

CLINICAL PRACTICE GUIDELINE:



2019
4th EDITION

MANAGEMENT OF ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION (STEMI)



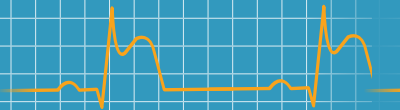
Academy of Medicine Malaysia



Ministry of Health Malaysia



NATIONAL HEART ASSOCIATION
OF MALAYSIA



STATEMENT OF INTENT

This guideline was developed to be a guide for best clinical practice, based on the best available evidence at the time of development. Specific attempts were made to use local data and publications to ensure local relevance. Adherence to this guideline does not necessarily lead to the best clinical outcome in individual patient care. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical presentation and management options available locally.

REVIEW OF THE GUIDELINE

This guideline is issued in 2019 and will be reviewed in 2024 or earlier if important new evidence becomes available.

CPG Secretariat
Health Technology Assessment Unit
Medical Development Division
Level 4, Block EI, Parcel E
Government Offices Complex
62590 Putrajaya, Malaysia

Available on the following websites:

<http://www.moh.gov.my>

<http://www.acadmed.org.my>

MESSAGE FROM THE DIRECTOR GENERAL OF HEALTH

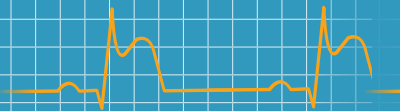


The 1st Clinical Practice Guideline (CPG) on ST Elevation Myocardial Infarction (STEMI) was published in 2001 with a 2nd and 3rd update in 2007 and 2014 respectively. Rapid developments have taken place, especially in the area of pre-hospital care. This 4th edition was developed to provide a clear and concise approach based on current evidence with the focus being on efforts to reduce the time from first medical contact, improve pre-hospital care as well support the application of guideline-directed therapies.

This CPG has been prepared by a panel of committee members from the National Heart Association of Malaysia (NHAM) and Ministry of Health (MOH). The committee members were multidisciplinary and comprised of cardiologists, internal medicine, family medicine, rehabilitation and emergency physicians from the government, private sector and universities. Relevant clinical trial data and published literature have been summarized and adapted to local practices. This guideline also implemented the work of our very own national STEMI network which links non-PCI-capable centres to PCI-capable centres so PCI services can be arranged in a timely manner for all patients.

Ischaemic heart disease has been a significant burden to this country, and it is projected that the burden will continue to increase with the rising number of cardiovascular risk factors and an ageing population. I believe this CPG will be an invaluable guiding document for healthcare providers involved in the management of STEMI and subsequently be translated to an improved clinical outcome for patients suffering from ischaemic heart disease.

DATUK DR NOOR HISHAM ABDULLAH
DIRECTOR GENERAL OF HEALTH OF MALAYSIA



MEMBERS OF THE EXPERT PANEL

Chairperson:

Dr Jeyamalar Rajadurai

Consultant Cardiologist
Subang Jaya Medical Centre

Members:

(in alphabetical Order)

Dr Abdul Kahar Abdul Ghapar

Consultant Cardiologist,
Head of Cardiology,
Hospital Serdang

Dr Amin Ariff Nuruddin

Consultant Cardiologist,
Head of Cardiology,
Institut Jantung Negara

Dr Ahmad Tajuddin Mohamad Nor

Consultant Emergency Physician,
Hospital Tengku Ampuan Rahimah,
Klang, Selangor

Dr Gunavathy Muthusamy

Consultant Physician/Endocrinologist,
Head of General Medicine,
Hospital Shah Alam

Dr Lee Kun Yun

Public Health Specialist,
Institute for Health Management,
Ministry of Health

Dr Narul Aida Salleh

Family Medicine Specialist,
Klinik Kesihatan Kuala Lumpur

Dr Ong Mei Lin

Consultant Cardiologist,
Gleneagles Penang

Dr Saari Mohamad Yatim

Consultant Rehabilitation Physician,
Hospital Serdang

Dr Sabariah Faizah Jamaluddin

Consultant Emergency Physician,
Hospital Sungai Buloh

Dr Wardati Mazlan Kepli

Clinical Pharmacist,
Hospital Serdang

Dr Wan Azman Wan Ahmad

Consultant Cardiologist,
University Malaya Medical Centre

EXTERNAL REVIEWERS

(in alphabetical order)

Dr Anwar Suhaimi

Rehabilitation Physician,
University Malaya Medical Centre

Dr Azerin Othman

Consultant Cardiologist,
Hospital Raja Perempuan Zainab II

Dr Kauthaman A Mahendran

Consultant Physician and Head,
Department of Medicine,
Hospital Melaka

Dr Keshab Chandran Nair

General Practitioner,
Klinik Anis,
17, Jalan Bunga Melur 2/18,
Section 2, 40000 Shah Alam

Dr Liew Houg Bang

Consultant Cardiologist,
Hospital Queen Elizabeth II

Dr Mastura Hj Ismail

Family Medicine Specialist,
Klinik Kesihatan Seremban 2

Dr Ong Tiong Kiam

Consultant Cardiologist,
Sarawak Heart Centre

Dr Pearl Leong Yuet Mae

President, Private Medical
Practitioners Association of
Selangor and KL
Pearl's Clinic Of Care
A-0-5, Plaza Damas 1,
Jalan Sri Hartamas 1,
Kuala Lumpur

Dr Rashidi Ahmad

Consultant Emergency Physician,
Universiti Malaya Medical Centre

Dr Ridzuan Mohd Isa

Consultant Emergency Physician,
Hospital Ampang

Dr Sahimi Mohamed

Head of Clinical Section,
Pharmacy Department,
Hospital Tengku Ampuan Afzan

Dr Shahrul Bahaya Kamaruzzaman

Head and Consultant Geriatrician,
Department of Medicine,
University Malaya Medical Centre

Dr. Sunita Bavanandan

Consultant Nephrologist,
Hospital Kuala Lumpur

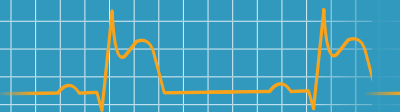
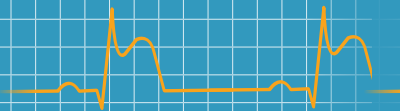


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RATIONALE AND PROCESS OF GUIDELINE DEVELOPMENT

Rationale

Acute Myocardial Infarction (AMI) continues to be a major cause of morbidity and mortality in Malaysia. With timely intervention and early reperfusion, the cardiovascular outcomes have improved. The biggest challenge has been to reduce the total ischaemic time, which is the time from onset of chest pain till the time when the infarct related artery is opened. A large portion of this delay has been the late presentation of the patient with AMI to medical attention (onset of chest pain to First Medical Contact – FMC).

The 1st Clinical Practice Guideline (CPG) on ST Elevation Myocardial Infarction (STEMI) was published in 2001 with a 2nd and 3rd update in 2007 and 2014 respectively. Rapid further developments have taken place especially in the area of pre-hospital care. This 4th edition was developed to provide a clear and concise approach based on current evidence with the focus being on efforts to reduce time to FMC and improve pre-hospital care. We have summarised and adapted relevant clinical trial data and published literature to the local practice.

This CPG has been prepared by a panel of committee members from the National Heart Association of Malaysia (NHAM) and Ministry of Health (MOH). The committee members were multidisciplinary and comprised of cardiologists, internal medicine, family medicine, rehabilitation and emergency physicians from the government, private sector and universities. The external reviewers were also multidisciplinary and in addition to specialists, general practitioners were also included. Patient and carer groups were however not included as external reviewers.

Objectives

These guidelines are intended to provide awareness and education in order to reduce the morbidity and mortality associated with STEMI by:

- Reducing total ischaemic time
- Developing a network for early referral and treatment of STEMI patients
- Updating the management of STEMI with respect to:
 - ◆ Diagnosis
 - ◆ Management
 - ◆ Secondary prevention

Process

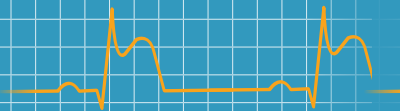
A review of current medical literature on AMI/STEMI since the publication of the last CPG on 30th Sept 2013 was performed. Literature search was carried out using the following electronic databases – PubMed and Cochrane Database of Systematic Reviews. The search was conducted for the period 1st September 2013 till 31st August 2018. The following MeSH terms or free text terms were used either singly or in combination:

“Myocardial infarction (MI); “STEMI”; ST Elevation Myocardial Infarction;” “definition of MI”; “Myocardial injury”; “ECG criteria of STEMI”, “Pre-hospital Management of STEMI”; “STEMI Networks”; “Pre-hospital thrombolysis”; “Fibrinolysis”; “Primary PCI”; “Reperfusion strategies in STEMI”; “Pharmaco-invasive strategy”; “Pharmacotherapy in STEMI”; “Oxygen therapy in MI”; “Complications post STEMI”, “cardiogenic shock”; “Heart Failure post STEMI”; “Risk stratification scores in STEMI”; “Cardiac rehabilitation”, “second prevention post STEMI”, “management of STEMI in women, the elderly, persons with diabetes and in those with chronic renal disease.”

The search was filtered to clinical trials and reviews, involving humans and published in the English language. The relevant articles were carefully selected from this huge list. In addition, the reference lists of all relevant articles retrieved were searched to identify further studies. Local CPGs were also studied. Experts in the field were also contacted to obtain further information. International guidelines mainly that from the American Heart Association/ American College of Cardiology (AHA/ACC) and the European Society of Cardiology (ESC) were used as main references.

All literature retrieved were appraised by members of the Expert Panel and all statements and recommendations made were collectively agreed by the group. The grading of evidence and the level of recommendation used in this CPG was adapted from the AHA/ACC and the ESC (pg 14).

After much discussion, the draft was then drawn up and submitted to the Technical Advisory Committee for Clinical Practice Guidelines, MOH Malaysia and key health personnel in the major hospitals of the MOH and the private sector for review and feedback.



Clinical Questions Addressed:

There were several topics and subtopics that were formulated addressing the diagnosis and management of STEMI.

For **diagnosis**: In a person presenting with chest pain:

- What features in the history would make one suspect this patient is having a myocardial infarction (MI)?
- Which ECG features would make one suspect this patient is having a MI?
- Which cardiac biomarkers would help confirm a diagnosis of MI early and with accepted sensitivity and specificity?

For **therapy**, the topics and subtopics were formulated using the PICO method as follows:

P: Population- Persons with ST elevation MI and:

- Duration of chest pain:
 - ◆ <1 hour
 - ◆ <3 hours
 - ◆ 3 - <12 hours
 - ◆ 12-24 hours
 - With ongoing symptoms and signs of ischaemia
 - With haemodynamic instability
 - Without ongoing ischaemia or haemodynamic instability
- Atrial Fibrillation
- Older persons
- Persons with diabetes
- Women
- Chronic Kidney disease
 - ◆ Not on renal replacement therapy
 - ◆ On renal replacement therapy

I: Intervention:

- Reperfusion strategy:
 - ◆ Primary Percutaneous Coronary Intervention (PCI)
 - ◆ Fibrinolytic therapy
 - Pre-hospital thrombolysis vs in-hospital thrombolysis
 - ◆ Pharmaco-invasive PCI
- Concomitant drug therapy
 - ◆ Anti-platelet therapy
 - ◆ Direct oral anti-coagulant (DOAC)
 - ◆ Angiotensin converting enzyme inhibitors (ACE-I),
 - ◆ Angiotensin receptor blockers (ARB)

- ◆ β -blockers
- ◆ Mineralocorticoid antagonists (MRA)
- ◆ Statins

C: Comparison:

- Reperfusion vs no reperfusion
- Fibrinolytic therapy vs primary PCI vs pharmaco-invasive PCI
- Single anti-platelet therapy vs dual anti-platelet therapy
- Clopidogrel vs prasugrel vs ticagrelor as second anti-platelet agent
- ACE-I vs no ACE-I

O: Outcome:

- Reduction in major cardiovascular disease event rate (MI, heart failure, stroke, cardiovascular (CV) death)
- Reduction in all-cause mortality

Type of Question- Involves:

- Therapy - Reperfusion strategy, concomitant drug therapy
- Harm –
 - ◆ Increase in cardiovascular event rate (MI, heart failure, CV death)
 - ◆ Increase in bleeding risk and stroke rate
 - ◆ Adverse effects due pharmacotherapy
- Prognosis – Reduction in MI, heart failure, CV death and improvement in all-cause mortality

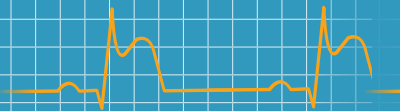
Type of Study

- Systematic review and meta-analysis
- Randomised controlled studies
- Cohort studies

Thus, there were numerous clinical questions formulated.

