonstrate that hereditary coagulopathies have a significant association with premature MI. Genetic mutations are part of differential diagnosis in cases with unexpected CAD occurring at a young age

12. **Drugs Illicit/Performance enhancing drugs**; Cardiovascular toxicity includes atherogenic, thrombotic and hematological effects as well as direct myocardial injury.



Psychosocial factors

The role of psychosocial stress is poorly recognized and underappreciated, and a higher prevalence of depression, anxiety, and hostility in younger patients likely contributes not only to addiction but to the pathogenesis of acute and chronic CVD.

Risk factors for MI at younger age

1. **Hypercoagulable states**; Thrombotic factors/fibrinolytic factors High levels of factor 5 or factor 10 Factor 5 leiden (most common), Higher levels of Factor 12 Antiphospholipid syndrome

2. **Homocysteine**; causes production of proinflammatory cytokines leading to oxidative damage (Methylene-tetra-hydrofolate reductase causes high levels of Homocysteine)

3. **Genetic factors** Factor II, Factor 5, Antithrombin deficiency, Protein C deficiency, Protein S deficiency, Lp(a), Products involved in pathogenesis of atherosclerosis .

4. **Intake of Anabolics & Stimulants**

   Cocaine & Cannabis Androgenic anabolic steroids

Diagnosis of myocardial infarction (MI) in young individuals

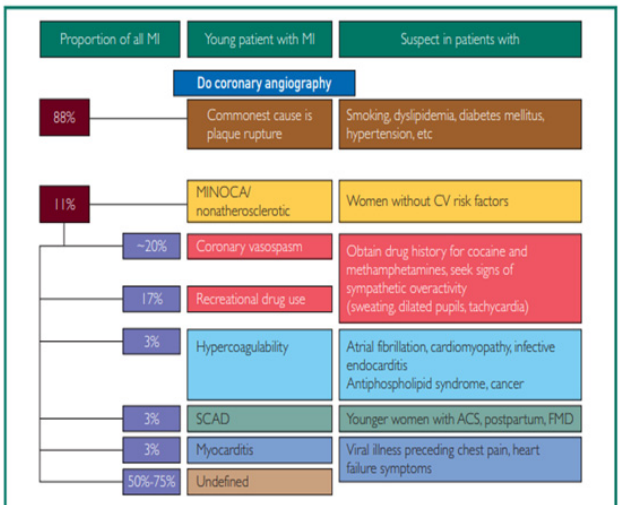


FIGURE 6. Diagnosis of myocardial infarction (MI) in young individuals. Data are compiled from multiple sources and reflect an approximation of the current prevalence of various causes of MI in young individuals. The most common cause of MI still is plaque rupture, accounting for around 88%. It should be suspected in patients with traditional cardiovascular (CV) risk factors, most commonly smoking and dyslipidemia. In 11% of patients, MI with nonobstructive coronary arteries (MINOCA) is observed. A history of recreational drug use, especially cocaine, should be sought and signs of sympathetic overactivity should be observed. Coronary embolism should be suspected in patients with atrial fibrillation, cancer, or cardiomyopathy. Spontaneous coronary artery dissection (SCAD) should be included in the differential diagnosis in young women, especially postpartum or with known fibromuscular dysplasia (FMD). Myocarditis should be high in the index of suspicion if there is a history of viral illness. Patients with MINOCA without any defined etiology should be encouraged to undergo further invasive testing to exclude coronary vasospasm. ACS = acute coronary syndrome.

MI Due to Atheromatous CAD Without Critical Coronary Stenosis (MINOCA)

- Angiographically young MI patients were divided into 2 subgroups; Plaque of 50% or greater (88%) or MINOCA (obstruction with plaque <50%).

- Angiographically Unruptured plaque characterization is now feasible with optical coherence tomography (OCT) and intravascular ultrasound (IVUS).
- Approximately one-third of cases of sudden death from ACS. Plaques with an intact fibrous cap (without plaque rupture) are seen more frequently in younger women (especially smokers) without known cardiac risk factors.
- 11 % Of ACS patients may have MINOCA
- Women had an almost 5 times higher incidence of MINOCA than men
- Many investigators include myocarditis and Takotsubo syndrome in MINOCA.
- For this review, we have not included Takotsubo cardiomyopathy because it principally affects older, usually postmenopausal, women
- If an intact fibrous cap of a coronary plaque is detected in a patient presenting with MI, it portends a favorable prognosis.

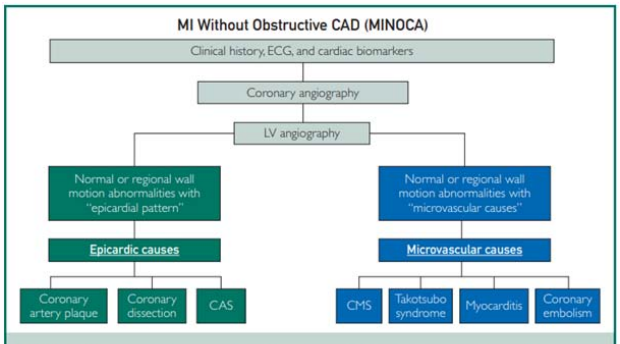


FIGURE 7. The diagnosis of myocardial infarction (MI) without obstructive coronary artery disease (CAD) (MINOCA) rests on obtaining a good clinical history, electrocardiography (ECG), cardiac biomarkers, and echocardiography. All these patients need to undergo coronary and left ventricular angiography. The potential causes can be ascertained from the types of regional wall motion abnormality (epicardic—plaque-based, coronary dissection, coronary artery spasm [CAS]; or microvascular—coronary microvascular spasm [CMS], Takotsubo syndrome, myocarditis, or coronary embolism). Adapted from *Eur Heart J Acute Cardiovasc Care*,[105] with permission.

Myocarditis & MI

The prevalence of myocarditis varies, but reported to be around 3% of patients with MINOCA.

Coronary Vasospasm (Microvascular Dysfunction)

Coronary Vasospasm (Microvascular Dysfunction)
The **true prevalence** of microvascular dysfunction in coronary arteries is unknown but it is associated with smoking & drug use .

- Higher in Asians
- Higher with ACS
- *Can lead to sudden cardiac death (AHA/ACC acknowledged)*
- Detected by provocative testing

Vasospastic Angina

- Vasospastic angina (Prinz-metal) typically presents with ST-elevation MI without provocation, is associated with stress, cold, or hyperventilation, and is characterized by prompt relief with sublingual nitroglycerine. Circadian variation is noted with this syndrome, with most attacks occurring during the morning hours. Vasospastic angina typically affects women smokers

MI Due to SCAD (Spontaneous Coronary Artery Dissection)

- SCAD is initiated by intimal disruption or intramural hematoma and is not due to underlying atherosclerosis, iatrogenic causes ,or trauma . It is commonly seen in younger women with a paucity of known cardiac risk factors. Recent series suggest that up to 1% to 4% of all cases presenting with ACS may be caused by SCAD and occur in younger women (<50 years). The factor most commonly associated with SCAD is fibromuscular dysplasia (FMD),
- Other factors associated with SCAD include pregnancy, connective tissue disorder, hormones, systemic inflammatory disorders (eg, Kawasaki disease, systemic lupus erythematosus)

Precipitating Factors for SCAD

Intense exercise or emotional stress, cocaine, retching, vomiting are the common precipitating factors for SCAD

Features of SCAD & Coronary artery spasm

Spontaneous coronary artery dissection	Coronary artery spasm
• 1% to 4% Overall prevalence	• 2% to 4% Overall prevalence
• Higher prevalence (up to 35%) in women <50 y	• Higher prevalence with provocative testing (20%)
• Important consideration in pregnancy and postpartum period	• Important cause of sudden cardiac death
• Look for fibromuscular dysplasia	• Higher prevalence in setting of acute coronary syndrome • Racial disparity, higher in Asians

Coronary embolism

- Coronary embolism is considered the cause of MI in 4% to

  13% of cases. These patients have no evidence of coronary atherosclerosis.

  In the Young Adult Myocardial Infarction and Ischemic Stroke (YAMIS) Study, major veno-arterial shunt was found in 25% of 101 young patients (16-39 years) who survived an MI and stroke.

  Paradoxical embolism as the cause should be considered in young adults in the presence of additional hypercoagulable risk factors (pregnancy, ischemic stroke, factor V Leiden).

Most common underlying disease in patients with CE was

- Atrial fibrillation (73%), followed by
- Cardiomyopathy (25%) and
- Valvular heart disease (15%). Less frequent cardiac etiologies of CE included
- Infective endocarditis and tumors.
- The systemic disorders associated with CE include Antiphospholipid antibody syndrome, malignancy, and autoimmune disorders.

No clear etiology could be discerned in 26.4%.