Eg of some of these Clinical Questions:

- In a person with STEMI presenting within the first hour of chest pain, is a reperfusion strategy with fibrinolytic therapy superior to Primary PCI leading to a reduction in rate of MI, stroke, heart failure and CV death?
- In a person with STEMI presenting within < 3 hours of chest pain, is a reperfusion strategy with fibrinolytic therapy superior to primary PCI leading to a reduction in rate of MI, stroke, heart failure and CV death?
- In a person with STEMI having undergone a reperfusion strategy with fibrinolytic therapy, is concomitant single anti-platelet therapy with aspirin alone superior to DAPT leading to a reduction in rate of MI, stroke, heart failure and CV death?



- In a person with STEMI having undergone a reperfusion strategy with primary PCI, does ACE-I therapy provide additional value in the reduction of MI, stroke, heart failure and CV death?
- In a person with STEMI having undergone a reperfusion strategy with fibrinolytic therapy, would PCI provide additional value in the reduction of MI, stroke, heart failure and CV death?
- In a person with STEMI presenting within 3 -12 hours of chest pain and with chronic kidney disease and on renal replacement therapy, is a reperfusion strategy with fibrinolytic therapy superior to primary PCI leading to a reduction in rate of MI, stroke, heart failure and CV death?

Target Group:

These guidelines are developed for all healthcare providers involved in the management of STEMI in adults.

Target Population:

These guidelines are developed to treat all adults with STEMI.

Period of Validity of the Guidelines:

These guidelines need to be revised at least every 5 years to keep abreast with recent developments and knowledge that is being learnt.

Applicability of the Guidelines and Resource Implications:

This guideline was developed taking into account our local healthcare resources. At present fibrinolytic therapy is available at most government hospitals while facilities for both fibrinolysis and PCI are present in the cardiac centres. STEMI networks have been established and are still being developed in the Klang Valley and other states/regions of the country.

The drugs used for secondary prevention – aspirin, clopidogrel, statins, ACE-I, β -blockers, spironolactone – are all available in the government formulary in almost all public hospitals as generics.

This guideline aims to educate health care professionals on strategies to optimise existing resources in the timely management of patients with STEMI.

Facilitators and Barriers:

The major barriers for the successful implementation of this CPG is the financial and resource implications of:

- transporting these patients to PCI capable centres quickly using well-equipped ambulances and accompanied by trained pre-hospital care personnel or medical officers
- availability of PCI centres providing 24/7 service
- PCI - costs of catheters and stents

Implementation of the Guidelines:

The implementation of the recommendations of a CPG is part of good clinical governance. To ensure successful implementation of this CPG we suggest:

- Increasing public awareness of CVD in general and educating them on the importance of seeking early medical attention when they have chest pains and chest pain equivalents.
- Continuous medical education and training of healthcare providers on the importance of timely reperfusion and appropriate management of patients with STEMI. This can be done by road shows, electronic media, and in-house training sessions.

Clinical audit by individual hospitals and units to ensure compliance using the suggested performance measures in Section 17, pg. 113.

Dr Jeyamalar Rajadurai

Chairperson

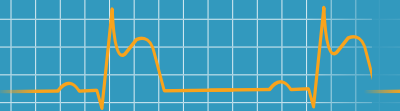


Table 1: Levels of evidence and grades of recommendation

GRADES OF RECOMMENDATION	
I	Conditions for which there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful and/or effective.
II	Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure/therapy.
	II-a: Weight of evidence/opinion is in favour of its usefulness/efficacy. II-b: Usefulness/efficacy is less well established by evidence/opinion.
III	Conditions for which there is evidence and/or general agreement that a procedure/therapy is not useful/effective and in some cases may be harmful.

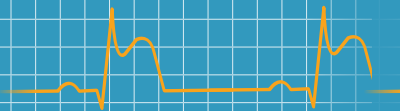
LEVELS OF EVIDENCE	
A	Data derived from multiple randomised clinical trials or meta-analyses.
B	Data derived from a single randomised clinical trial or large non-randomised studies.
C	Only consensus of opinions of experts, case studies or standard of care.

Adapted from the American College of Cardiology Foundation / American Heart Association and the European Society of Cardiology

(Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees and at <http://www.escardio.org/guidelines-surveys/escguidelines/about/Pages/rules-writing.aspx>).

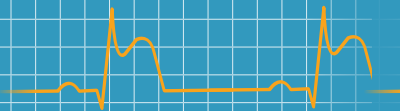
GLOSSARY

Abbreviation	Description
ABC	Airway, Breathing, Circulation
ABCD	Airway, Breathing, Circulation and Defibrillation
ACC	American College of Cardiology
ACE-I	Angiotensin Converting Enzyme Inhibitor
ACS	Acute Coronary Syndrome
ACT	Activated Clotting Time
ADP	Adenosine diphosphate
AF	Atrial Fibrillation
AHA	American Heart Association
AMI	Acute Myocardial Infarction
APTT	Activated Partial Thromboplastin Time
ARB	Angiotensin Receptor Blocker
AST	Aspartate Aminotransferase
AV	Atrio-ventricular
BBB	Bundle Branch Block
Bd	Bis Die (twice daily)
BiPaP	Bi-level Positive Airway Pressure
BMS	Bare Metal Stents
BP	Blood Pressure
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CCU	Cardiac Care Unit
CHD	Coronary Heart Disease
CIN	Contrast Induced Nephropathy
CK	Creatine Kinase
CKD	Chronic Kidney Disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CK-MB	Creatine Kinase-Myocardial Band
CPG	Clinical Practice Guidelines



Abbreviation	Description
CPR	Cardiopulmonary Resuscitation
CrCL	Creatinine Clearance
CRP	Cardiac Rehabilitation Programme
cTn	Cardiac Troponins
cTnI	Cardiac Troponin I
cTnT	Cardiac Troponin T
CV	Cardiovascular
CVD	Cardiovascular Disease
CPAP	Continuous Positive Airway Pressure
D5W	5% dextrose in water
DAPT	Dual Antiplatelet Therapy
DBT	Door to Balloon Time
DES	Drug Eluting Stents
DM	Diabetes Mellitus
DNT	Door to Needle Time
DOAC	Direct Oral Anticoagulants
DVT	Deep Venous Thrombosis
ECG	Electrocardiogram
EF	Ejection Fraction
eGFR	Estimated Glomerular Filtration Rate
ESC	European Society of Cardiology
FMC	First Medical Contact
GFR	Glomerular Filtration Rate
Gp	Glycoprotein
GRACE	Global Registry of Acute Coronary Events
GTN	Glyceryl trinitrate
HF	Heart Failure
HRT	Hormone Replacement Therapy
HTA	Health Technology Assessment

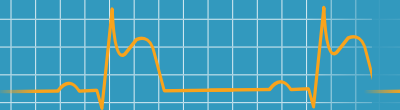
Abbreviation	Description
IABP	Intra-aortic Balloon Pump
IC	Intracoronary
ICD	Implantable Cardioverter-Defibrillator
INR	International Normalised Ratio
IO	Intraosseous
IRA	Infarct-Related Artery
IV	Intravenous
LBBS	Left Bundle Branch Block
LDH	Lactate Dehydrogenase
LDL	Low Density Lipoprotein
LDL-C	Low Density Lipoprotein Cholesterol
LMWH	Low Molecular Weight Heparin
LV	Left Ventricular
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
MDRD	Modification of Diet in Renal Disease
MI	Myocardial Infarction
MOH	Ministry of Health Malaysia
MRI	Magnetic Resonance Imaging
MSCT	Multi-Slice Computed Tomography
NaCl	Sodium Chloride
NaHCO₃	Sodium Bicarbonate
NCVD	National Cardiovascular Disease Database
NHAM	National Heart Association Malaysia
NSAID	Non-steroidal Anti-Inflammatory Drug
NSTEMI	Non ST Segment Elevation Myocardial Infarction
OAC	Oral Anticoagulants
Od	Once daily
PCI	Percutaneous Coronary Interventions



Abbreviation	Description
PCWP	Pulmonary Capillary Wedge Pressure
PEA	Pulseless Electrical Activity
PHC	Pre Hospital Care
RBBB	Right Bundle Branch Block
ROSC	Return of Spontaneous Circulation
r-TPA	Recombinant Tissue Plasminogen Activator
RV	Right Ventricular
RVI	Right Ventricular Infarction
SBP	Systolic Blood Pressure
SC	Subcutaneous
Scr	Serum Creatinine
SpO₂	Pulse Oximeter Oxygen Saturation
STEMI	ST Segment Elevation Myocardial Infarction
Tds	Ter die sumendus (three times per day)
TIA	Transient Ischaemic Attack
TIMI	Thrombolysis in Myocardial Infarction
TMP	TIMI Myocardial Perfusion Grade
TNK-tPA	Tenecteplase
TVR	Target Vessel Revascularization
UFH	Unfractionated Heparin
ULRR	Upper Limit Reference Range
URL	Upper Reference Limits
VF	Ventricular Fibrillation
VPC	Ventricular Premature Contractions
VSD	Ventricular Septal Defect
VT	Ventricular Tachycardia

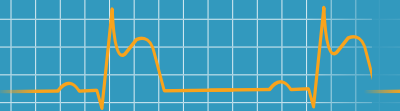
WHAT'S NEW IN THE CURRENT GUIDELINES

	Previous CPG STEMI (2014)	Current CPG STEMI (2019)
Distinguishing the difference between myocardial injury and Myocardial Infarction (MI) - Recognition that all myocardial injury is not necessarily due to MI.	No clear differentiation between myocardial injury and MI	Myocardial injury is reflected by a troponin level above the 99th percentile of upper reference limit (URL). Myocardial injury may be due to: <ul style="list-style-type: none"> • Ischaemia • Non-ischemic causes MI is myocardial injury due to ischaemia. STEMI is MI with ST elevation seen on the resting ECG.
Pre-hospital Care (PHC)/personnel	Brief statement about Pre-hospital Care/personnel	<ul style="list-style-type: none"> • Providing a structured format of response to an emergency call for "chest pain." • To treat STEMI promptly preferably by Primary PCI by transporting the patient directly to a PCI capable hospital. • Outlining key care processes to shorten door to balloon (device) time (DBT) and improve quality of care during transport. • Encouraging pre-hospital thrombolysis if transport time to a PCI capable centre is long and trained doctor/PHC personnel are available. If this is not available, for in-hospital thrombolysis at the nearest hospital. • Identifying training of PHC personnel as an important priority.



<p>STEMI Networks</p>	<p>No mention of STEMI networks</p> <ul style="list-style-type: none"> • FMC to ECG interpretation: preferably within 10 min • For Primary PCI: <ul style="list-style-type: none"> ◆ Door to balloon time < 90minutes ➤ If transported from a non- PCI hospital: Door to Balloon time < 120 minutes • For fibrinolysis: <ul style="list-style-type: none"> ◆ Door to needle time < 30 minutes 	<ul style="list-style-type: none"> • Identifying the key points in establishing a STEMI network. • Encouraging the setting up of STEMI Networks throughout the country. • Establishing time intervals to reduce total ischaemic time and achieve timely early reperfusion. • FMC to ECG interpretation < 10 min • For Primary PCI: <ul style="list-style-type: none"> ◆ FMC directly by ambulance to PCI capable centre: DBT< 90 minutes ◆ FMC at non-PCI (spoke) hospital: DBT: < 120 minutes ➤ Door in Door Out (DIDO): < 30 minutes. ➤ Transfer to PCI capable centre: < 60 minutes. • For fibrinolysis: <ul style="list-style-type: none"> ◆ FMC to thrombolysis < 30 minutes (this could be in-hospital or pre-hospital in an ambulance equipped with the necessary facilities)
<p>Diagnosing reinfarction- Troponins can also be used for reinfarction</p>	<p>In a patient with recurrent chest pain following STEMI, a $\geq 20\%$ increase in the value of Creatine Kinase-Myocardial Band (CKMB) from the last sample suggests reinfarction.</p>	<p>If a patient is suspected of having a reinfarction on clinical grounds, a $\geq 20\%$ increase in the value of either troponins or CKMB between 2 samples 3-6 hours apart supports the diagnosis</p>
<p>Fibrinolysis</p>		<p>If the time from STEMI diagnosis to wire crossing is more than 120 minutes, then pre-hospital or nearest in-hospital fibrinolysis is an option. Then consider transfer for a pharmaco-invasive strategy.</p> <p>New section on Fibrinolysis in an unstable patient</p>

<p>PCI post-Fibrinolysis</p>	<p>As part of a pharmaco-invasive strategy in stable patients who have been given fibrinolytics and an elective PCI can be performed within 3 - 24 hours. IIa,B</p>	<p>As part of a pharmaco-invasive strategy in stable patients who have been given fibrinolytics and an elective PCI can be performed within 3 - 24 hours. I,A</p>
	<p>Early PCI should be considered in the following situations:</p> <ul style="list-style-type: none"> • Failed reperfusion or re-occlusion after fibrinolytic therapy. IIa,B • Cardiogenic shock or acute pulmonary oedema that develops after initial presentation. I,B 	<p>Early PCI should be considered in the following situations:</p> <ul style="list-style-type: none"> • Failed reperfusion or re-occlusion after fibrinolytic therapy. I,A • Cardiogenic shock or acute pulmonary oedema that develops after initial presentation. I,A • STEMI TIMI risk score of ≥ 6.0 at admission. I,C • If symptoms are completely resolved and ST segment completely normalises either spontaneously or after GTN (sublingual or spray) or anti platelet therapy. I,C
<p>Primary PCI</p>		<ul style="list-style-type: none"> • Patients presenting with ischaemic type chest pains > 30 mins and continuing to have chest pains but with a non interpretable ST-segment on the ECG, such as those with bundle branch block (assumed new onset RBBB) or ventricular pacing, may be having a MI and may be considered for a PCI strategy depending on resources. IIa,A. There is no role for fibrinolysis in these patients. • Radial access is recommended over femoral access if performed by an experienced radial operator. I,A • Stenting is recommended (over balloon angioplasty) for primary PCI. I,A



		<ul style="list-style-type: none"> Stenting with new-generation DES is recommended over BMS for primary PCI. I,A Routine use of thrombus aspiration catheters is not recommended. III, A
Delayed angiography and PCI - Symptom onset >12h		A primary PCI strategy is indicated in the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias. I,B
Pharmacotherapy PCI in STEMI patients with AF		New section
Pharmacotherapy (anti-platelets + anti-thrombotics > 1 year)		<ul style="list-style-type: none"> Rivaroxaban 2.5mg twice daily in combination with aspirin 100mg daily in high risk post-MI patients >12 months and up to 2 years. IIa,B Aspirin and ticagrelor 60 mg twice a day for >12 months may be considered for up to 3 years, in high risk patients who have tolerated DAPT without a bleeding complication. IIb,B

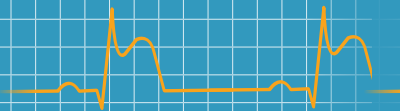
SUMMARY

Key Message #1: -Epidemiology of STEMI

- From the latest report of the National Cardiovascular Database - Acute Coronary Syndrome (NCVD-ACS) Registry 2014-2015:
 - ◆ The STEMI mortality in Malaysia remains high- the in-hospital, 30-day and 1-year mortality following STEMI being 10.6%, 12.3% and 17.9% respectively.
 - ◆ Patients receiving reperfusion (Primary PCI or fibrinolytic) had better survival compared to patients who did not receive any reperfusion.
 - ◆ Patients who had PCI during the index hospitalisation (including those who underwent Primary PCI and PCI both fibrinolysis) had better short-term and long-term survival as compared to those who did not undergo in-hospital PCI. This data is consistent with other published registries.

Key Message #2: - Diagnosis of STEMI

- Myocardial Infarction (MI) is defined pathologically as myocardial cell death due to prolonged ischaemia.
 - ◆ It is diagnosed by the rise and/or fall in cardiac troponins, with at least one value above the 99th percentile of the upper reference limits (URL), and accompanied with **at least one** of the following:
 - i. Clinical history consistent with chest pain of ischaemic origin.
 - ii. New ischaemic ECG changes or development of pathological Q waves.
 - iii. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
 - iv. Identification of an intracoronary (IC) thrombus by angiography or autopsy.
- MI may be due to STEMI or Non ST Elevation Acute Coronary Syndrome (NSTEMI-ACS).
- STEMI is diagnosed when there is:
 - ◆ ST elevation of ≥ 1 mm in 2 contiguous leads or
 - ◆ a new onset LBBB in the resting ECG
 - ◆ in a patient with ischaemic type chest pains of > 30 minutes and
 - ◆ accompanied by a rise and fall in cardiac biomarkers. (Table 6, pg 48 for ECG diagnosis of STEMI)
- New onset Right Bundle Branch Block with ST elevation of ≥ 1 mm in 2 contiguous leads does not interfere with the diagnosis of STEMI.
- Patients having prolonged ischaemic type chest pain of > 30 minutes and having:
 - ◆ a normal ECG or ST segment depression may be having NSTEMI-ACS. This encompasses both Unstable Angina (UA) and Non -ST Elevation MI (NSTEMI).



- ◆ a non-interpretable resting ECG (eg paced rhythm, RBBB etc) may be having NSTEMI-ACS. If pain persists, these high-risk patients may be considered for early Percutaneous Coronary Intervention (PCI) if facilities are available. Fibrinolysis is not advisable.
- ◆ There are separate guidelines for NSTEMI-ACS.

Key Message #3: - Clinical Presentation and Pitfalls in Diagnosis

- Atypical presentations can occur in the elderly, women and in diabetic persons.
- If the initial ECG is non-diagnostic, it may need to be repeated at frequent intervals to detect evolving changes of STEMI. Additional chest leads (V 7-9) and right ventricular leads may also be helpful.
- Too early a measurement of the cardiac biomarkers can sometimes result in misleadingly low levels.

Key Message #4: - Pre-Hospital Management:

- The public and Pre-hospital Care (PHC) personnel should be educated on the importance of early diagnosis and the benefits of early treatment.
- Patients with suspected STEMI should be given soluble or chewable 300 mg aspirin and 300 mg clopidogrel.
- These patients should be rapidly transported to the hospital for early initiation of reperfusion strategies.

Key Message #5: - STEMI Network:

- The objective of a STEMI network is to link non-PCI-capable centres to PCI-capable centres with the aim of providing PCI services in a timely manner for patients:
 - ◆ With STEMI
 - ◆ Who have been given fibrinolytic therapy and:
 - have failed reperfusion, or;
 - as part of a pharmaco-invasive strategy, or;
 - have high-risk features requiring early intervention.
- The optimal treatment of these patients should be based on the implementation of networks between hospitals ('hub' and 'spoke') and linked by an efficient ambulance service.

Key Message #6: - Initial Management:

- Early management of STEMI is directed at:
 - ◆ Pain relief.
 - ◆ Establishing early reperfusion.
 - ◆ Treatment of complications.

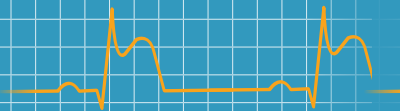
Key Message #7: - Reperfusion Strategies:

“Time is muscle” - Every patient with STEMI should have the occluded artery reopened (reperfusion therapy) as soon as possible after the onset of symptoms.

- Reperfusion therapy is indicated in all patients with symptoms of ischaemia of <12 hours duration and persistent ST-segment elevation.
- Primary PCI is superior to fibrinolysis for STEMI when performed in a timely manner at experienced centres. (see Flow Charts 1 & 2, pg 33 & 34)
 - ◆ If the patient **presents at a PCI centre**, then the time from FMC (First Medical Contact) to wire crossing should be **≤ 90 minutes**.
 - ◆ If transferred from **a centre with no PCI facilities**, the time from FMC to wire crossing should be **≤ 120 minutes** (including transfer delay). This is made up of:
 - door-in-door-out (DIDO) of non-PCI-capable hospital (spoke): ≤ 30 minutes.
 - Transport time to PCI -capable centre (hub): ≤ 60 minutes.
 - Door of PCI capable centre to wire crossing: ≤ 30 minutes.
 - If the time delay to primary PCI is >120 minutes, the best option is to give fibrinolytic therapy and make arrangements to transfer the patient to a PCI capable centre for a pharmaco-invasive strategy.
- When fibrinolytic therapy is administered, the Door to Needle time (DNT) should be ≤ 30 minutes.
- Whenever possible, patients given fibrinolytic therapy should be considered for a pharmaco-invasive approach (elective angiogram within 3-24 hours post fibrinolysis).

Key Message #8: - Adjunctive Therapies:

- All patients with STEMI receiving **fibrinolytic therapy** should receive:
 - ◆ 300 mg aspirin
 - + **(Plus) loading dose**
 - 75 mg of clopidogrel (> 75 years of age) or
 - 300 mg clopidogrel (≤75 years of age)
 - ◆ followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily. The duration of dual antiplatelet therapy (DAPT) should be between 1 month to 1 year, the duration being a balance between the ischaemic risks vs the bleeding risks.
- All patients with STEMI undergoing **Primary PCI** should receive loading doses of:
 - ◆ 300 mg aspirin
 - + **(Plus)**
 - 300-600 mg clopidogrel **or**
 - 180 mg ticagrelor **or**



- ▶ 60 mg prasugrel (after the coronary angiogram)
- ◆ This is followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily or 90 mg twice daily ticagrelor or 10 mg prasugrel daily.
- ◆ Patients who underwent PCI require DAPT for up to a year depending on the thrombotic/ischaemic versus bleeding risks. In patients with high bleeding risks, a shorter period of DAPT of 6 months may be considered.
- Medications that have been shown to improve survival if given early are:
 - ◆ ACE-Is
 - ◆ ARBs if ACE-I intolerant
 - ◆ β -blockers
 - ◆ Mineralocorticoid Receptor Antagonists (MRA)
 - ◆ High dose statins.

Key Message #9: - Complications Post STEMI:

- Important complications following STEMI are arrhythmias and heart failure.
- Heart failure may be due to extensive myocardial damage or mechanical complications.
- Chest pain post STEMI may be due to:
 - ◆ Reinfarction/Recurrent MI
 - ◆ Post infarct angina
 - ◆ Pericarditis
 - ◆ Non-cardiac causes such as gastritis

Key Message #10: - Risk Stratification Post STEMI:

- All patients post-STEMI should be risk-stratified either clinically or by using the STEMI TIMI and/or GRACE risk scores (pages 120-122).
- High-risk patients should be referred to cardiology centres for early coronary angiography and revascularization.

Key Message #11: - Secondary Prevention:

- Secondary prevention interventions can reduce mortality and cardiovascular event rate post-STEMI. This includes:
 - ◆ smoking cessation and other lifestyle changes
 - ◆ regular exercise
 - ◆ control of CV risk factors- hypertension, diabetes, smoking, dyslipidaemia
 - ◆ drug therapy;

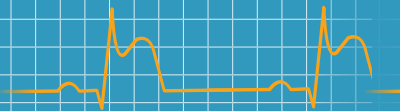
- anti-platelet agents
- statins therapy
- β -blockers:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%
- ACE-I/ARB:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%, anterior infarct and diabetes
- Healthcare providers should provide patient education and encourage compliance.
- Cardiac rehabilitation is an integral component of secondary prevention.

Key Message #12: - STEMI in Special Groups:

- Diagnosis of STEMI in older patients, persons with diabetes and women is difficult and a high index of suspicion is important.
- Treatment is the same although the older population and women tend to have higher bleeding risk.
- In patients with Chronic Kidney Disease (CKD):
 - ◆ Treatment of STEMI should be individualised.
 - ◆ Primary PCI is the preferred reperfusion strategy but morbidity and mortality are high.
 - ◆ In view of bleeding risks, the dosages of anti-platelet agents and anti-thrombotics need to be adjusted accordingly.
 - ◆ Aspirin, β - blockers, ACE-I and statins are beneficial in patients with mild to moderate CKD. In patients on dialysis, only aspirin, β - blockers and ACE-I remain beneficial.

Key Message #13:- Resumption of driving:

- There is no unanimous consensus as when to resume driving after STEMI.
- In general, for:
 - ◆ Private drivers:
 - After one month if no complications and LVEF $>$ 35%.
 - In those with complications such as LVEF $<$ 35%, acute decompensated heart failure, arrhythmias etc- it may be longer.
 - ◆ Commercial drivers:
 - should be assessed at 3 months post-STEMI for fitness to resume duties.
- For fitness for commercial air travel, see Table 16, pg 111.



Key Message #14: - Performance Measures:

Indicators for STEMI at presentation	Targets
ECG done within 10 minutes of FMC	90%
FMC to Device time \leq 90 minutes if in same hospital	60%
FMC to Device time \leq 120 minutes if transferred from another hospital	60%
FMC to needle time $<$ 30 minutes	75%
Medications at discharge: <ul style="list-style-type: none"> • Aspirin • P2 Y₁₂ inhibitors • High intensity statins 	90% 90% 90%
If LVEF $<$ 40%) <ul style="list-style-type: none"> • ACE-I/ARB • β-blocker • MRA 	70% 70% 70%
Cardiac rehabilitation	50%

Outcome Measures indicators include:

- In hospital mortality $<$ 10%
- 30-day mortality $<$ 14%
- 1-year mortality $<$ 18%

KEY RECOMMENDATIONS

Key Recommendation 1:

- A quick targeted history should be taken and is essential in raising the suspicion that the chest pain or chest pain equivalent is ischaemic in origin.

Key Recommendation 2:

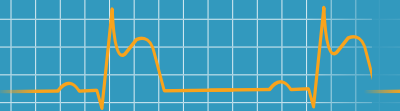
- In all patients presenting with chest pain or chest pain equivalents, a 12 lead ECG should be done and interpreted < 10 min of the First Medical Contact (FMC).
- If the initial ECG is non diagnostic and the index of suspicion of STEMI is high:
 - ◆ the ECG should be repeated at close intervals of at least 15 minutes to look for progressive ST changes.
 - ◆ compared with previous ECG's.
 - ◆ additional chest leads (V 7-9) and right ventricular leads should be done to identify posterior and right ventricular infarcts.