Myocardial bridging

This is a congenital anomaly in which a coronary artery is embedded within a tunnel of the subepicardial myocardium or has a band of myocardium overlying it. This can impede blood flow during systole that can persist during diastole resulting in myocardial ischaemia, which has been associated with myocardial infarction. Traditionally treatment involved surgical splitting of the band but there are now reports of successful treatment by stent implantation

Obesity & Young MI

- 80% of young patients with MI have a higher BMI. Compared to older MI age group (>45 years), patients in the younger group were more likely to be male and have a higher BMI (31 kg/m2 vs. 29 kg/m2
- Role of metabolically healthy obesity, the obesity paradox, and various lifestyle modifications for weight loss that would be important in the management of young obese individuals who present with an MI

Pregnancy and MI

- Incidence of MI is 3 per 100,000 pregnancies
- Higher maternal mortality rates (5%)
- Multivariate predictors included older maternal age.
- Most MIs occurred during the third trimester or during the early postpartum period.
- Atherosclerosis is not very common, and many pregnant women have SCAD Spontaneous Coronary Artery , microvascular dysfunction, thrombus, or coronary emboli
- Higher incidence of ST-segment elevation MI (75%) in the anterior wall (69%) is noted.
- Treatment should be individualized based on the needs and health of the mother and child and requires a multidisciplinary approach. Optimal care may include bare metal stents and postponing delivery by 2 to 3 weeks after MI. During MI, Aspirin and b-blocker use are safe in pregnancy, but other drugs (statins/angiotensin-converting enzyme inhibitors/fibrinolytic therapy) either

have been found to be unsafe or have not been tested during pregnancy. Heparin is the anticoagulant of choice (during stent placement) because it does not cross the placenta. Bleeding may be more problematic during longer-term heparin use.

- The complication rates of MI are high in pregnant patients, and in one study 38% experienced heart failure/shock, 12% had ventricular arrhythmias, and 20% had recurrent angina

CLINICAL PRESENTATION YOUNG MI

- Two-thirds of all MIs in young patients present with non-ST-elevation
- In general, clinical presentation in young patients with MI is **indistinguishable from that of older patients**, and most patients present with chest pain due to plaque rupture.(88%)
- **First** History of angina symptoms before MI is less common, seen in approximately one-fourth of patients.
- **Second**, 69% of patients younger than 45 years do not report chest pain before MI.
- **Third**, the onset of symptoms is within 1 week of MI.
- In addition, younger women typically have longer delays in reporting symptoms and getting medical attention in the setting of MI; possible reasons could be varying prodromal symptoms, inaccurate assessment for personal cardiac risk, competing and conflicting priorities affecting their decision making, less consistent response of the health care system to symptoms, and poor access to primary care.
- In young patients who present with MI in the setting of normal coronary arteries, recent recreational drug use should be recorded and signs of sympathetic overactivity should be noted (sweating, mydriatic pupils, tachycardia)
- Clinical and family history of recurrent arterial and/or venous thrombosis should be diligently evaluated
- Similar to other MIs, patients with SCAD present with chest pain (95.9%) and elevation of cardiac biomarkers (26%-87% with ST-segment elevation MI). Ventricular arrhythmia or sudden cardiac death is the presenting symptom in 3% to 11% of patients.

Clinical Presentation of Young Patients With Myocardial Infarction

- Two-thirds present with non–ST-elevation myocardial infarction
- Chest pain characteristics similar to those in older patients
- Women have 5-times higher odds of having myocardial infarction with nonobstructive coronary artery disease
- Look for drug use (cocaine) or source of thromboembolism
- Suspect myocarditis in patients with a history of viral illness who present with worsening heart failure or chest pain

Clinical presentation of Myocarditis

- Presenting symptoms of myocarditis vary from dyspnea or chest pain to life-threatening shock or arrhythmias, and therefore, this diagnosis requires a high index of suspicion.
- Two main presentations of myocarditis are new or worsening congestive heart failure or symptoms of chest pain akin to those of ACS.
- Preceding viral illness (respiratory or gastrointestinal symptoms), younger age, and inflammatory markers (high C-reactive protein level) can point to a diagnosis of myocarditis .
- *Treatment with acyclovir, ganciclovir, and valacyclovir for herpesvirus and interferon beta for adenoviral or enteroviral infection can be considered.*

MI due to Drug Abuse (less common in India)

- *In young patients who present with MI in the setting of normal coronary arteries, recent recreational drug use should be recorded and signs of sympathetic overactivity should be noted (sweating, mydriatic pupils, tachycardia).*
- *Obtaining a good drug history is paramount in younger patients presenting with MI.*
- *Rates of MI associated with cocaine use range between 0.7% and 6%, Its use was associated with an almost 5-times higher risk of MI over baseline , especially within the first hour after use.*

  Patients with cocaine induced persistent ST elevation not resolved by nitrates, should be offered thrombolytic therapy Betablockers should be avoided as it can precipitate severe vasospasm.
- *Marijuana and risk of CVD.; use of marijuana was associated with higher mortality.*

When the Initial Work-up for MINOCA is Negative then search for

- *Precipitating causes:*
- *Drug history (cocaine, methamphetamine, marijuana)*
- *Preceding viral illness favours myocarditis*
- *Type II myocardial infarction due to supply/ demand mismatch*

Cardiac MRI (late gadolinium enhancement) may be done

- Subepicardial enhancement indicates myocarditis
- Subendocardial enhancement indicates ischemia , dissection, thromboembolism

Treatment of microvascular dysfunction

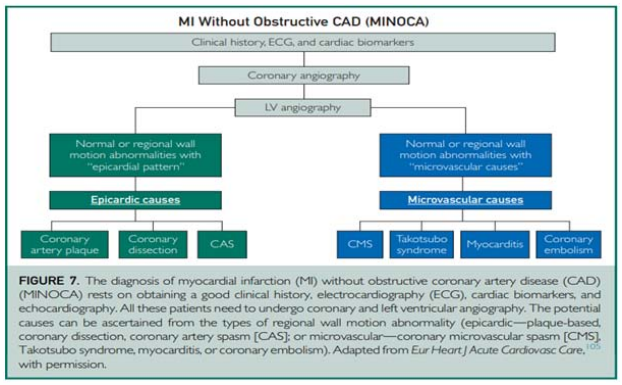


FIGURE 7. The diagnosis of myocardial infarction (MI) without obstructive coronary artery disease (CAD) (MINOCA) rests on obtaining a good clinical history, electrocardiography (ECG), cardiac biomarkers, and echocardiography. All these patients need to undergo coronary and left ventricular angiography. The potential causes can be ascertained from the types of regional wall motion abnormality (epicardic—plaque-based, coronary dissection, coronary artery spasm [CAS]; or microvascular—coronary microvascular spasm [CMS], Takotsubo syndrome, myocarditis, or coronary embolism). Adapted from *Eur Heart J Acute Cardiovasc Care*, [105] with permission.

The treatment of patients with coronary microvascular dysfunction should be guided by the outcomes and the results of the invasive testing.

- *Once detected, Most patients need basic CVD prevention (diet, exercise, and weight loss)*
- *Long-term nitrates with or without non-dihydropyridine calcium-channel blockers. Their doses in isolation or in combination can be gradually increased to the maximum tolerated dose.*
- *b-Blockers (especially nonselective), in general, are avoided because they can exacerbate and prolong vasospasm.*
- *Nicorandil (a nitrate and potassium channel activator), magnesium, antioxidants, rho kinase inhibitor, and statins have been tried with some success in these patients*

Conclusion

- *Young MI patients have a cluster of risk factors including eccentric atherosclerotic plaques with inflammatory features,*
- *Higher incidence of tobacco use, obesity, and increased healthy lifestyle risk factors, such as inactivity and alcohol intake.*
- *Compared with older patients where MI is prevalent among men and women, young MI patients are more likely to be men, have a family history of FCHL and higher levels*

of Lp(a).

- *In addition, cannabis and cocaine use, as well as the use of AASs are risk factors for MI in young patients.*
- *Genomic differences, especially in the pathways of coagulation and lipid metabolism, have also been identified between young and older patients with MI.*
- *The relative contributions of gene pathways related to lipid metabolism, inflammation, cellular proliferation, vascular tone, or other as yet undiscovered pathways may provide important insights.*
- *Both familial hypercholesterolaemia mutations and high polygenic scores are associated with increased odds of early-onset MI.*

Healthy lifestyle factors (HLFs) and MI in younger patients are

(i) average body mass index< 25 kg/m2 ;

(ii) no or moderate alcohol intake;

(iii) higher healthy diet score;

(iv) higher physical activity score; and

(v) never smoking

The different pathophysiology and risk factor profile of young and older MI patients could help identify young subjects at increased risk and guide primary and secondary prevention strategies

Clinical implications

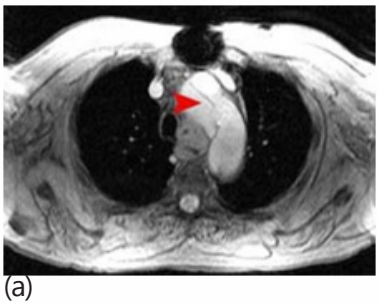
- *Taking into account the differences in the profile of young and older MI patients, customization of the established primary and secondary prevention strategies may be considered.*
- *Since, it is rather difficult to identify hereditary atherosclerotic burden in young population, clinicians have to prevent the thrombotic events.*
- *Clinical awareness for the development of CAD even at younger age is required. The value of asymptomatic screening for CAD has to be explored especially in subgroups of patients with strong family history of premature CAD or presence of non-traditional risk factors [e.g. increased Lp(a) or C-reactive protein serum levels].*
- *Surveillance and monitoring for the early onset of arterial hypertension, an abnormal lipid profile, central obesity, and strong counselling against smoking should be implemented, especially when other predisposing thrombotic factors co-exist e.g. use of oral contraceptives in young women.*
- *Clinicians must be conscious of the prevalence of drug abuse among young people, which has been steadily growing over the year*
- *The major area of concern is that 50% of total young MI patients may not receive any reperfusion therapy due to late diagnosis.*