Key Recommendation 3:

- Patients with suspected STEMI should be given soluble or chewable 300mg aspirin and 300 mg clopidogrel.
- These patients should be rapidly transported to the hospital for early initiation of reperfusion strategies.
- If the anticipated time from FMC to PCI mediated reperfusion (wire crossing the lesion) is > 120 minutes, then pre-hospital or nearest in-hospital fibrinolysis is an option.

Key Recommendation 4:

- "Time is muscle" - Every patient with STEMI should have the occluded artery reopened (reperfusion therapy) as soon as possible after the onset of symptoms.
- Reperfusion therapy is indicated in all patients with symptoms of ischaemia of <12hours duration and persistent ST-segment elevation.



Key Recommendation 5:

- Primary PCI is superior to fibrinolysis for STEMI when performed in a timely manner at experienced centres. (see Flow Chart 2, pg 34).

Key Recommendation 6:

- When fibrinolytic therapy is administered, the Door to Needle time (DNT) should be ≤ 30 minutes.
- Whenever possible, patients given fibrinolytic therapy should be considered for a pharmaco-invasive approach (elective angiogram within 3-24 hours post fibrinolysis).

Key Recommendation 7:

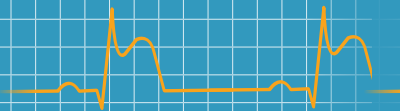
- All patients with STEMI receiving **fibrinolytic therapy** should receive:
 - ◆ 300 mg aspirin
+ **(Plus) loading dose**
 - 75 mg of clopidogrel (> 75 years of age) or
 - 300 mg clopidogrel (≤ 75 years of age)
 - ◆ followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily. The duration of dual antiplatelet therapy (DAPT) should be between 1 month to 1 year, the duration being a balance between the ischaemic vs the bleeding risks.
- All patients with STEMI undergoing Primary PCI should receive loading doses of:
 - ◆ 300 mg aspirin
+ **(Plus) loading dose**
 - 300-600 mg clopidogrel or
 - 180 mg ticagrelor or
 - 60 mg prasugrel (after the coronary angiogram)
 - ◆ This is followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily or 90 mg twice daily ticagrelor or 10 mg prasugrel daily.
 - ◆ Patients who underwent PCI require DAPT for up to a year depending on the thrombotic/ischaemic versus bleeding risks. In patients with high bleeding risks, a shorter period of DAPT of 6 months may be considered.

Key Recommendation 8:

- All patients with STEMI should receive medications that have been shown to improve survival if given early. These include:
 - ◆ ACE-Is
 - ◆ ARBs if ACE-I intolerant
 - ◆ β -blockers
 - ◆ Mineralocorticoid Receptor Antagonists (MRA)
 - ◆ High dose statins.

Key Recommendation 9:

- All patients post-STEMI should be risk-stratified either clinically or by using the STEMI TIMI and/or GRACE risk scores (pages 120-122).
- STEMI patients who present initially to non PCI-capable hospitals should be referred for early coronary angiography with a view to revascularization in the presence of any of the following:
 - ◆ Post-infarct angina
 - ◆ Inducible ischaemia
 - ◆ Late ventricular arrhythmias
 - ◆ In the presence of a depressed LV function (LVEF \leq 35%) and significant regional wall motion abnormalities
 - ◆ STEMI TIMI risk score \geq 6.0 (Appendix III, pg 120)



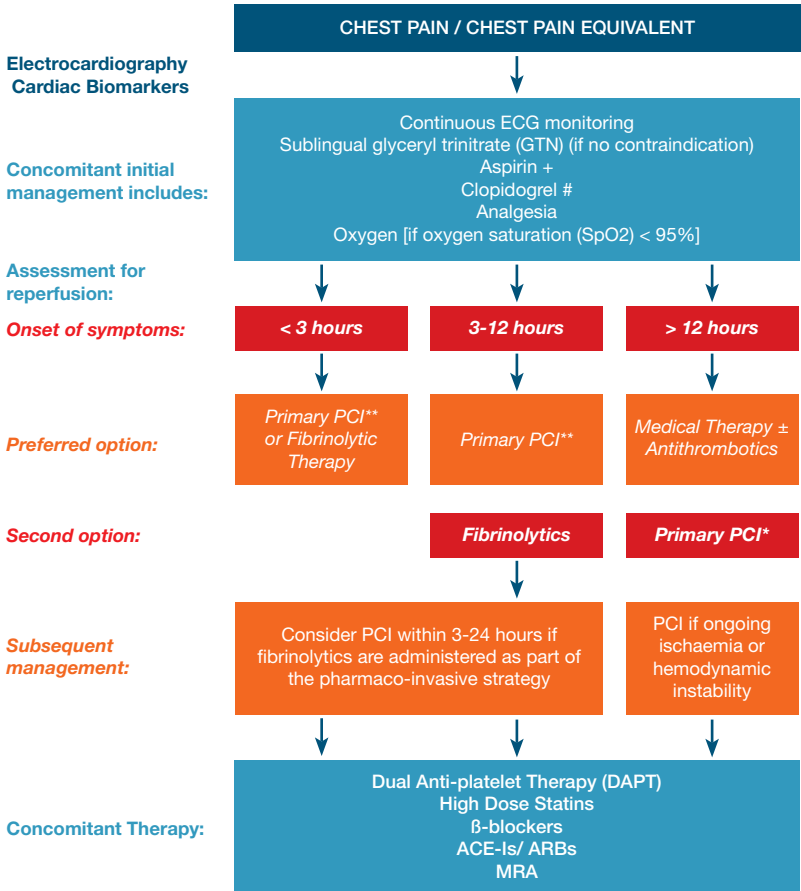
Key Recommendation 10:

- Post STEMI, all patients should receive secondary prevention interventions that have been shown to reduce mortality and cardiovascular event rate. These include:
 - ◆ smoking cessation and other lifestyle changes
 - ◆ regular exercise
 - ◆ control of CV risk factors- hypertension, diabetes, smoking, dyslipidaemia
 - ◆ drug therapy;
 - anti-platelet agents
 - statins therapy
 - β -blockers:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%
 - ACE-I/ARB:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%, anterior infarct and diabetes

Key Recommendation 11:

- Regular audit of performance measures (Table 19, pg 113) and outcomes measures are important to monitor and improve quality of care.

Flow Chart 1: Management of patients presenting with STEMI



or ticagrelor or prasugrel (after coronary angiogram)

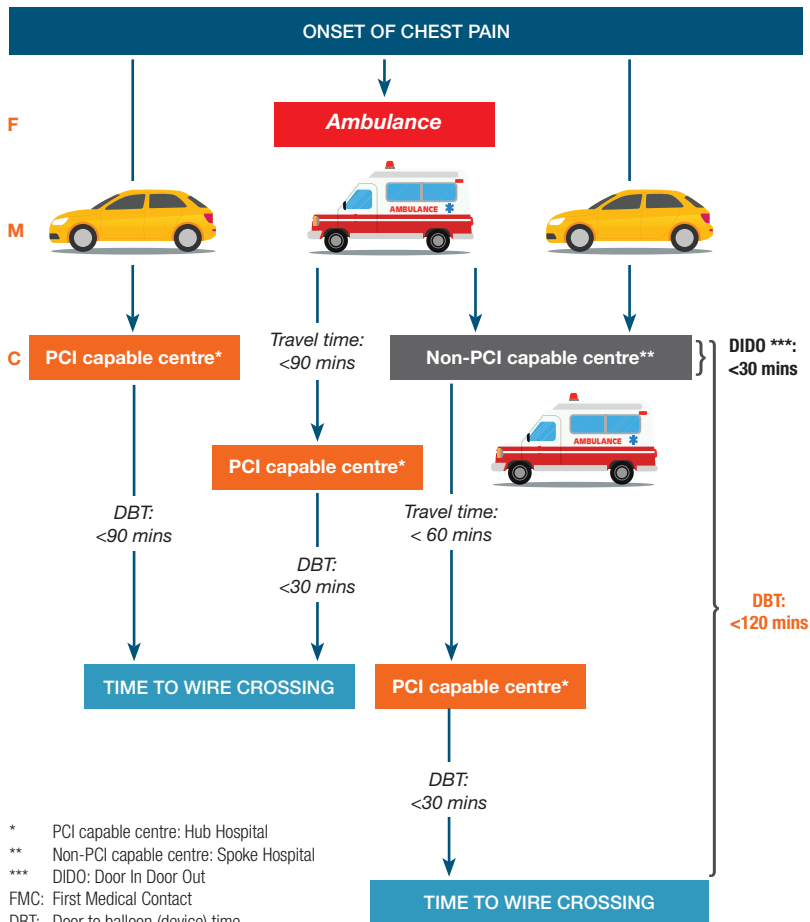
* When clinically indicated

** Preferred option in:

- high-risk patients
- presence of contraindications to fibrinolytic therapy and/or
- if the anticipated time intervals/transport times are within that stated in Flow Chart 2.



Flow Chart 2: Time intervals to determine choice of reperfusion strategy



If time intervals/transfer times are anticipated to be longer than stated, initiate fibrinolysis first and then consider same day transfer for PCI as part of pharmaco-invasive strategy (3-24 hours post lysis) or for transfer later depending on the clinical condition of the patient and the available resources.

Table 2: Level of evidence and grade of recommendation for acute therapy of STEMI

INTERVENTION	GRADE OF RECOMMENDATION	LEVEL OF EVIDENCE
REPERFUSION THERAPY		
Recommendation 1: *Primary PCI: Strategy of choice if: <ul style="list-style-type: none"> • Done within the time intervals stated in Flow chart 1 and 2. • There are contraindications to fibrinolysis. • High-risk patients. 	I I I	A A A
Recommendation 2: *Fibrinolytic therapy: Strategy of choice if: <ul style="list-style-type: none"> • DBT > 90 minutes if FMC in a PCI centre and > 120 min if transferred from non-PCI centre. • No contraindications to fibrinolysis. 	I I	A A
CONCOMITANT PHARMACOTHERAPY		
Recommendation 3: Aspirin: Loading dose of 300 mg followed by maintenance dose of 75 mg – 150 mg daily. + (PLUS) Clopidogrel: Loading dose of 300 mg followed by maintenance dose of 75 mg daily (for at least 1 month). OR Ticagrelor: Loading dose of 180 mg followed by maintenance dose of 90 mg twice daily (bd) to be administered to patients undergoing primary PCI. OR Prasugrel: Loading dose of 60 mg followed by maintenance dose of 10 mg (to be administered only prior to primary PCI).	I I I I	A A B B
Recommendation 4: Antithrombotics to be given to patients: <ul style="list-style-type: none"> • Who received fibrinolytic therapy and did not undergo PCI. <ul style="list-style-type: none"> ◆ Enoxaparin ◆ Heparin ◆ Fondaparinux • Underwent PCI and have atrial fibrillation (AF). <ul style="list-style-type: none"> ◆ Warfarin + DAPT or DOAC + DAPT • With mural thrombus. 	I I IIa IIa I	A B B B C
Recommendation 5: β-blockers: For all patients if no contraindications	I	A
Recommendation 6: ACE-Is: For all patients with no contraindications.	I	A
Recommendation 7: High dose Statins: For all patients if no contraindications.	I	A

*Please refer to Flow Chart 1 & 2, pg 33 & 34 for details.

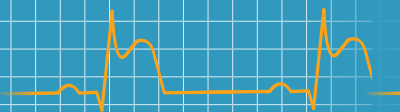
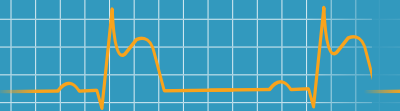


Table 3: Level of evidence and grade of recommendation for secondary prevention post-STEMI

INTERVENTION	GRADE OF RECOMMENDATION	LEVEL OF EVIDENCE	COMMENTS
Recommendation 8: Smoking Cessation	I	B	
Exercise	I	B	At least 30-60 minutes most days of the week.
CONCOMITANT PHARMACOTHERAPY			
Recommendation 9: Aspirin	I	A	Maintenance dose: 75-150 mg daily.
+ Clopidogrel	I	A	Maintenance dose 75 mg daily to be given for 1 month following fibrinolytic therapy and for at least 1-year post- primary PCI.
OR			
+ Ticagrelor	I	B	Maintenance dose 90 mg twice daily for at least 1-year post-primary PCI
OR			
+ Prasugrel	I	B	Maintenance dose 10 mg daily for at least 1-year post- primary PCI
+ β-blockers	I	A	Consider long-term therapy (>1 year) for patients with LVEF \leq 40%.
	IIb	B	Routine administration (> 1-year) in all patients post STEMI with no angina / ischaemia and normal LV function.
+ ACE-Is	I	A	Started on first day and continued long-term (>1 year) for patients with LVEF \leq 40%, anterior infarcts and diabetes.
	IIb	B	Routine administration in all patients post STEMI > 1 year
+ ARBs	I	B	Started on first day and continued long-term(>1-year) for patients with LVEF \leq 40%, anterior infarcts and diabetes.
	IIb	B	Routine administration in all patients post STEMI > 1 year
+ Statins	I	A	Aim for low density lipoprotein-cholesterol (LDL-C) < 1.8 mmol/L).

Table 4: Indications for PCI in STEMI

INTERVENTION	GRADE OF RECOMMENDATION/ LEVEL OF EVIDENCE
<p>Primary PCI in patients presenting < 12 hours of ischaemic symptoms and PCI can be performed:</p> <ul style="list-style-type: none"> • < 90 minutes if initial presentation is at a PCI centre or • < 120 minutes if initial presentation is at a non-PCI centre 	<p>IA</p> <p>IA</p>
<p>Primary PCI in patients presenting 12 to 24 hours of symptom onset with evidence of ongoing ischaemia</p>	I,B
<p>Primary PCI in patients who have:</p> <ul style="list-style-type: none"> • High-risk features – section 7 (C). pg 64 • Contraindications to fibrinolytics – section 7 (B). pg 63-64 	<p>I,A</p> <p>I,A</p>
<p>Rescue PCI in patients who have evidence of failed reperfusion of the infarct-related artery (IRA) diagnosed by persistent ST elevation and/or recurrent/ongoing chest pain.</p>	I,A
<p>Facilitated PCI is a strategy of immediate PCI < 1 hour after an initial pharmacological regimen. (fibrinolytics +/- GPIIb/IIIa Inhibitors)</p>	III,A
<p>Post-fibrinolysis and:</p> <ul style="list-style-type: none"> • Routine angiography with a view to PCI and stenting between 3-24 hours in all STEMI patients (pharmaco-invasive therapy). • Delayed selective angiography depending on presence of hemodynamic instability or residual ischaemia. 	<p>I,A</p> <p>I,A</p>
<p>PCI of totally occluded vessel within 3-28 days after MI and no reversible ischaemia.</p>	III,B



1. INTRODUCTION

The most recent data from the National Department of Statistics Malaysia indicated that in 2014, ischaemic heart disease (IHD) was the principal cause of mortality (13.7%). For men, it was the principle cause of death (15.2%) and for women, it was second after pneumonias.¹

Most deaths in STEMI occur within the first hour due to fatal arrhythmias. In addition, **TIME LOST IS MYOCARDIUM LOST**. Thus, early diagnosis and prompt reperfusion is important.

Based on the latest Malaysian Annual Report of the National Cardiovascular Database- Acute Coronary Syndrome (NCVD-ACS) Registry 2014-2015 it was noted that:²

- The demographics of patients with Acute Coronary Syndrome (ACS) have not changed over the last 10 years.
 - ◆ They are young with a mean age of 58.6 years, and about a quarter are below the age of 50 years. This age is lower than that seen in Thailand, Singapore and in Western populations.³⁻⁵ The patients presenting with ST segment Elevation Myocardial Infarction (STEMI) are even younger with a mean age of 56 years.
 - ◆ Majority of men presented with STEMI (50.5%) whereas women presented with Non ST Elevation Acute Coronary syndrome (NSTEMI-ACS) (70.8%). NSTEMI-ACS encompasses both Unstable Angina (UA) and Non ST-Elevation Myocardial Infarction (NSTEMI).
 - ◆ There was a high prevalence of hypertension, dyslipidaemia and diabetes – the prevalence of these risk factors has not changed over the last 10 years.
- The in-hospital mortality following STEMI was 10.6% and that following NSTEMI-ACS was 8.0%.
- The STEMI patients were generally more ill.
 - 67.4% were in the intermediate-high TIMI risk score.
 - 19.0% were in Killip class III/IV.
- Fibrinolytic therapy was the most common mode of reperfusion (69.1%), and only 13.7% were treated with primary PCI. Even in PCI capable centres, only 16.4% of STEMI patients underwent Primary PCI. About 14% of patients did not receive any form of reperfusion treatment due to late presentation, missed and delayed diagnosis.
 - ◆ The median door-to-needle time (DNT) was 45 minutes and only 35.2% achieved the recommended DNT time of < 30 minutes. However, as a Key Performance Indicator for the Emergency Department (ED) the DNT of < 30 mins was achieved in 87.1% of patients diagnosed with STEMI at presentation.⁶

- ◆ The median door-to-device (balloon) (DBT) time was 69 minutes and 63.6% achieved the recommended DBT time of < 90 minutes.
- More than 90.0% of the patients were discharged on dual antiplatelet therapy (DAPT) and statins. About 69.0% and 56.1% were on β -blockers and Angiotensin Converting Enzyme Inhibitors (ACE- I)/ Angiotensin Receptor Blockers (ARB) upon discharge.
- The in-hospital, 30-day and 1-year mortality following STEMI remains high at 10.6%, 12.3% and 17.9% respectively. This in-hospital mortality is almost double that reported in the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry-GWTG (Get With the Guidelines) database in the United States for the period January 2012 to December 2013 which was only 4.6%.⁷
- Patients receiving reperfusion therapy (PCI or fibrinolytic) had overall better survival than those who did not receive any form of reperfusion.
- Patients who underwent PCI during the index hospitalisation did better irrespective of it being primary PCI, rescue PCI, as part of pharmaco-invasive therapy or delayed PCI. Mortality was (PCI during the index hospitalisation compared to no PCI):
 - ◆ In-hospital: 7.9% vs 12.8%,
 - ◆ 30-day: 9.0% vs 14.9%
 - ◆ 1 year: 13.1% vs 21.8%.
- These figures are consistent with that of other registries.^{8,9}

To improve outcomes, it is important to:

- make an early diagnosis.
- reduce delays in the pre-hospital phase and delays related to systems.
- have a system in place for timely reperfusion (fibrinolysis or PCI).
- provide a seamless clinical pathway for high risk patients to have early revascularization.

The last Clinical Practice Guidelines (CPG) on Management of Acute ST Segment Elevation Myocardial Infarction (STEMI) - 3rd Edition was published in 2014. The objectives of this update are to:

- Determine the best practice in terms of pre-hospital and in-hospital care logistics and risk assessment.
- Decide the best reperfusion strategy for the patient.
- Optimise secondary prevention strategies.



The focus is to:

- Develop seamless systems and pathways in the management of STEMI patients.
- Improve the quality of care and outcomes.
- Shorten the total ischemic time by:
 - ◆ patient education so that they seek medical attention early.
 - ◆ improvements in the pre-hospital care, ambulance services and emergency department management.
 - ◆ establishment of STEMI networks of STEMI-referral (non-PCI capable) hospitals and STEMI-receiving (PCI capable) hospitals. This network in the Klang Valley is called MySTEMI.
- Work with payers and policy makers for reimbursement.

Guidelines are intended to help in the management of patients. All the recommendations stated in this guideline may not be available to all eligible patients. Patient care should be individualised, and sound clinical judgement still plays an important role in decision-making.

Key message #1:

- The STEMI mortality (in-hospital, 30 day and 1 year) remains high.
- Data from the latest 2014-2015 NCVD-ACS Registry indicated that patients receiving reperfusion (Primary PCI or fibrinolytic) had better survival compared to patients who did not receive any form of reperfusion.
- Patients who had any form of PCI during the index hospitalisation had better short-term and long-term survival compared to those who did not undergo PCI. This is consistent with other registries.

2. DEFINITION AND PATHOGENESIS OF MYOCARDIAL INFARCTION

Acute Coronary Syndrome (ACS) is a clinical spectrum of Coronary Artery Disease (CAD) ranging from Unstable Angina (UA), non-ST segment Elevation Myocardial Infarction (NSTEMI) to STEMI depending upon the degree and acuteness of coronary occlusion (Figure 1, pg 43). In UA, myocardial injury is absent and cardiac biomarkers are normal. In myocardial injury, cardiac biomarkers are raised.

It is important to distinguish between myocardial injury and myocardial infarction (MI). Myocardial injury may be due to:¹⁰

- ischaemia and/or
- non-ischaemic causes (eg myocarditis, renal failure)

MI is myocardial injury due to ischaemia.¹⁰ It is defined pathologically as myocardial cell death due to prolonged ischaemia.¹⁰

The preferred cardiac biomarkers are the troponins (both I and T). Elevation of cardiac troponins indicates myocardial necrosis. A level above the 99th percentile of the URL is abnormal and indicative of myocardial injury.¹⁰ All locally available commercial assays indicate this level, the exact value varying depending on the reagents used. The point of care kits, however, although giving a more rapid result, are not sensitive enough to detect this low level.

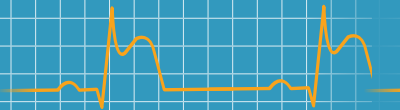
Troponins should always be interpreted in the clinical setting. Many troponin elevations, especially below certain cut-off points and troponin elevations without a rise and fall, are myocardial injuries and not MI.

A rise and/or fall in the troponin level is indicative of acute injury, while a persistently elevated level is indicative of chronic injury.¹⁰

MI is diagnosed when there is a rise and/or fall in cardiac troponins, with at least one value above the 99th percentile of the URL, and accompanied with **at least one** of the following:

- i. Clinical history consistent with chest pain of ischaemic origin of > 30 minutes.
- ii. ECG changes of ischaemia/infarction and/or the development of pathological Q waves.
- iii. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- iv. Identification of an intracoronary (IC) thrombus by angiography or autopsy.

MI may be **STEMI** or **NSTE-ACS** based on the ECG. (Figure 1, pg 43)



STEMI is diagnosed when there is:

- ST elevation of > 1 mm in 2 contiguous leads or
- a new onset LBBB in the resting ECG
- in a patient with ischaemic type chest pains of > 30 minutes and
- accompanied by a rise and fall in cardiac biomarkers.

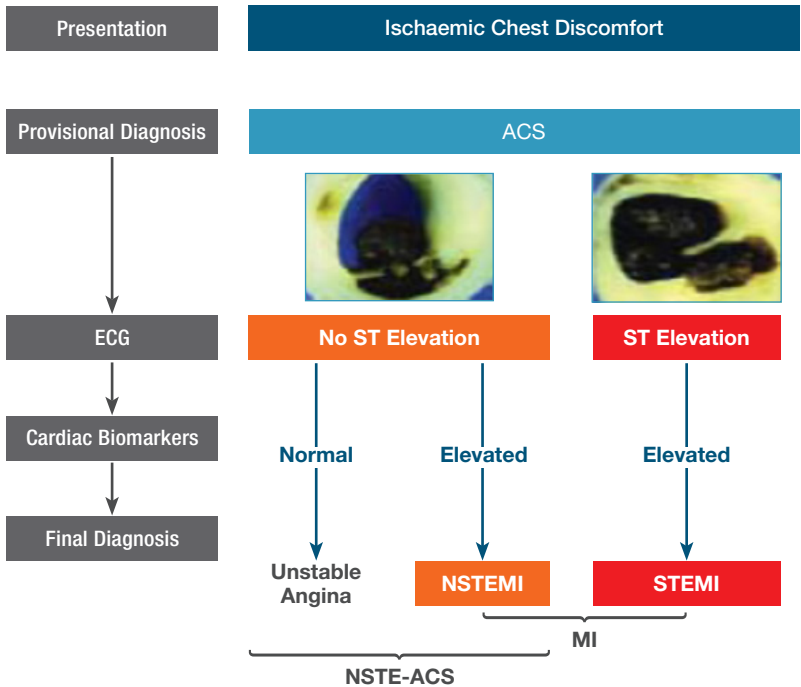
New onset Right Bundle Branch Block with ST elevation of ≥ 1 mm in 2 contiguous leads does not interfere with the diagnosis of STEMI.

In **NSTE-ACS**, ST elevation is absent on the resting ECG. In addition, patients having prolonged ischaemic type chest pain and having a non-interpretable resting ECG (eg paced rhythm, new RBBB etc) without ST elevation are having NSTE-ACS. There are separate guidelines for NSTE-ACS.

According to the 4th Universal definition, MI can be classified as 5 types depending on the pathology, clinical features, prognosis and treatment strategies.¹⁰ (Table 5, pg 44). This CPG focuses on STEMI which is almost always Type 1 MI (spontaneous MI related to atherosclerotic plaque rupture, with ulceration, fissuring, erosion or dissection). Occasionally the other types of MI may also present as STEMI.

'Reinfarction' is used for MI that occurs within 28 days of the incident event (incident MI) while recurrent MI occurs after 28 days.¹¹

Figure 1: Clinical spectrum of ACS.*



*Adapted from Amsterdam EA, Wenger N, Brindis RG et al. "2014 ACC/AHA Guidelines for the management of patients with Non ST Elevation Acute Coronary Syndromes" Circulation. 2014;130:e344-e426.