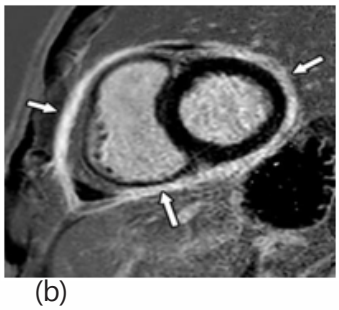
Differential Diagnosis Of The Acute Coronary Syndrome – A Doctor ' S Dilemma

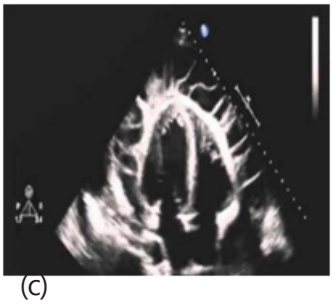
Dr . Birupaksha Biswas
MD (Clinical Pathology)
Special Interest in Critical care Medicine
drbiswasassted.medicalglory@gmail.com

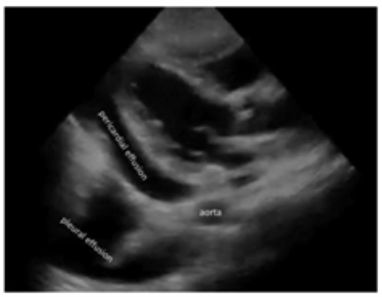
Whereas , it been documented that nearly 70 % patients with a suspected A C S predominantly due to the coronary pathology die within the transit time vis -a -vis from the onset of the symptoms to catheterization (door to needle time) OR from an alternative diagnosis which leads to a loophole in the proper history taking / specific workups of the patient which might aid & thereby may be helpful for the in- patient treatment, certain differentials to the chest pain or no chest pain due to autonomic pathology which is thought to be a resultant of a long standing diabetes (as both diabetes & hypertension hold a deep relevance for atherosclerosis) , must be considered.

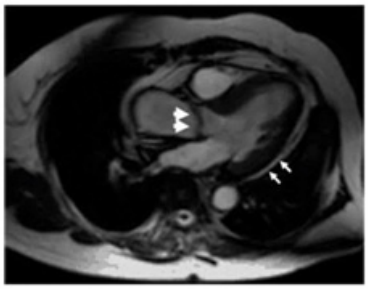
Generally , with respect to cardiac pathologies , aortic dissection , Infective or Non Infective (constrictive & restrictive) pericarditis or pericardial effusions , Severe Aortic stenosis (< 1 cm sq. & a mean gradient > 40 mm of Hg, Transaortic velocity > 4 m / sec) which may be eliminated by a quick E C G & a 2 - D Echocardiogram with a colour Doppler / TTE or a CT / MR angiogram revealing possibly a Concave ST segment on EC G (points towards pericarditis) & at times the EC HO catches up with the pericardial inflammation , Approximately 20 - 50 ml fluid in the pericardial space , and CT or MR angiogram will confirm the presence of a proximal or a distal tear in the intima of the aorta (Stanford classification) obviously supplemented with a quantitative cardiac enzyme workup (Trop I , CK - MB : CK ratio , LDH), markers of inflammation , meticulous history taking of any background co morbidities (consider a diagnosis of uraemic pericarditis), preceding infections , type of pain & the radiation with a close look at the haemodynamics of the patient might exclude / include the above mentioned . (Whereas pericarditis , carditis or pericardial effusions may be a direct result of a S T E M I)


(a)


(b)


(c)


(d)



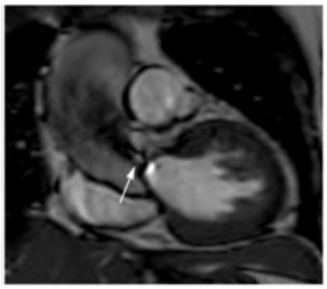

(e)

Figure : (a) A cardiac MRI showing an aortic dissection. (b) Four-chamber double inversion-recovery black blood MRI image shows circumferential pericardial thickening in acute pericarditis. (c) Pericarditis as seen in the ECHO. (d) Pericardial effusion as seen in ECHO. (e) Cardiac M RI showing a severe aortic stenosis.

With respect to the Gastrointestinal lesions , Peptic ulcer Disease , G astro Esophageal Reflux disease , isolated oesophagitis & often acute pancreatitis or cholecystitis may mimic an imminent A CS . On a gross , Evaluation of the G . I system looks to be cumbersome , therefore some quick blood tests not limited to an lipase estimation , CRP , lipid profile , a quick ultrasound , a CT + - contrast & if necessary a E G D (Esophagogastroduodeno-scopy) , M R C P nearly eliminates the the possibility of the G I causes. An obviously history taking in which a clinician DO FALTER , does not go without saying.

As the thoracic organs seem to be really good friends , Respiratory pathologies mimics & leads to serious cardiovascular outcomes, as it was classically documented in the management of AR DS in COVID -19. To name some , a pulmonary embolus , Pulmonary arterial hypertension , Any cause of pleurisy , tracheobronchitis , some neoplastic lesions & rarely pneumothorax may mimic an E C S . A Simple C T - thorax & a 2 D echo , E C G , a Chest X Ray to the least as mentioned, least of again a history with clinical examination nearly rules out all. For a P. E a classical finding of an embolus in the pulmonary artery (Or S1 Q3 T 3 as per textbooks) , any variety of a pneumothorax , PAH as documented in the echo of > 20mm Hg (2018 W .H .O update further categorised into mild , moderate & severe PAH ~ > 45 mm of Hg) , pleurisy due to Infective / non Infective causes may be delineated again supplemented with a recording of the crucial history & haemodynamics.

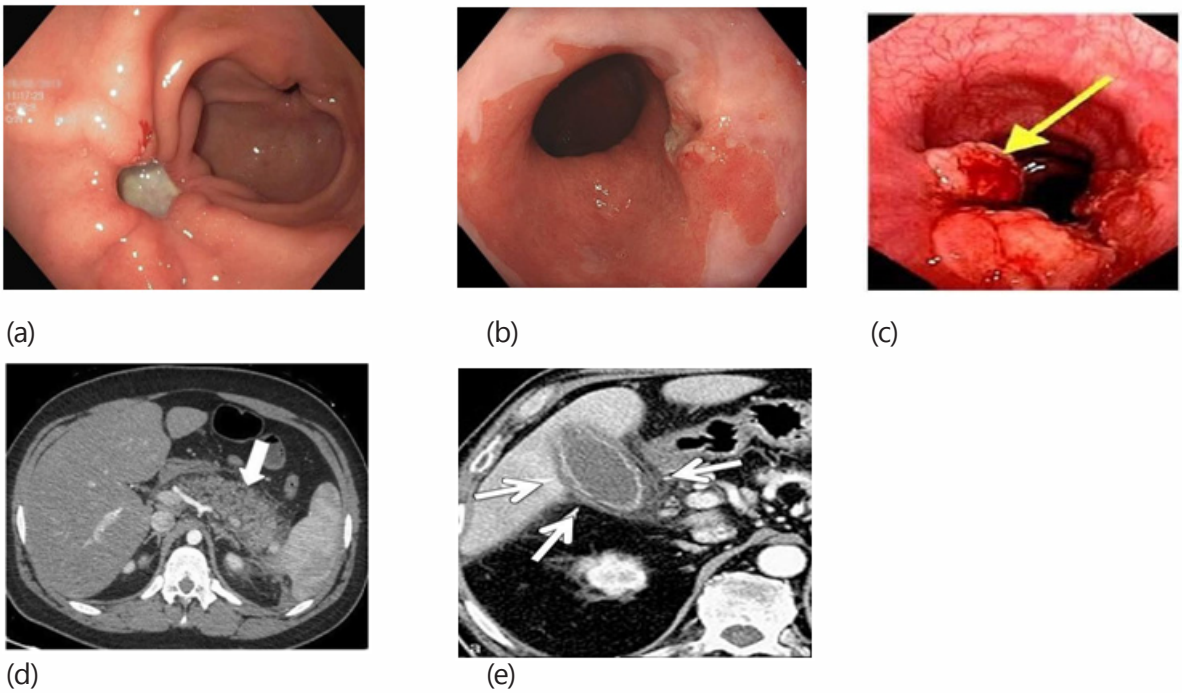
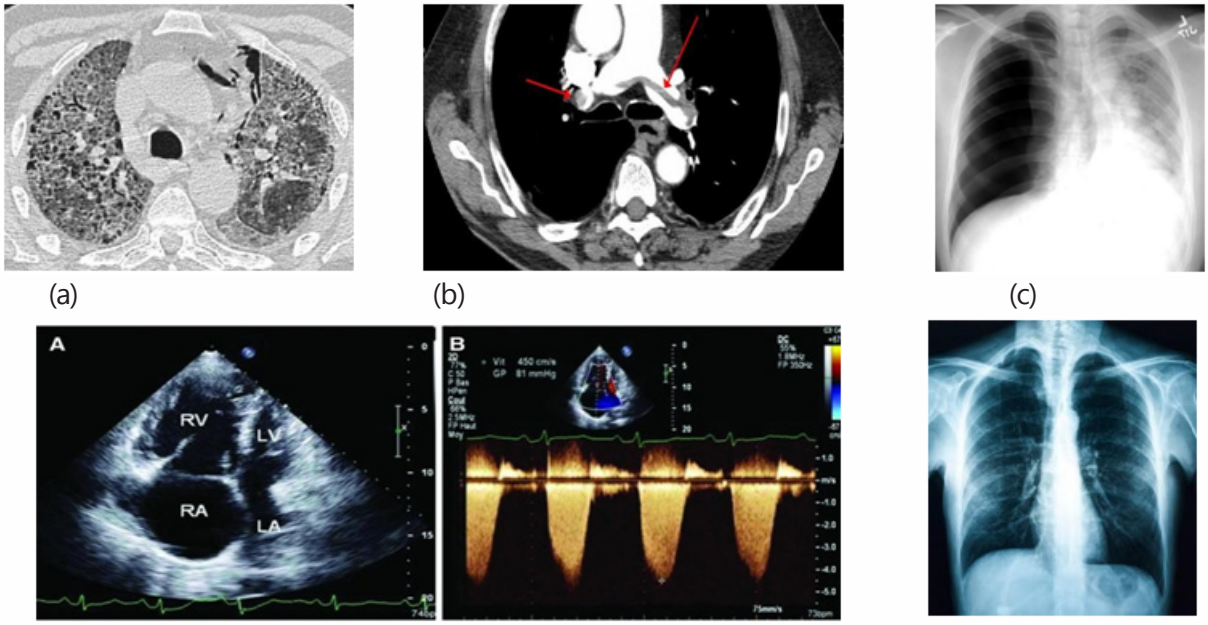