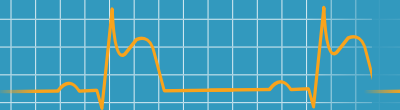


Table 5: Clinical Classification of MI

<p>Type 1: Spontaneous MI due to coronary athero-thrombosis</p> <p>Spontaneous MI related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis.</p>
<p>Type 2: MI secondary to an imbalance between myocardial oxygen demand and supply unrelated to acute coronary athero-thrombosis</p> <p>MI that occurs due to an imbalance between myocardial oxygen supply and/or demand. It may occur in the presence of coronary atherosclerosis without plaque rupture or in the absence of atherosclerosis eg coronary endothelial dysfunction, coronary artery spasm, coronary embolism, coronary artery dissection, tachy/bradyarrhythmias, anaemia, respiratory failure, sepsis, hypotension, and hypertension with or without left ventricular hypertrophy (LVH).</p>
<p>Type 3: MI resulting in death when biomarker values are unavailable</p> <p>Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes or new LBBB, but death occurring before blood samples could be obtained, before cardiac biomarker could rise, or in rare cases cardiac biomarkers were not collected.</p>
<p>Type 4a: MI related to PCI</p> <p>MI associated with PCI is arbitrarily defined by elevation of cardiac troponin (cTn) values $5 \times > 99^{\text{th}}$ percentile URL in patients with normal baseline values ($\leq 99^{\text{th}}$ percentile URL) or a rise of cTn values $> 20\%$ if the baseline values are elevated but are stable or falling. In addition, either</p> <ul style="list-style-type: none"> (i) symptoms suggestive of myocardial ischaemia, or (ii) new ischaemic ECG changes or new LBBB, or (iii) angiographic loss of patency of a major coronary artery or a side branch or persistent slow-or no-flow or embolization, or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality is required.
<p>Type 4b: MI related to stent thrombosis</p> <p>MI associated with stent thrombosis is detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.</p>
<p>Type 5: MI related to coronary artery bypass surgery (CABG)</p> <p>MI associated with CABG is arbitrarily defined by elevation of cardiac biomarker values $10 \times 99^{\text{th}}$ percentile URL in patients with normal baseline cTn values (99^{th} percentile URL). In addition, either</p> <ul style="list-style-type: none"> (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Adapted from Thygesen K et al. Fourth universal definition of myocardial infarction. Eur Heart J 2019; 40 (3): 237–269

Key message #2:

- MI is defined pathologically as myocardial cell death due to prolonged ischaemia.
- It is diagnosed by the rise and/or fall in cardiac troponins, with at least one value above the 99th percentile of the URL, and accompanied with at least one of the following:
 - i. Clinical history consistent with chest pain of ischaemic origin of > 30 minutes.
 - ii. ECG changes of ischaemia/ infarction and/or the development of pathological Q waves.
 - iii. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
 - iv. Identification of an intracoronary (IC) thrombus by angiography or autopsy.
- STEMI is diagnosed when there is:
 - ◆ ST elevation of ≥ 1 mm in 2 contiguous leads or
 - ◆ a new onset LBBB in the resting ECG
 - ◆ in a patient with ischaemic type chest pains and
 - ◆ accompanied by a rise and fall in cardiac biomarkers.

3. DIAGNOSIS

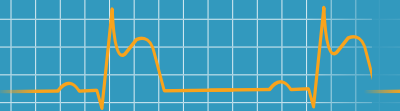
The diagnosis of STEMI is based on:

- the presence of evolutionary changes of ST elevation in the resting ECG
- history of ischaemic-type chest pain or its equivalent and
- supported by a rise and/or fall in the cardiac biomarkers

3.1 History

A thorough, targeted history is important in making the diagnosis of STEMI. Chest pain in STEMI begins abruptly and lasts for more than thirty minutes.¹² It is usually located in the centre of the chest and may radiate to the jaw or down the left arm. It may occur at rest or with activity. The pain may just be a tightness or heaviness in the chest, but it is usually described as a pressure, squeezing or a severe crushing pain with a sense of impending doom, and is associated with sweating, nausea, vomiting and shortness of breath. The pain may be of a burning quality and localised to the epigastria or interscapular region resulting in a misdiagnosis.

In the elderly, females and patients with diabetes, the index of suspicion should be high because they may present with atypical symptoms such as unexplained fatigue, shortness of breath, dizziness, light-headedness, unexplained sweating and syncope. They may not necessarily have chest pain.



Other important points to note in the history are the presence of:

- Previous history of ischaemic heart disease, PCI or CABG.
- Risk factors for atherosclerosis.
- Symptoms suggestive of previous transient ischaemic attack (TIA) or other forms of vascular disease.

Key Recommendation 1:

- A quick targeted history should be taken and is essential in raising the suspicion that the chest pain or chest pain equivalent is ischaemic in origin.
- Upon clinical suspicion of ACS, a 12-lead ECG should be performed and interpreted immediately within 10 minutes of FMC.

3.2 Electrocardiographic changes (Table 6 & 7, pg 48 & 49)

The diagnosis of STEMI depends upon the presence of characteristic ECG changes.

The presence of ST elevation in two contiguous leads in a patient with symptoms of ischaemia is the cardinal feature of STEMI.

The cut-off points for new or presumed new ST segment elevation at the J point (in the absence of Left Ventricular Hypertrophy (LVH) and LBBB) is:¹⁰

- the presence of ≥ 0.1 mV ST segment elevation in all leads except leads V2-V3
- a cut-off point of ≥ 0.25 mV (in males < 40 years), ≥ 0.2 mV (in males ≥ 40 years) and ≥ 0.15 mV in females is used in leads V2-V3

In patients with BBB (new or presumed new), comparison with a previous ECG may be helpful in determining if the changes are pre-existent. The presence of a new onset or presumed new LBBB in a patient with typical chest pain of ischaemic origin may indicate an infarct and should be treated as STEMI.¹³

Patients with ischaemic type chest pain > 30 minutes and new presumed new RBBB accompanied with:¹⁰

- ST segment elevation ≥ 1 mm - should be managed as STEMI
- ST-segment depression or T wave abnormalities (excluding those in leads V1-V4) – should be managed as NSTEMI. If pain persists, they should be considered for an early PCI strategy.

Acute anterior STEMI with a Right Bundle Branch Block (RBBB) is usually an extensive MI due to involvement of the proximal left anterior descending artery or the left main coronary artery. It carries a poor prognosis and these patients should also undergo early reperfusion strategies.¹⁷ Occasionally, patients with inferior STEMI can

also develop a RBBB due to involvement of the atrioventricular (A-V) branch of the right coronary artery. In these patients, often the myocardium involved is small and the prognosis is not that bad.¹⁴

Generally, patients with new onset Bundle Branch Block (BBB) have more comorbidities and a worse prognosis.^{15,16}

In the early stages of MI, the initial ECG may be normal, equivocal or show hyperacute T-wave changes only. In these patients, if the index of suspicion of STEMI is high, the ECG should be repeated at close intervals of at least 15 minutes to look for progressive ST changes. Comparison with previous ECGs may also be helpful. In addition, there are some conditions with ECG changes that can mimic that of STEMI. (Appendix I, pg 118)

Patients with inferior STEMI should have an ECG recording of the right precordial lead (V4R) to identify concomitant right ventricular (RV) involvement.^{17,18} The cut-off point is ≥ 0.5 mm (≥ 1 mm in men < 30 years old).¹⁰

In those with ST segment depression in leads V1-V3, it is advisable to have an ECG recording of the posterior chest wall (V7-V9) to identify a true infero-basal (formerly known as infero-posterior) STEMI.¹⁹ The cut-off point for ST segment elevation in the posterior leads is ≥ 0.05 mV (≥ 0.1 mV in men < 40 years).¹⁰

ST elevation of > 1 mm in lead aVR may accompany anterior or inferior STEMI. This is also a predictor of left main/3 vessel CAD and carries an adverse prognosis.²⁰⁻²²

Occasionally patients with ongoing chest pains and myocardial ischaemia may have a normal or un-interpretable ECG. If the clinical suspicion of ongoing MI is high, imaging techniques such as bedside echocardiogram may be helpful.

Key Recommendation 2:

- In all patients presenting with chest pain or chest pain equivalent, a 12 lead ECG should be done and interpreted < 10 min of the First Medical Contact (FMC).
- If the initial ECG is non diagnostic and the index of suspicion of STEMI is high:
 - ◆ the ECG should be repeated at close intervals of at least 15 minutes to look for progressive ST changes.
 - ◆ compared with previous ECG's.
 - ◆ additional chest leads (V 7-9) and right ventricular leads should be done to identify posterior and right ventricular infarcts.

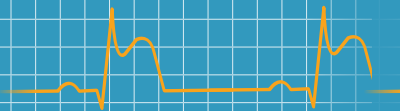


Table 6: ECG patterns of various STEMI locations and the diagnostic cut off points (in the absence of LVH or LBBB)^{10,23}

LOCATION	LEADS	ECG FINDINGS
Anteroseptal	V1 – V3	<ul style="list-style-type: none"> • ST elevation in leads V2-3: ≥ 0.25 mV (in males < 40 years), ≥ 0.2 mV (in males ≥ 40 years) ≥ 0.15 mV in females, • Q wave
Extensive anterior	V1 – V6	<ul style="list-style-type: none"> • ST elevation of ≥ 0.1 mV in all leads except leads V2-V3. In leads V2-3 : ≥ 0.25 mV (in males < 40 years), ≥ 0.2 mV (in males ≥ 40 years) ≥ 0.15 mV in females, • Q wave
Posterior	V7 – V8	<ul style="list-style-type: none"> • ST elevation ≥ 0.05 mV (≥ 0.1 mV in men < 40 years), • Q wave
Posterior	V1 – V2	<ul style="list-style-type: none"> • ST depression, Tall R wave
Anterolateral	I, AVL, V5 – V6	<ul style="list-style-type: none"> • ST elevation ST elevation of ≥ 0.1 mV, • Q wave
Inferior	II, III, AVF	<ul style="list-style-type: none"> • ST elevation ST elevation of ≥ 0.1 mV, • Q wave
Right Ventricular (RV)	V4R	<ul style="list-style-type: none"> • ST elevation > 0.5 mm (≥ 1 mm in men < 30 years old).

Table 7: Location of Ischaemia/infarction in STEMI²⁴

LEADS WITH ST SEGMENT ELEVATION	AFFECTED MYOCARDIAL AREA	OCCLUDED ARTERY (CULPRIT VESSEL)
V1 – V2	Septal	Proximal LAD
V3 – V4	Anterior	LAD
V5 – V6	Apical	Distal LAD, left circumflex or RCA
I, aVL	Lateral	circumflex
II, III, aVF	Inferior	RCA 90%, circumflex: 10%
V7,8,9 (reciprocal ST segment depression often seen in V1-3)	Posterolateral (also referred to as posterior or inferobasal)	RCA or circumflex

3.3 Serum cardiac biomarkers

The history and ECG are of paramount importance in making the diagnosis of STEMI and determining the reperfusion strategy. A rise and fall in the levels of serum cardiac biomarkers support the diagnosis of STEMI. One should not, however, wait for the results of these biomarkers before initiating reperfusion therapy.

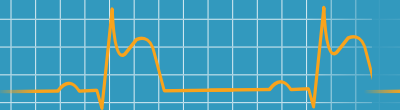
These cardiac biomarkers include:

- Cardiac Troponin T (cTnT) and Cardiac Troponin I (cTnI).
- Creatine Kinase-Myocardial Band (CK-MB).
- Creatine Kinase (CK).
- Myoglobin -This appears rapidly after myocardial necrosis but has not achieved widespread use in cardiac practice.²⁵

For the relative timing, rate of rise, peak value, duration of elevation and properties of these cardiac biomarkers following STEMI, see Figure 2, pg 51 and Table 8, pg 51.

Troponins have near absolute specificity and high clinical sensitivity for myocardial necrosis. It rises within 3-4 hours of the onset of MI and is more likely to be positive 6 hours after symptom onset. Troponins may also be raised in other conditions (see Appendix II, pg 119).

High Sensitive (hs) troponins can detect even lower concentrations of troponins in the setting of myocardial necrosis leading to an earlier diagnosis of MI.¹⁰ They are useful as a rule-out for MI. The negative predictive value is > 95% as a single test on admission and almost 100% when repeated after 3 hours.²⁶ Sex-dependent values are recommended for hs-troponin assays.²⁷⁻²⁹



CK-MB (measured by mass assay) is the next best alternative. It is less tissue-specific than troponins and values differ between the gender. The criterion most commonly used for the diagnosis of acute MI is 2 serial elevations above the 99th percentile of a reference control group or a single result more than twice the URL.^{29,30}

CK-MB first appears 4-6 hours after symptom onset, peaks at 24 hours, and returns to normal in 48-72 hours. Its value in the early and late (>72 h) diagnosis of acute MI is limited. Values for CK-MB should rise and fall; values that remain elevated without change are almost never due to MI.

These cardiac biomarkers (troponins and CK-MB) should be measured at the time of first assessment and repeated 6-9 hours later:

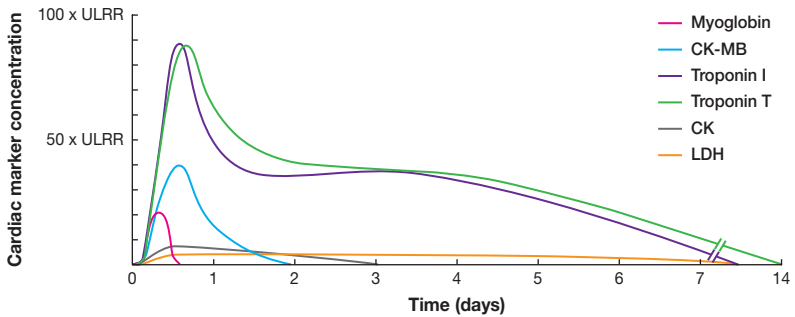
- To document the rise and/or fall exceeding the 99th percentile URL for the diagnosis of MI.
- If the first measurement is non-diagnostic and the clinical suspicion of MI is high.

It used to be thought that troponins are not useful for the detection of reinfarction because they can remain elevated for up to 10-14 days and sometimes longer.²⁶ However, if a patient is suspected of having a reinfarction on clinical grounds, a $\geq 20\%$ increase in the value of either troponins or CK-MB between 2 samples 3-6 hours apart supports the diagnosis.²⁹⁻³¹

To ensure the reliability of these tests, each individual laboratory should maintain high quality laboratory practice and confirm the range of reference values in their specific setting.

Total CK measurement is also not recommended owing to its poor specificity and large distribution in skeletal muscles.²⁹

Figure 2: Time Course of Elevation of Serum Cardiac Biomarkers after STEMI²⁵

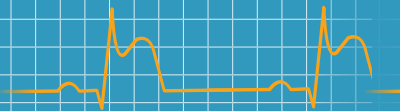


ULRR: Upper Limit Reference Range

Table 8: Properties of serum cardiac biomarkers²⁵

PROTEIN	FIRST DETECTION*	DURATION OF DETECTION	SENSITIVITY	SPECIFICITY
CK-MB	2 – 3 hours	1 – 2 days	+++	+++
Troponin I	3 – 4 hours	7 – 10 days	++++	++++
Troponin T	3 – 4 hours	7 – 14 days	++++	++++
CK	4 – 6 hours	2 – 3 days	++	++
Myoglobulin	1.5- 2 hours	8- 12 hours	+++	+

* Hours after symptom onset.



3.4 Other diagnostic modalities

Echocardiography is a particularly useful bedside imaging technique. It is useful in detecting:

- New regional wall motion abnormalities.
- LV and RV function.
- Mechanical complications of acute MI e.g. free wall rupture, acute ventricular septal defect (VSD), and mitral regurgitation.

Other imaging techniques such as chest radiography, computed tomographic coronary angiography (CTCA), magnetic resonance imaging (MRI) and radionuclide techniques may be useful investigations in the patient presenting with acute chest pain in difficult diagnostic situations.

They help to detect:

- Coronary atherosclerotic plaques, myocardial ischaemia and/or scars from previous MI.
- Non-ischaemic conditions causing chest pain such as valvular heart disease, perimyocarditis, pulmonary embolism, aortic dissection and pneumothorax.

In STEMI, there is no role for routine CTCA. Use of CT should be confined to selected cases where acute aortic dissection or pulmonary embolism is suspected.

Key Recommendation 3:

- The diagnosis of STEMI is made based on history of characteristic ischaemic type chest pain accompanied by ECG changes of ST elevation of at least 1 mm in at least 2 contiguous leads or new onset LBBB.
- A rise and fall of the cardiac biomarkers support the diagnosis of STEMI.
- Troponins and CKMB are the cardiac biomarkers of choice.

4. PRE-HOSPITAL MANAGEMENT

Public awareness about heart disease should be increased so that individuals will seek appropriate treatment early, thus reducing time from symptom onset to FMC. Most deaths following STEMI occur in the pre-hospital phase.

Patients with ischaemic-type chest pain should go to the nearest hospital rather than a clinic.

In STEMI, it is important to reduce total ischaemic time i.e. the time from symptom onset to the time of institution of reperfusion strategies. Total ischaemic time is a combination of:

1. Time from arterial occlusion to symptom onset.
2. Time from symptom onset to FMC.
3. FMC to initiation of reperfusion strategies (Primary PCI or fibrinolysis).

The public should be educated about:

- Symptoms of ACS.
- The importance of seeking early treatment at the nearest hospital.
- The benefits of early treatment – opening the blocked coronary artery as soon as possible to limit myocardial damage to the minimum and preserve heart function.

“TIME IS MYOCARDIUM.”

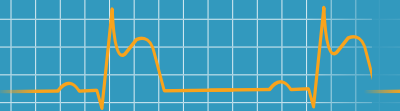
Immediate measures to be taken in suspected cases of ACS.

4.1. For the general public

- Seek immediate medical attention at the nearest hospital.
- Call for an ambulance (dial 999) or get someone to take you immediately and directly to the nearest hospital.
- Do not drive yourself.
- If not on regular aspirin and with no history of allergy, chew 300mg aspirin immediately. Soluble and chewable aspirin formulations are preferable to solid aspirin either chewed or swallowed.^{32,33} Regular aspirin is preferred over enteric coated aspirin in this situation because of its faster onset of action.³⁴
- The 999 despatchers will provide additional care instructions before the arrival of the pre-hospital care (PHC) providers.

4.2 For patients with known coronary heart disease (CHD)

- If the chest pain is suggestive of ACS (section 3.1, pg 45), take one dose of sublingual glyceryl trinitrate (GTN) by tablet or spray, and be rapidly transported to the nearest hospital.



- Patients should be educated that taking GTN with certain drugs can cause complications such as vasodilatation and hypotension; this includes taking it within 48 hours of drugs such as **phosphodiesterase inhibitors** [sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra)].

4.3 For patients with known CHD and history of previous PCI and/or CABG

- If the chest pain is suggestive of ACS (section 3.1, pg 45), take one dose of sublingual GTN by tablet or spray, and be rapidly transported to the nearest hospital.
- Go as soon as possible preferably to a PCI capable hospital.

4.4 Pre-hospital Care (PHC)

When a patient presents with chest pain, it is of paramount importance to determine if:

- The pain is cardiac in origin.
- If cardiac in origin, is it due to:
 - ◆ STEMI – requires immediate treatment preferably by Primary PCI if this can be done in a timely manner.
 - ◆ UA/NSTEMI.

In STEMI there is:

- Prolonged duration of ischaemic-type chest pain of > 30 minutes **and**
- ECG changes showing ST elevation of > 1 mm in 2 contiguous leads or a new (or presumed new) onset LBBB.

In **STEMI, TIME IS MYOCARDIUM** and the patient should be transported rapidly to a centre capable of providing reperfusion therapy to reopen the occluded infarct related artery.

In **UA/NSTEMI**, the initial management is medical in accordance with the CPG on UA/NSTEMI.

The pre-hospital management of STEMI patients should ideally be based on regional networks designed to deliver reperfusion therapy rapidly and effectively, with efforts made to make primary PCI available to as many patients as possible.

When there is a 999 call, the caller is first directed to Telekoms who will verify the authenticity of the caller. It is then directed to a Medical Emergency Coordination Centre (MECC), who will then:

A. Identify the chief complaint- If the complaint is chest pain or a chest pain equivalent (eg chest heaviness, discomfort which may be associated with sweating and/or shortness of breath), use a validated protocol addressing:



- ◆ nature of complaint and severity including level of alertness.
 - ◆ difficulty breathing.
 - ◆ changing of skin colour (pallor / blue).
 - ◆ previous history of heart attack or angina.
 - ◆ use of medications in the past 12 hours.
- Provide pre-arrival instructions including immediate self-care or bystander care while waiting for the ambulance arrival.

Ambulance teams dispatched to the scene should be trained and equipped to identify STEMI (with the use of Advanced Cardiac Care Device which is capable of ECG recording, transmission, and real-time ECG monitoring and telemetry). This results in direct referral to PCI centres and earlier initiation of reperfusion strategies. This strategy is cost-effective and short-term mortality is also reduced.³⁵⁻³⁷

B. If the ECG shows changes of STEMI:

I,A

I,A

I,A

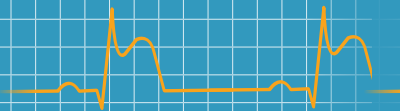
- PHC providers should administer initial therapy:
 - ◆ Soluble or chewable aspirin (300mg)^{38,39} and
 - ◆ Clopidogrel- Loading dose of 300mg, if > 75 years of age- the loading dose is 75mg.⁴⁰⁻⁴²
 - ◆ *Fibrinolysis when applicable.⁴⁴⁻⁴⁷ - Fibrinolysis treatment initiated by PHC providers resulted in shorter DNT, translating into greater health and cost benefits.⁴⁸

I,A

- STEMI patients:
 - ◆ should be given appropriate care and monitored during transport.
 - ◆ should be transferred to a PCI-capable centre, bypassing non-PCI centres if this can be done in a timely manner.⁴⁹⁻⁵¹
 - ◆ that present to a non-PCI-capable hospital and awaiting transportation for primary or rescue PCI should be attended in an appropriately monitored area and accessible to the PHC personnel.
 - ◆ To reduce reperfusion times, other key care processes include:⁵²
 - Pre-hospital activation of the catheterisation team.
 - Single call transfer protocol from an outside facility.
 - Direct access to catheterisation lab with Emergency Department (ED) bypass for both patients diagnosed with STEMI and transported directly to the ED via ambulances and those transferred from non-PCI centers.⁵³⁻⁵⁷

I,C

- PHC services, emergency departments, and critical care units should have a written updated STEMI management protocol, preferably shared within geographical networks with the same cardiology services.



- I,C • All hospitals and PHC services participating in the care of patients with STEMI should record and audit delay times and work to achieve and maintain quality targets.⁵⁸
- I,C • It is recommended that primary PCI-capable centres deliver a 24/7 service and be able to perform primary PCI without delay.⁵⁸

I,A *If the anticipated time from FMC to PCI-mediated reperfusion (wire-crossing the lesion) is >120 minutes, then pre-hospital or nearest in-hospital fibrinolysis is an option.^{46,59}

C. If the ECG does not show STEMI:

- the patient should be transported to the nearest hospital preferably with cardiology services.

4.5 Pre-hospital Care Personnel

Pre-hospital care personnel should be trained to:

- identify patients at high risk of developing ACS such as those with prior heart disease, the elderly, presence of multiple cardiovascular risk factors - diabetes, smoking, hypertension, dyslipidaemia, and a family history of premature heart disease.
- interpret the ECG, identify and treat common arrhythmias.
- identify patients with STEMI based on history and characteristic ECG changes after consultation with the ED physician/medical officer.
- assess, stabilise and monitor the patient's haemodynamics continuously prior to and during transfer.
- I,A • administer fibrinolysis out of hospital after excluding the contraindications in patients who cannot be transferred to a PCI-capable centre in a timely manner.^{46,59}

Key Messages #4:

- The public and PHC personnel should be educated on the importance of early diagnosis and the benefits of early treatment.

Key Recommendation 3:

- Patients with suspected STEMI should be given soluble or chewable 300 mg aspirin and 300 mg clopidogrel.
- These patients should be rapidly transported to the hospital for early institution of reperfusion strategies.
- If the anticipated time from FMC to PCI mediated reperfusion (wire crossing the lesion) is > 120 minutes, then pre-hospital or nearest in-hospital fibrinolysis is an option.

5. STEMI NETWORK

The objective of a STEMI network is to link non-PCI-capable centres to PCI-capable centres with the aim of providing PCI services in a timely manner for patients:

- With STEMI
- Who have been given fibrinolytic therapy and:
 - ◆ have failed reperfusion or,
 - ◆ as part of a pharmaco-invasive strategy or,
 - ◆ have high risk features requiring early intervention.

The optimal treatment of these patients should be based on the implementation of networks between hospitals ('hub' and 'spoke') with various levels of technology, linked by an efficient ambulance service.

The main features of such a network are:⁶⁰

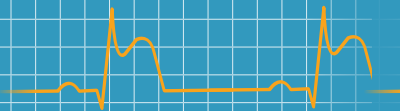
- Clear definition of geographic areas of responsibility.
- Shared written protocols based on risk stratification and transportation by a trained physician, nurse, or PHC personnel in appropriately equipped ambulances.
- Pre-hospital triage and management of STEMI patients (see section 4, pg 53-56)

Ideally, primary PCI centres (hub) should perform the procedure systematically on a 24/7 basis for all STEMI patients. In centres with limited resources, a primary PCI programme should still be encouraged and eventually aim to offer a 24/7 service.

At present, a STEMI network is available in the Kelang valley (MYSTEMI) and in Pahang. It is hoped that similar networks will be set up throughout the country.

Essentials of STEMI systems of care include:^{54,55,58,60}

- A single telephone emergency number (999).
- Ambulances equipped with 12-lead ECGs and defibrillators, and staffed with well-trained PHC personnel, capable of basic and advanced life support.
- Automatic ECG interpretation or ECG telemetry.
- Direct telephone access between the medical officer and the cardiology team on call.
- Protocols for standardized care (diagnosis, therapy, and transfer).
- Cardiologist as a network leader with close collaboration with the emergency physician, internal medicine and family medicine specialists.
- Involvement of healthcare authorities in both private and public sectors.
- Addressing insurance and other reimbursement issues.
- Public information campaigns stressing the importance of early treatment.
- Regular meetings of the involved parties.
- A prospective registry to assess progress and need for change.
- Quality Improvement Measures and Quality Improvement Programs.