Figure : (a) A Peptic ulcer as seen in the OGD. (b) A Barrett's eosophagus as a resultant of chronic severe esophagitis on EGD. (c) Adenocarcinoma of eosophagus due to chronic GERD on EGD. (d) Severe necrotic pancreas with fat stranding as seen on the CECT whole abdomen. (e) The inflamed gall bladder as seen in CECT whole abdomen in acute / chronic pancreatitis.



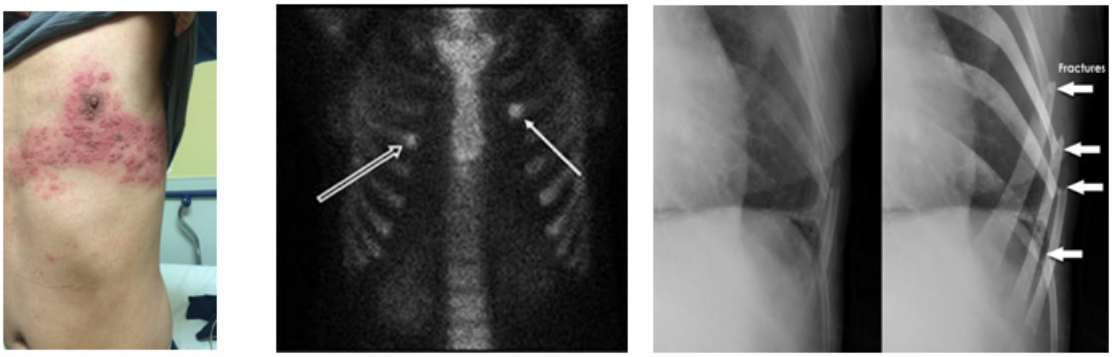
(a) (b) (c) (d) (e)

Figure : (a) Classical ARDS as seen in the CT thorax. (b) A huge pulmonary embolus as seen in the C T of the Pulmonary artery. (c) A classical pneumothorax Right sided hypertranlucency with atelectasis with a left mediastinal shift as seen in the X Ray. (d) Pulmonary arterial hypertension as seen with the dilated Right sided chambers of the heart with increased pressures as seen on the ECHO. (e) Tracheobronchitis as seen on the X ray.

Miscellaneous causes are those that are also to be considered, Herpes Zoster infections(Shingles) , Costocondritis , Rib fractures & rarely due to Psychiatric issues may lead to a erroneous diagnosis. Whereas the first three may be excluded simply from a history & General examinations , the latter one is supposed to be an exclusion of Diagnosis & a psychiatric referral may be warranted.

Besides all, the drug history must be elucidated. Tetracyclines , Clindamycin , Doxycycline, NSAIDs' are notorious to cause an acute chest discomfort.

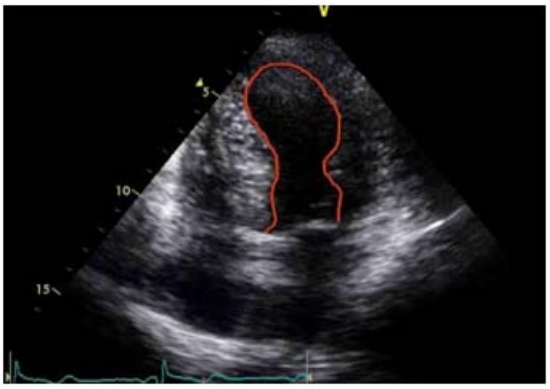
Some rare cases like the Mid Ventricular Takotsubo Cardiomyopathy (Broken Heart syndrome as a result of excess sympathomimetic activity where classical S T E M I changed are available but coronary angiography do not reveal a pathology



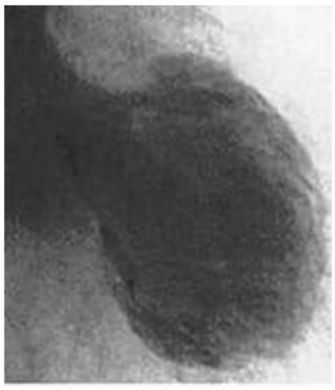
(a) (b) (c)

Figure: (a) Shingles due to HZV. (b) The 99mTc-MDP bone scan shows a focal increase in MDP uptake at the anterior end of left 3rd rib (arrow) and the right 4th rib (open arrow) on the anterior static image for Costocondritis. (c) Rib Fractures as seen on the Chest X Ray.

, EC HO reveals an apical balloning) & various forms of vasculitis involving the small, medium & large arterias(Churg Strauss syndrome , Takayasu Arteritis , Microscopic polyangitis , Polyarteritis Nodosa) are potential causes to mimic or cause an A C S . A radiological diagnosis with an evaluation of the serum inflammatory markers along with the both P & C AN CA ' s may be useful, obviously coupled with a good clinical examination.



(a)



(b)

Figure: (a) ECHO in apical 4-chamber view, showing dilatation of the apex and the mid segments of the left ventricular wall, diagnostic of Takotsubo Cardiomyopathy. (b) Takotsubo Cardiomyopathy as seen in the Left Ventriculography.

The take home message would be , Alternatives are always to be considered . As mentioned in the title , it is uncanny for a clinician to rely only on extreme orthodox thinking regarding the diagnosis. Therefore Acute Chest discomforts must be evaluated swiftly for better results.

"Curiosity is gluttony. To see is to devour." - Victor Hugo

Targeting residual CV risk in Statin Era: Cholesterol or Inflammation

Dr. Rajiv Agarwal
MD, DM Cardiology, FACC
Principal Director Cardiology
Max Smart Super Speciality Hospital, Saket, New Delhi

Lipid lowering has been one of the most effective strategies for both primary and secondary prevention of cardiovascular disease especially myocardial infarction. Studies have shown the importance of low density lipoprotein (LDL) lowering and that lower is better with no lower threshold for benefit. However aggressive lipid lowering does not eliminate cardiovascular risk and considerable cardiovascular risk remains even in patients optimally treated by current guidelines.

Guidelines recommend lipid LDL lowering goals that are more stringent in those with established atherosclerotic cardiovascular disease (ASCVD) or in those without a cardiovascular event but at high risk. For example in the European guidelines, there is an LDL goal of 100 to 70 mg/dl in patients with low to moderate risk, whereas those with established ASCVD or high risk should aim for LDL cholesterol below 55 mg/dl (*2019 ESC/EAS guidelines for the management of dyslipidemia. Eur Heart J 2019*). There is also a provision for keeping LDL cholesterol below 40 in those with recurrent coronary events or polyvascular disease involving more than one territory (coronary, cerebrovascular, peripheral arterial). It is noteworthy that the Lipid Association of India (LAI) proposes an LDL goal below 30 mg/dl in the extreme risk category. (*Proposed low-density lipoprotein cholesterol goals for secondary prevention and familial hypercholesterolemia in India with focus on PCSK9 inhibitor monoclonal antibodies: Expert consensus statement from Lipid Association of India. Puri R, Mehta V, DuellB et al. J Clin Lipidol 2020;14:e1-e13*). These levels of extreme cholesterol reduction may be achieved by high intensity statin therapy but may often require additional oral drugs like ezetimibe and now bempedoic acid. Rarely injectable medicines are required like PCSK9 inhibitors and newer drugs like inclisiran are in the pipeline, all of which are expensive and beyond the reach of many patients.

High intensity statins are known to reduce LDL cholesterol levels by 50-70% in various randomized trials. Likewise the CV risk is also reduced from 24-44% in various studies, leaving a considerable amount of residual risk. The Cholesterol Treatment Trialists' (CTT) meta-analysis looked at 22 trials of statin versus control (n=1,34,537; mean LDL cholesterol diûerence 1·08 mmol/L; median follow-up 4·8 years) which showed a 21% relative risk (RR) reduction in CVD events.(1 mmol of cholesterol equals about 39 mg/dl.) A further five trials of more versus less statin (n=39,612; mean LDL diûerence 0·51 mmol/L, median follow up 5·1 years) showed a further 16% RR reduction in CVD event. Yet even after this, there was a mean LDLc on treatment of 70 mg/dl and a 5 yr risk of a major vascular event of 13%. *(Lancet 2010)*

Early observational studies showed a log linear relationship between LDLc reduction and reduction of CV risk, such that proportionate or relative risk reduction (RRR) of vascular events with lipid lowering therapy is fairly constant. Thus a reduction of LDLc level from 160 to 120 mg/dl will produce the same 20% reduction in CV events as will a further reduction of LDLc from 120 to 80

mg/dl. This was demonstrated in the large randomized Heart Protection Study (HPS) which also showed that there was no lower threshold of useful lipid lowering below which further treatment would be futile or at which side effects would be prohibitive. (*Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo controlled trial. Lancet 2002;360:7-22*)

This was further substantiated by further trials including the Treat to New Targets (TNT) trial. (*LaRosa JC, Grundy SM, Waters DD, et al. Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary artery disease. N Engl J Med. 2005;352:1425–35.*) An exhaustive list of trials shall not be attempted here.

This log linear reduction of CV risk with cholesterol reduction is true not just for statins but for other therapies including diet, other oral drugs like ezetimibe, injectables like PCSK9 inhibitors and even ileal bypass. (*Silverman MG et al. JAMA. 2016;316(12):1289-1297*).

At average cholesterol levels, the risk of vascular events decreases by approximately 1% for every 2 mg/dl reduction in LDLc levels but the absolute risk reduction achieved will be less at lower baseline cholesterol levels. This is because, in mathematical terms, the absolute risk reduction (ARR) is a product of baseline risk and relative reduction of risk (RRR). Thus aggressive lipid lowering below currently accepted levels is likely subject to the law of diminishing returns. (*Laufs et al. Eur Heart J. 2014 Aug 7;35(30):1996-2000*)

Lipid reduction should be pursued along with a reduction of other measurable cardiovascular risk factors including hypertension, diabetes and insulin resistance, tobacco and smoking, and obesity. A healthy life style is also essential to promote physical and mental health and reduce coronary events. Since we do not fully understand the pathogenesis of atherosclerosis, we need to emphasize a multi factorial approach, instead of exclusive focus on any one factor.

Today we consider an LDL cholesterol below 70 mg/dl as acceptable for most patients from the point of view of clinical risk reduction, cost and achievability with current oral medicines. Even this moderately aggressive target may require additional oral or injectable medicines in 5-10% of patients. Considerable residual risk remains however at this level of LDLc and the best strategy for such patients remain an important therapeutic consideration.

The mechanism of atherosclerosis and even cardiovascular events is multifactorial and governed by several traditional and non-traditional risk factors with lipids being only one of them. The list includes additional lipid targets like small dense LDL, nonHDL cholesterol, triglyceride, Lp(a) and Remnant like particles. Other factors include long term anti platelet therapy, with or without aspirin, anti thrombotic therapy including dual pathway inhibition by Rivaroxaban and therapies directed at dysgycemia even without diabetes like SGLT2 inhibitors and GLP1 receptor agonists. In particular the role of inflammation in the causation of atherosclerosis has found wide acceptance based on laboratory and clinical studies. Thus residual CV risk may be thought to reside in each of these mechanisms despite using current evidence based therapies for conventional risk factors. *(Lawler P et al. Eur Heart J 2021;42:113-131)*.

The correlation of high sensitivity C reactive protein (hsCRP) levels with coronary events is well known. HsCRP is a non specific downstream marker of inflammation. While high lipid levels especially oxidized LDL may contribute to inflammation and macrophage activation in the atherosclerotic plaque, the levels of hsCRP may even be elevated in patients with normal or controlled cholesterol levels. HsCRP is a reliable marker of systemic inflammation, with values stable over time and correlated with risk of CV events in >30 prospective epidemiologic studies, and even treatment

studies.(*Ridker PM et al. J Am Coll Cardiol 2016;67:712-723*). Values below 1 mg/dl denote low CV risk, 1-3 mg/dl moderate risk and 3-10 mg/dl high CV risk. Values beyond 10 mg/dl may be an acute phase response to recent infection or stress and may be disregarded for CV prognosis. Similarly, plasma Interleukin-6 levels have also been correlated with risk of CV events in multiple trials.

In AFCAPS/TexCAPS trial, no clinical benefit of statin therapy was observed among those with LDLC<150 mg/dL who had hsCRP <2 mg/L, yet a substantial clinical benefit was observed among those with LDL <150 mg/dL with hsCRP >2 mg/L. Thereafter, the JUPITER trial of primary prophylaxis with Rosuvastatin in high risk patients without a vascular event was conducted as a direct test of the hypothesis raised in AFCAPS/TexCAPS - would statin therapy reduce event rates among those with elevated hsCRP but low levels of cholesterol, a group at high risk that is currently outside all treatment guidelines?(*Paul M Ridker, Circ Cardiovasc Qual Outcomes. 2009;2:279-285*). In the trial 17082 primary prevention subjects with LDL <130 mg/dl, hsCRP>2 mg/dl, were randomized to Rosuvastatin 20 mg or placebo. Rosuvastatin decreased LDL by 50%, hsCRP by 37% with 44% RRR in combined clinical end point (CV death, MI, stroke, revasc, hosp for Unstable angina). Best results were achieved when both LDL and hsCRP targets were achieved. In fact a 79% RRR was possible with Rosuvastatin in the trial if both LDL<70 and hsCRP<1 were achieved. Thus JUPITER was the first study to show the importance of hsCRP reduction in CV risk reduction. (*Ridker PM et al. N Engl J Med 2008;359:2195-2207*). The importance of lowering hsCRP has also been shown in post-hoc analysis of secondary prevention trials like PROVE-IT and IMPROVE-IT (*Ridker PM et al. N Engl J Med 2005;352:20-28, Bohula EA et al. Circulation 2015;132:1224-1233).* Residual inflammatory risk associated with high CRP levels has been demonstrated even at very low LDL levels, achieved with PCSK9 inhibitors in the Fourier and SPIRE series of trials (Ridker PM et al J Am Coll Cardiol 2018;72:3320-3331).

Reduction of hsCRP levels can be achieved with statins as above but also by reduction of unhealthy lifestyle, diet, obesity and smoking. Bempedoic acid is another lipid lowering agent with proven CV risk reduction (CLEAR-Outcomes Trial) that can lower hsCRP levels. Newer anti-diabetic drugs like GLP-1 receptor agonists and SGLT2 inhibitors also lower hsCRP levels.

Canakinumab is a monoclonal antibody that directly inhibits inflammatory cytokine Interleukin-1. On treatment hsCRP and IL-6 level reduction in the CANTOS trial were shown to reduce CV events. The patients already had well controlled lipids with average LDL 82 mg/dl and no effect of the study drug on lipid levels. However this trial was a failure as it showed increase in fatal infection and no reduction in overall mortality. (*Ridker PM et al Eur Heart J 2018;39:3499-3507*).

A more practical approach to hsCRP reduction may be with Colchicine, a low cost oral drug, primarily used for gout and pericarditis. In LODOCO-2 trial of stable ischemic heart disease and in COLCOT trial after acute myocardial infarction, colchicine at a daily dose of 0.5 mg/day has been shown to reduce elevated hsCRP levels and CV event risk at 2-2.5 year follow up with few side effects. (Nidorf SM et al. N Engl J Med 2020;383:1838-47, Tardif JC et al. N Engl J Med 2019). Total mortality was not reduced and the approach is not widely used despite a total of nearly 10,000 patients enrolled in the above named placebo controlled trials.

In a recent collaborative analysis of 3 contemporary randomized clinical trials, the relative contribution of inflammation and cholesterol as predictors of CV events was investigated among patients receiving contemporary evidence based therapy including statins. A total of 31245 patients from the PROMINENT, REDUCE-IT, and STRENGTH trials were enrolled, (average baseline LDL 76 and hsCRP

2.2 mg/dl). Patients were analysed as per quartiles of increasing LDL and hsCRP levels. Among patients receiving contemporary statins, reducing inflammation as assessed by hsCRP <2 mg/dl was a stronger predictor for reduced risk of future major CV events, CV mortality and all-cause death than reduction of LDL below 70 mg/dl. In other words once LDL cholesterol of 70 mg/dl is achieved, one should pursue residual inflammation and other risks more aggressively rather than going for ever lower cholesterol levels. (*Ridker P, Bhatt DL et al Lancet 2023;401:1293-1301*).

This suggests a new approach whereby, once we achieve a moderately aggressive lipid target target of LDL <70, we should assess hsCRP levels also and try to reduce it by the measures listed above, rather than only adding another lipid lowering agent. This is not an either-or approach but we need to lower both lipids and inflammation along with other risk factors. This is also not trivial as most patients and even doctors will adopt a finite amount of preventive care. This preventive care, therefore, should be carefully chosen to prioritize first those interventions that will be most effective and practicable.

Future research may be directed at how best to lower the hsCRP levels, including newer drugs.(*Zahid A, Li B, Kombe AKK et al, Pharmacological Inhibitors of the NLRP3 Inflammasome.Front Immunol 2019;doi:10.3389/fimmu.2019.02538*) For the present we should at least start to measure hsCRP levels in all our patients with CV events or at high risk. This will itself be a significant change in our risk perception and management of these patients.

Perioperative Management of Ischemic Heart Disease

Dr Soumi Das
Associate Professor,
Department of Cardiac Anaesthesia I.P.G.M.E&R, Kolkata.
E mail id: soumidasanaesth79@gmail.com

Ischemic heart disease is a disease of inadequate supply of blood and oxygen to a portion of myocardium supplied by coronary artery which is partial to completely occluded by atheromatous plaque. It is also known as coronary artery disease. Most common cause is atherosclerotic disease of epicardial coronary arteries resulting in regional reduction in myocardial blood flow and inadequate supply by involved coronary artery.

Ischemic heart disease may present in the following ways:

i) Chronic stable angina

ii) Acute coronary syndrome - unstable angina and myocardial infarction - Non ST elevated MI and ST elevated MI.

iii) Sudden cardiac death

Following are the predisposing risk factors for ischemic heart disease:

- High blood pressure
- High cholesterol level
- Smoking
- Family history of coronary artery disease
- Diabetes
- Obesity

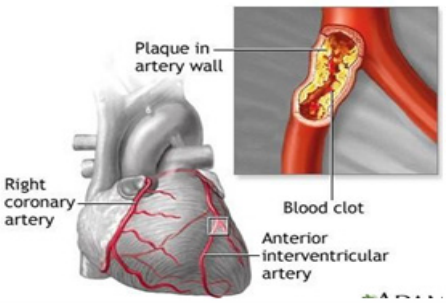


Figure 1 : of atherosclerotic vessel

Pathophysiology of ischemic heart disease:

A mismatch between myocardial oxygen delivery and demand is the underlying pathophysiology of myocardial ischemia, which brings us to the various determinants of myocardial oxygen demand and supply.

Three major determinants of myocardial oxygen demand are:

i) Myocardial wall tension (PR/2T)

ii) Contractility

iii) Heart rate

Determinants of oxygen supply are:

i) Coronary blood flow which depends on : diastolic arterial pressure, left ventricular end diastolic pressure, patency of coronary arteries, coronary vascular tone.

ii) Arterial oxygen content :

$CaO2\ (ml/L) = [1.34 \times Hb(g/dl) \times SaO2] + [(0.0031 \times PaO2(mm\ Hg))$

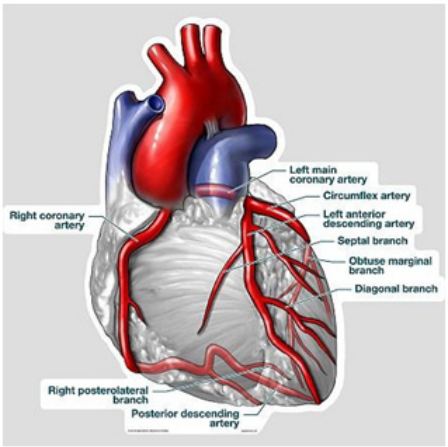


Figure 2: Coronary artery anatomy and blood flow

Management of Ischemic Heart Disease:

- Correction of risk factors.
- Lifestyle modification - reduce stress, improve exercise tolerance.
- Treatment of co-morbidities that may exacerbate ischemia like hypertension, anaemia, hypoxemia, hyperthyroidism, fever, adverse drug effect.
- Medical management to balance myocardial oxygen supply - demand.
- Anti-coagulation.
- Correction of coronary lesions by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

Pre-operative Evaluation prior to non cardiac surgery:

Goals of pre-operative evaluation

i) Evaluation of patient's current medical status.

ii) Clinical risk profiling.

iii) Decision on further testing.

iv) Treatment of modifiable risk factors.

v) Strategize management of the cardiac conditions during the peri-operative period.

Pre-operative evaluation in a patient with IHD will therefore include:

- Taking history of present illness characteristic of ischemic heart disease: angina pectoris, chest discomfort, heaviness, squeezing, atypical location of pain as in arising in arm radiating to back, interscapular region, root of neck. jaw, teeth, dyspnoea, poor exercise tolerance, syncope etc.
- Type of IHD, h/o prior MI, duration of IHD, present condition and ongoing treatment.
- H/O comorbidites like hypertension, obesity, respiratory disease, smoking, alcohol intake, obstructive sleep apnoea, diabetes mellitus, renal disease, hyperlipidemia, cerebrovascular event, coagulation disorders, features of congestive heart failure, family history.

During physical examination to look for signs of left or right ventricular failure, raised jugular venous pressure, pedal oedema, orthostatic hypotension, carotid bruit, S3 on auscultation, etc.

Apart from routine, following investigations are done for IHD patients pre-operatively:

- Baseline ECG - ST-T wave changes, arrythmia.
- Cardiac enzymes - CPK MB, cardiac specific troponins.
- Specialized testing like exercise ECG, myocardial perfusion scanning, echocardiography, coronary angiography.
- Non invasive cardiac stress testing - AHA/ ACC 2014 guidelines propose preoperative stress testing if all the following criteria are met - elective surgery, patients with poor or unknown functional capacity, patients having elevated perioperative risk of major adverse cardiac events, testing will have an impact on decision making for peri-operative care.

Stepwise approach to patient with IHD prior to non cardiac surgery (ACC/AHA 2014 guidelines)

i) Is there clinical need for emergency non cardiac surgery?

ii) Are there active cardiac conditions?

iii) Does the patient have clinical risk factors?

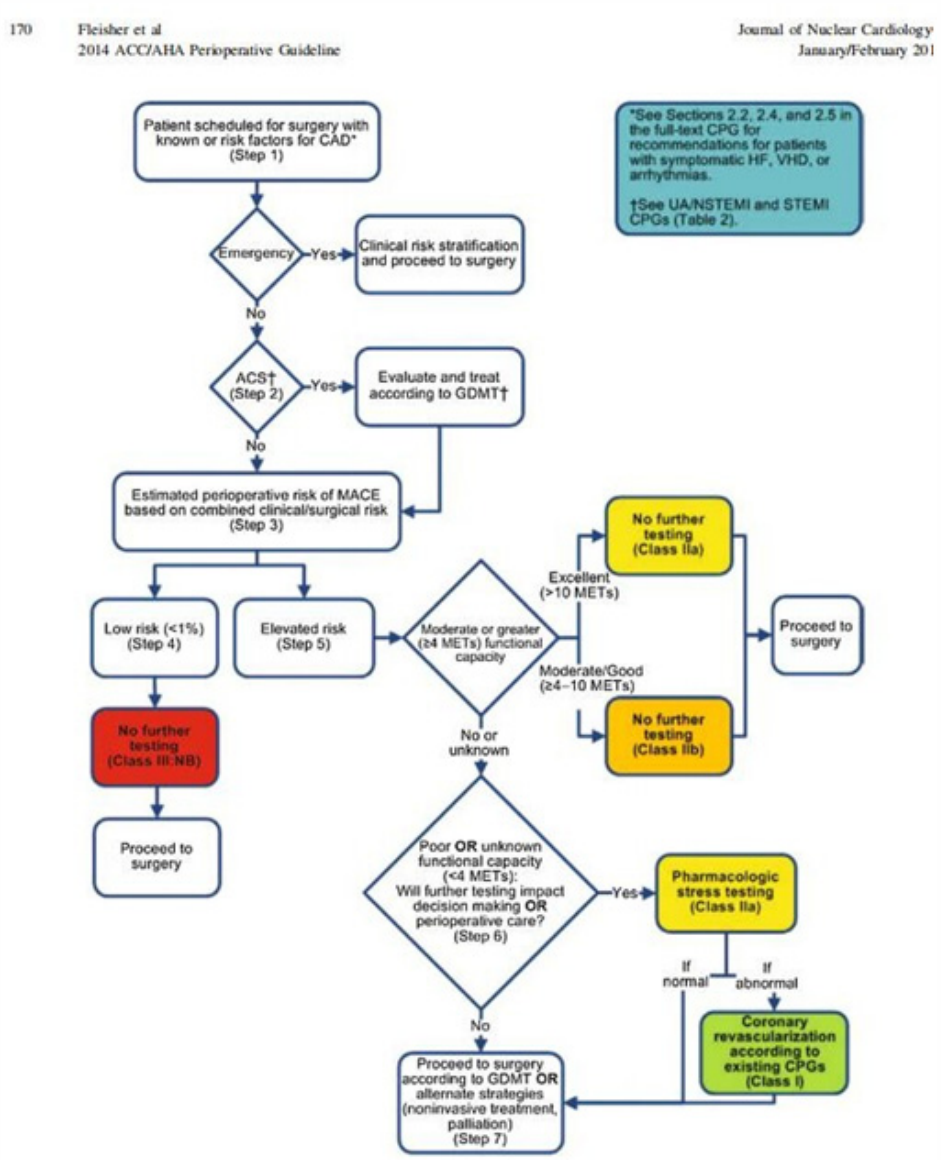
iv) Does the planned surgery have cardiac risk (surgical risk)?

v) Does the patient have good functional capacity without symptoms?

Table 3. Summary of Recommendations for Supplemental Preoperative Evaluation

Recommendations	COR	LOE	References
The 12-lead ECG			
Preoperative resting 12-lead ECG is reasonable for patients with known coronary heart disease or other significant structural heart disease, except for low-risk surgery	IIa	B	64-66
Preoperative resting 12-lead ECG may be considered for asymptomatic patients, except for low-risk surgery	IIb	B	59, 65–67
Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures	III: No Benefit	B	36, 68
Assessment of LV function			
It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function	IIa	C	N/A
It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function	IIa	C	N/A
Reassessment of LV function in clinically stable patients may be considered	IIb	C	N/A
Routine preoperative evaluation of LV function is not recommended	III: No Benefit	B	69–71
Exercise stress testing			
For patients with elevated risk and excellent functional capacity, it is reasonable to forgo further exercise testing and proceed to surgery	IIa	B	72–76
For patients with elevated risk and unknown functional capacity it may be reasonable to perform exercise testing to assess for functional capacity if it will change management	IIb	B	75–77
Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedures	IIb	B	78–86
For patients with elevated risk and moderate to good functional capacity, it may be reasonable to forgo further exercise testing and proceed to surgery	IIb	B	72–74
For patients with elevated risk and poor or unknown functional capacity it may be reasonable to perform exercise testing with cardiac imaging to assess for myocardial ischemia	IIb	C	N/A
Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery	III: No Benefit	B	87, 88
Noninvasive pharmacological stress testing before noncardiac surgery			
It is reasonable for patients at elevated risk for noncardiac surgery with poor functional capacity to undergo either DSE or MPI if it will change management	IIa	B	89–93
Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery	III: No Benefit	B	88, 87
Preoperative coronary angiography			
Routine preoperative coronary angiography is not recommended	III: No Benefit	C	N/A

COR indicates Class of Recommendation; DSE, dobutamine stress echocardiogram; ECG, electrocardiogram; HF, heart failure; LOE, Level of Evidence; LV, left ventricular; MPI, myocardial perfusion imaging; and N/A, not applicable.



Step 1: Is there clinical need for emergency non cardiac surgery?

- Emergency surgery
- Patients who have suspected coronary artery disease, heart failure, or severe valvular disease.
- No sufficient time for an extensive evaluation of the severity of cardiovascular disease.
- Benefit of proceeding with surgery outweighs risk of waiting for further evaluation.
- Proceed to surgery (class I recommendation).

Step 2: Does the patient have active cardiac condition?

- Recent MI - delay elective surgery for at least 60 days.
- Coronary revascularization - no benefit of prophylactic revascularization in patients with stable or asymptomatic CAD except ongoing acute coronary syndrome.

Indications for pre-operative coronary artery revascularization prior to non cardiac surgery are: acceptable coronary revascularization risk with viable myocardium and left main coronary artery stenosis, triple vessel CAD with LV dysfunction, left main equivalent, intractable coronary ischemia despite maximal medical therapy.

176 Fleisher et al
2014 ACC/AHA Perioperative Guideline
Journal of Nuclear Cardiology®
January/February 2015

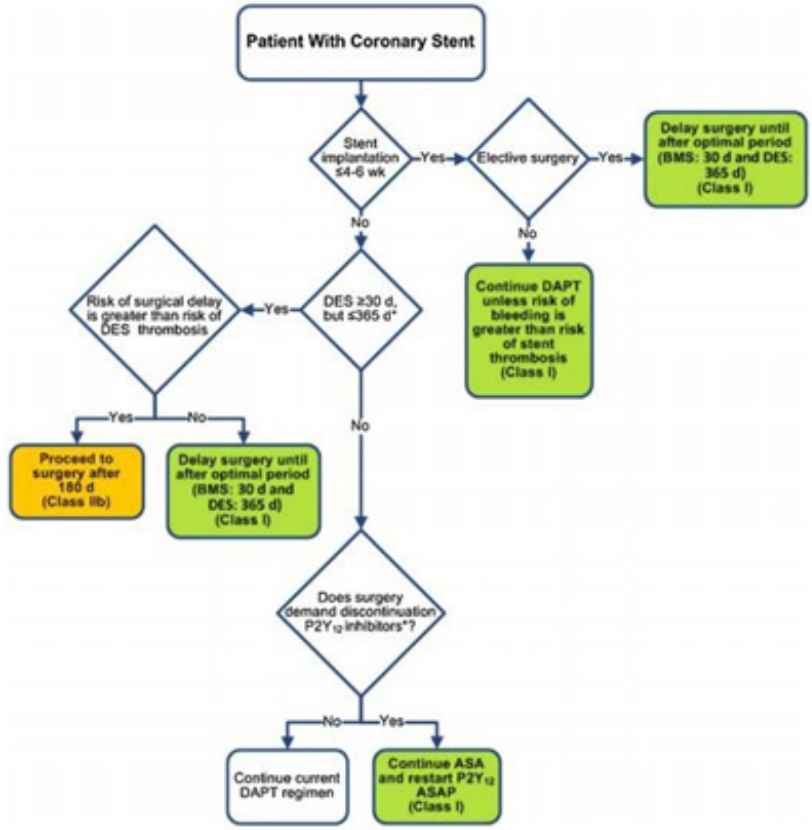


Figure 2. Algorithm for antiplatelet management in patients with PCI and noncardiac surgery. Colors correspond to the Classes of Recommendations in Table 1. *Assuming patient is currently on DAPT. ASA indicates aspirin; ASAP, as soon as possible; BMS, bare-metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; and PCI, percutaneous coronary intervention.

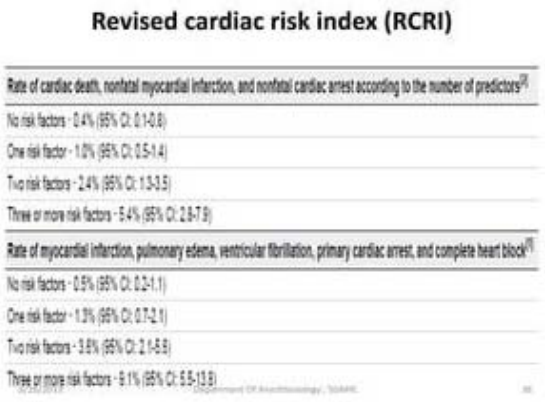
In case of recent PCI, 2014 ACC/AHA guidelines recommend delay in elective surgery. For urgent or emergency surgery a multi-disciplinary discussion regarding risk-benefit ratio. Aspirin should be continued where possible.

Step 3: Does the patient have clinical risk factors?

Risk factors used for risk prediction are: Revised cardiac risk index (Lee's), American college of physician risk calculation.

Lee's Revised cardiac risk index (RCRI)

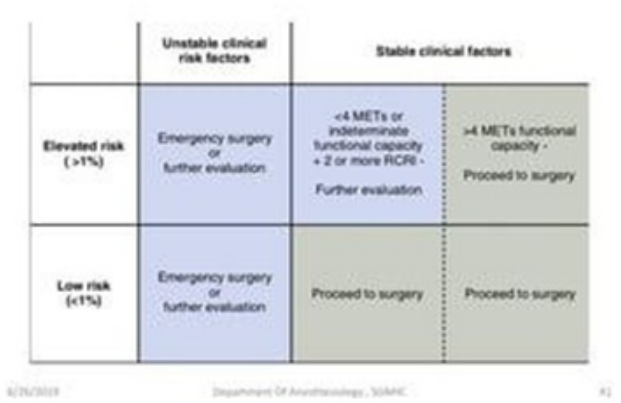
1. High-risk surgery
   Abdominal aortic aneurysm
   Peripheral vascular operation
   Thoracotomy
   Major abdominal operation
2. Ischemic heart disease
   History of myocardial infarction
   History of a positive finding on exercise testing
   Current complaints of angina pectoris
   Use of nitrate therapy
   Presence of Q waves on ECG
3. Congestive heart failure
   History of congestive heart failure
   History of pulmonary edema
   History of paroxysmal nocturnal dyspnea
   Physical examination showing rales or S_3 gallop
   Chest radiograph showing pulmonary vascular redistribution
4. Cerebrovascular disease
   History of stroke
   History of transient ischemic attack
5. Insulin-dependent diabetes mellitus
6. Preoperative serum creatinine concentration > 2 mg/dL



Step 4: Does the planned surgery have a cardiac risk?

Low risk patients - patients whose estimated risk of death is less than 1% and requires no additional cardiovascular evaluation.

High risk patients - patients whose estimated risk of death is more than 1% and requires additional cardiovascular testing.



Step 5: Does the patient have good functional capacity without symptoms? Cardiac functional status as determined by METs or metabolic equivalent.

Pre-operative Medical Optimization prior to planned surgery:

Beta blockers, aspirin, ACE inhibitors, ARBs, statins.

Intraoperative anaesthesia management goals and consideration:

To maintain a favourable myocardial oxygen supply demand relationship by increasing myocardial oxygen supply and/or decreasing myocardial oxygen demand. The former by maintaining low-normal heart rate, high blood oxygen content, high-normal aortic pressure, reduced coronary vascular resistance, low left ventricular end diastolic pressure. The latter by maintaining low-normal heart rate, low myocardial wall tension, avoiding increased myocardial contractility.

Choice of Anaesthetic Technique: General or regional anaesthesia alone or in combination as part of a balanced technique depending on surgery and patient requirements.

A) General Anaesthesia: maintenance of haemodynamic stability with attenuation of the haemodynamic responses to intubation and surgical stimulation.

Premedication- anxiolytics- benzodiazepines.

Induction- etomidate preferred, alternatively, propofol. Ketamine is avoided. Attenuation

of laryngoscopy and intubation by opioids, lidocaine or induction agents.

Maintenance of anaesthesia by either volatile agents or TIVA, analgesics (opioids) and muscle relaxants.

Monitoring- ASA standard monitors- ECG, pulse oximetry, temperature, EtCO2.

Cardiovascular monitors- intra-arterial BP, central venous pressure, pulmonary artery pressures through PA catheter, transoesophageal echocardiography.

Other monitors- cerebral oximetry, urine output, point of care lab testing like ABG, electrolytes, glucose etc.

Extubation should be smooth to avoid sympathetic stimulation.

B) Regional Anaesthesia- either spinal or epidural anaesthesia in intermediate and low risk surgeries involving extremities, perineum, lower abdomen. Strict guidelines are followed for those who are on anti-coagulants. Hypotension related to central neuraxial blockade is treated with adequate preload and vasopressors such as phenylephrine.

Postoperative management:

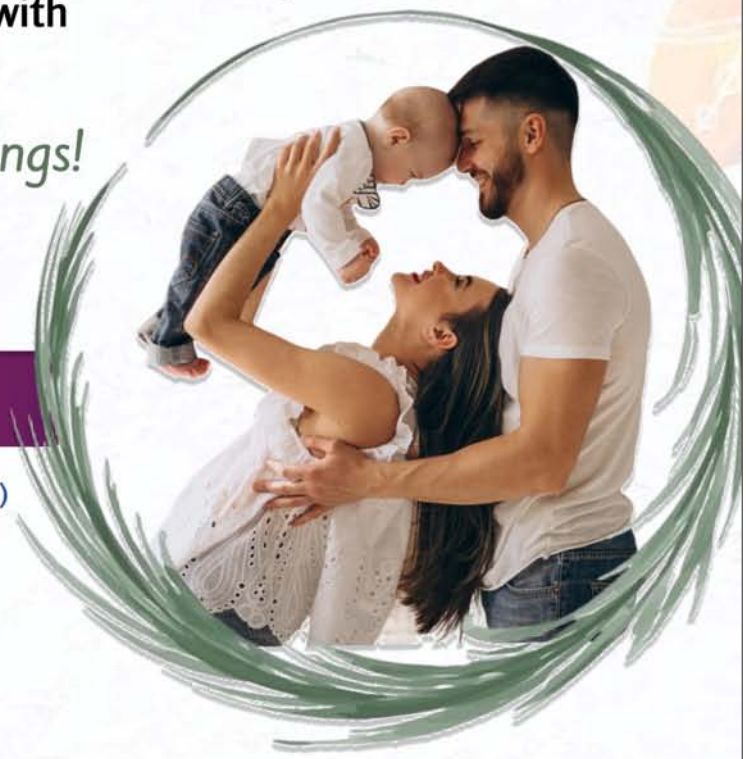
Goals- to prevent ischemia, monitor myocardial injury, treat myocardial ischemia and infarction. The above goals are brought to effect by continuous ECG monitoring in CCU/ICU, effective pain management, prevention of hypovolemia, hypotension, hypoxemia, hypercarbia, maintaining Hb levels > 7g/dl and above 8g/dl in patients more than 80yrs. Weaning and extubation done with utmost precaution to avoid a pressor response.

References:

1. 2014 ACC/AHA guideline of perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery.
2. Stoelting's Anesthesia and Co-existing disease. 7th ed.
3. Harrison's principle of internal medicine. 20th ed.
4. Perioperative myocardial ischemia in non cardiac surgery ATOTW 375-2018.

GENESIS
FERTILITY & LAPAROSCOPY CENTRE
Life begins here...

Unlock the Door to
PARENTHOOD with
Genesis Fertility Centre
Your Path to New Beginnings!



Dr. Narmada Katakam

MD (OBG) (Osm) PGCERTME (UK) DFSRH (UK)
CESR (UK) FRCOG (UK),
Fertility Specialist & Gynaecologist
(Accredited by British Fertility Society, UK)
Specialist in Minimal Access Surgery
(Laparoscopy & Hysteroscopy)

Our Services

IUI | IVF | ICSI | Surrogacy
Donor Treatment
Egg Freezing | Hysteroscopy
laparoscopy

Contact:
Kothapet | 91005 42910
Sainikpuri | 81210 02910

www.genesisfertilitycentre.co.in

TVR LAPAROSCOPY CENTER
Estd. 2020

I. M. A (AMS) Headquarters
Fellowship program

8 batches finished
Successful surgeons
Logbook oriented training

Basic Laparoscopic Surgery

Course (4 Months)

For Surgeons
Gynecologists

302,Sri Kalki Chambers
Madinaguda /Miyapur
Hyderabad - 500049

Dr. T. Varun Raju
Advanced Laparoscopic Surgeon
H. O. D (St Hospital), Author
Course Director
27 years experience

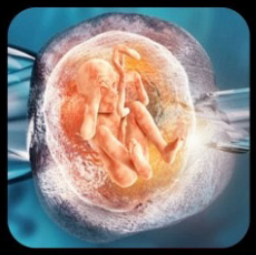
HYDERABAD - TELANGANA

#Live Surgery exposure
#20 tasks on simulation models
#Animal tissue lab
#Instruments & video classes
#Laparoscopic suturing tasks
#External examiners
#Convocation by IMA-AMS

Book your seat :- 9866159160 www.drvarunraju.com 8886177750

THE SRIJJAN IVF BHILAI

— TEST TUBE BABY CENTER —



INFERTILITY TRAINING INSTITUTE

FOGSI Recognised Courses
2 Weeks Courses, 1 Week Courses

IMA - AMS Recognised Courses
1 Year Courses

- IUI
- IVF
- ICSI
- IMSI

Dr. Sangeeta Sinha
IVF Specialist
Sr. Gynaecologist & Infertility Specialist
MBBS, DGO, FMAS, PGA (ART) UK
Trained From London

REVIVAL MEDICAL CENTER

A UNIT OF THE SRIJJAN IVF, BHILAI

LAPAROSCOPY TRAINING INSTITUTE

FOGSI Recognised Courses
2 Weeks Courses, 1 Week Courses

IMA - AMS Recognised Courses
1 Year Courses

- Painless Delivery
- Hysteroscopy
- High Risk Pregnancy
- Laparoscopic Surgery

Dr. Rajesh Sinha, MS
Senior Consultant
Laparoscopic Surgeon
NH MMI Narayana Superspeciality Hospital, Raipur

97525 95605, 99813 33570

2nd Floor, Revival Medical Center, C-4,
GE Road, Near Maurya Talkies, Bhilai (C.G.)

Design HUB 83598 90299


Be a Donor,
Be a Hero
INDIAN MEDICAL ASSOCIATION
(GUJARAT STATE BRANCH)
I PLEDGED FOR ORGAN DONATION

Dr. Ketan Desai
Chief Patron
Past President, IMA, MCI & IMA

RELAUNCH
OF IMA DREAM PROJECT SOON

Aao Gaon Chalen

1st Prize — **Cash Prize: Rs. 3,00,000/-**
(Rupees Three Lakh to the Local Branch)

2nd Prize — **Cash Prize: Rs. 2,00,000/-**
(Rupees Two Lakh to the Local Branch)

3rd Prize — **Cash Prize: Rs. 1,00,000/-**
(Rupees One Lakh to the Local Branch)

Aao Gaon Chalen
Mega Inaugural Camp

25th JUNE 2023, Sunday

Gujarat

Let's give health to every Indian

All branches are requested to adopt one village

Certificate and Dr. Ketan Desai - Aao Gaon Chalen Award to the President & Secretary of the Local Branch.


Dr. R. V. Asokan
National President-Elect


Dr. Bharat Kr. Agarwal
National President


Dr. Anilkumar J. Nayak
Hony. Secretary General


Dr. Shitij Bali
Hony. Finance Secretary


Dr. Bipin M. Patel
Chairman, IMA Standing Committee for Aao Gaon Chalen


Dr. V. K. Monga
Convenor, IMA Standing Committee for Aao Gaon Chalen