5.1 Total Ischaemic Time

Recommendations to reduce total ischaemic time in a STEMI network:

For Primary PCI:

- **Target from FMC to “wire crossing” (Door to Balloon (Device) Time):**
 - ◆ **FMC in PCI capable hospital (“Hub”): ≤ 90 minutes**
 - ◆ **FMC in Non-PCI capable hospital (“Spoke”): ≤ 120 minutes**
- **Symptom onset to Door 1 (Emergency Department (ED) of spoke):**
 - ◆ Community health education
- **Door 1 (ED of spoke) to First Medical Contact (FMC) - ≤ 10 minutes**
 - ◆ Patient should be triaged to the Fast Lane.
 - ◆ Door 1 to ECG interpretation and decision (within 10 minutes).
- **Door 1 (ED of spoke) to departure - ≤ 30 minutes**
 - ◆ Time to ECG; goal < 10 minutes.
 - ◆ Time to ambulance commitment; goal < 10 minutes.
 - ◆ Time to ambulance arrival and departure; goal < 10 minutes.
 - ◆ Total time in ED (**Door In, Door Out- DIDO**); goal ≤ 30 minutes.
- **Door 1 (ED of spoke) to Door 2 (ED of hub) - Travel time ≤ 60 minutes**
- **Door 2 (ED of hub) to wire crossing- ≤ 30 minutes**

For Fibrinolysis:

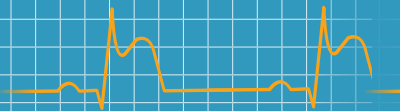
- If transfer time to the PCI capable hospital is prolonged fibrinolysis is advised.^{49,59}
Transfer times:
 - ≤ 90 minutes - If transferred from a non-PCI centre (spoke) to a PCI centre (hub): DIDO in the spoke hospital of < 30 minutes + travel time of < 60 minutes.
 - ≤ 60 minutes - If ambulance transport direct to PCI centre.
- ◆ The goal is 10 minutes from diagnosis to initiation of fibrinolysis. (Door to needle time <30 minutes)
- ◆ If reperfusion is not successful, the patient should be transferred to a PCI capable hospital for rescue PCI.
- ◆ If reperfusion is successful, the patient:
 - Can be transferred to a PCI capable hospital if:
 - ◇ It is part of a pharmaco-invasive strategy.
 - ◇ Has high risk features requiring early intervention.
 - Managed at the spoke hospital if the patient has low risk features.

I,A

Key Messages #5:

The objective of a STEMI network is to link non PCI-capable centres to PCI-capable centres with the aim of providing PCI services in a timely manner for patients:

- With STEMI
- Who have been given fibrinolytic therapy and:
 - ◆ have failed reperfusion or,
 - ◆ as part of a pharmaco-invasive strategy or,
 - ◆ have high risk features requiring early intervention.
- The optimal treatment of these patients should be based on the implementation of networks between hospitals ('hub' and 'spoke') with various levels of technology, linked by an efficient ambulance service.



6. IN-HOSPITAL MANAGEMENT

Early management of STEMI is directed at:

- Pain relief.
- Establishing early reperfusion
- Treatment of complications.

6.1 Initial recognition and management

When the patient with suspected STEMI reaches the emergency department, evaluation and initial management should be prompt (**FAST TRACK - RED ZONE**) because the benefits of reperfusion therapy are greater the earlier it is instituted.⁶¹⁻⁶⁵

- A quick targeted history should be taken, and vital signs noted. The diagnosis should be confirmed with an ECG, which should be done as soon as possible, within 10 minutes of the patient's arrival in the emergency department.^{66,67}
- In patients suspected of having a STEMI in view of the prolonged ischaemic-type chest pain of > 30 minutes but without obvious ST elevation seen in the resting ECG, the following steps may be taken: (Section 3.1 and 3.2, pg 45-49 and Table 6, pg 48)
 - ◆ repeating the ECG at 15-minute intervals to detect evolving changes of STEMI.
 - ◆ the use of additional chest leads may be helpful in detecting STEMI at uncommon and difficult to detect sites:
 - Additional posterior chest wall leads (V7-V9) can detect a posterior MI (circumflex occlusion).⁶⁸⁻⁷²
 - Right precordial leads (V3R and V4R) may be necessary to identify concomitant Right Ventricular (RV) infarction in the presence of an inferior wall MI.^{69,71,73}
- A missed STEMI carries a poorer prognosis because of the missed opportunity for reperfusion and myocardial salvage.⁷²

THUS, EARLY DIAGNOSIS AND PROMPT TREATMENT OF STEMI IS VITAL.

- Continuous ECG monitoring using a monitor with defibrillation capacity should be commenced as soon as the diagnosis of STEMI is made.⁷⁴
- Pain should be relieved with titrated IV morphine at 2-5 mg by slow bolus injection every 5-15 minutes as necessary. Watch for adverse events – hypotension and respiratory depression. Antiemetic (IV metoclopramide 10 mg or promethazine 25 mg) should be given with morphine and 8-hourly as necessary.
- Venous access established and blood taken for cardiac biomarkers (CKMB), full blood count, renal profile, glucose and lipid profile. A baseline lipid profile can help guide the dose of high dose statin to be administered. Preferably two IV lines should be set up.
- Intramuscular injections and NSAIDs should be avoided.



- The patient's suitability for reperfusion by either fibrinolytic therapy or primary PCI should be quickly assessed.
- The following should be done immediately and concomitantly in the emergency department (See Flow Chart 1, pg 33):
 - ◆ Assessment and stabilisation of the patient's haemodynamics.
 - ◆ One dose of sublingual GTN by tablet or spray if chest pain persists (avoid if SBP < 90 mmHg).
 - ◆ 300 mg of soluble or chewable aspirin if not given earlier.^{38,39}
 - ◆ Clopidogrel at a dose of 300 mg should be given, if not given earlier.^{41,42}
 - ◆ Alternatively, the following may be given as loading doses if primary PCI is being considered:
 - 300-600 mg of clopidogrel^{40,75}
 - 180 mg of ticagrelor^{76,77}
 - ◆ Oxygen is administered in patients with hypoxaemia (SpO₂ < 95% or PaO₂ < 60 mmHg). Routine oxygen is not recommended in patients with SpO₂ ≥ 95%.⁷⁸⁻⁸⁰

I,C

I,C

I,A

I,A

IIa,B

I,B

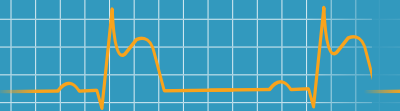
I,B

Key Message #6:

- Early management of STEMI is directed at:
 - ◆ Pain relief.
 - ◆ Establishing early reperfusion.
 - ◆ Treatment of complications.

Key Recommendation 4:

- "Time is muscle" - Every patient with STEMI should have the occluded artery reopened (reperfusion therapy) as soon as possible after the onset of symptoms.
- Reperfusion therapy is indicated in all patients with symptoms of ischaemia of <12 hours duration and persistent ST-segment elevation.



7. REPERFUSION STRATEGIES

A patient's immediate and long-term prognosis following STEMI can be predicted by using the:

- Thrombolysis in Myocardial Infarction (TIMI) STEMI risk score⁸¹ (Appendix III, pg 120) - This was specifically developed for patients with STEMI **or**
- GRACE risk score (Appendix IV, pg 121-122).^{82,83} -this predicts in-hospital and 6-month mortality in patients with ACS.

I,C Risk assessment is a continuous process that should be repeated throughout hospitalisation and at the time of discharge.

The appropriate and timely use of some form of reperfusion therapy is more important than the choice of therapy.

I,A Early and prompt reperfusion is crucial as **TIME LOST** is equivalent to **MYOCARDIUM LOST**.^{62,84,85}

I,A Primary PCI is superior to fibrinolytic therapy as a reperfusion strategy.⁴⁹⁻⁵¹

I,A However, in patients who present within 3 hours of symptom onset and are at low-risk, both treatment strategies appear to have similar benefits.^{86,87}

Generally, in most of our hospitals, fibrinolytic therapy is more readily available and constitutes the main reperfusion strategy.

If both choices are available, the reperfusion strategy of choice is still primary PCI if it can be done in a timely manner by experienced operators in PCI capable centres.

The following factors are important considerations:

- Time from symptom onset to FMC.
- Time to PCI (time from hospital arrival to wire crossing i.e. Door to Balloon (Device) time- DBT/DDT).
- Time to hospital fibrinolysis (time from hospital arrival to administration of fibrinolytic therapy i.e. DNT).
- Contraindications to fibrinolytic therapy.
- High-risk patients.

The best reperfusion strategy will depend upon:

A. Time from onset of symptoms to STEMI Diagnosis

• Early presentation (within 3 hours of symptom onset)

If both treatment options are readily available, they have been shown to be equally effective except for the following situations where primary PCI is the preferred strategy:^{86,87}

- ◆ Fibrinolytic therapy is contraindicated.
- ◆ In high-risk patients.
- ◆ PCI time delay (DBT minus (-) DNT) is more than 60 minutes.⁸⁸

• Late presentation (3 to 12 hours of symptom onset)

◆ Primary PCI is preferred.¹⁰⁻¹² The STEMI diagnosis to wire crossing should be within 90 minutes if the patient presents at a PCI-capable facility.

◆ If transferred from a centre with no PCI facilities, the STEMI diagnosis to wire crossing should be less than **≤ 120 minutes** (including transfer delay).⁸⁹ This is made up of:

- DIDO of non PCI-capable hospital (spoke): ≤ 30 minutes.
- Transport time to PCI-capable centre (hub): ≤ 60 minutes.
- Door of PCI-capable centre to wire crossing: ≤ 30 minutes.

◆ If the time delay to primary PCI is longer than > 120minutes, the best option is to give fibrinolytic therapy and make arrangements to transfer the patient to a PCI-capable centre for a pharmaco-invasive strategy.^{65,90-92}

• Very late presentation (> 12 hours)

◆ Both primary PCI and fibrinolytic therapy are not routinely recommended in patients who are asymptomatic and haemodynamically stable.^{93,94}

◆ However, reperfusion therapy would still be beneficial in patients with persistent ischaemic symptoms, hemodynamic or electrical instability. In this subgroup, primary PCI is the preferred strategy.

B. Contraindications to fibrinolytic therapy

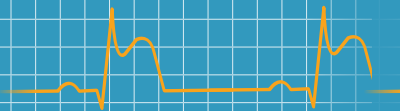
Absolute contraindications

• Risk of intracranial haemorrhage

- ◆ History of intracranial bleed.
- ◆ History of ischaemic stroke within 3 months.
- ◆ Known structural cerebral vascular lesion (e.g. arteriovenous malformation).
- ◆ Known intracranial neoplasm.

• Risk of bleeding

- ◆ Active bleeding or bleeding diathesis (excluding menses).
- ◆ Significant head trauma within 3 months.
- ◆ Suspected aortic dissection.



Relative contraindications

- Risk of intracranial haemorrhage
 - ◆ Severe uncontrolled hypertension on presentation (blood pressure (BP) > 180/110 mmHg)*.
 - ◆ Ischaemic stroke more than 3 months.
 - ◆ History of chronic, severe uncontrolled hypertension.
- Risk of bleeding
 - ◆ Current use of anticoagulant in therapeutic doses [International Normalised Ratio (INR) > 2] or direct oral anticoagulant (DOAC).
 - ◆ Recent major surgery < 3 weeks.
 - ◆ Traumatic or prolonged CPR > 10 minutes.
 - ◆ Recent internal bleeding (e.g. gastrointestinal or urinary tract haemorrhage) within 4 weeks.
 - ◆ Non-compressible vascular puncture.
 - ◆ Active peptic ulcer.
- Others
 - ◆ Pregnancy.
 - ◆ Prior exposure (> 5 days and within 12 months of first usage) to streptokinase (if planning to use same agent).⁹⁵

* The BP should be reduced prior to institution of fibrinolytic therapy

C. High-risk patients

High-risk patients include those with:

- Large infarcts.
- Anterior infarcts.
- Hypotension and cardiogenic shock.
- Significant arrhythmias.
- Elderly patients.
- Post-revascularization (post-CABG and post-PCI).
- Post-infarct angina.

Primary PCI is the preferred strategy in patients in Category B who have contraindications to fibrinolytic therapy and those in Category C, the high risk patients.⁹⁶⁻⁹⁸

Ia,A

Primary PCI is more cost-effective than thrombolysis-based care and should become the treatment of choice for all STEMI patients provided it could be delivered 'in a timely fashion'.

Ia,A

Patients presenting with ischaemic type chest pains > 30 minutes and continuing to have chest pains but with a non-interpretable ST-segment on the ECG, such as

those with bundle branch block or ventricular pacing, may be considered for a PCI strategy if resources are available.^{99,100}

III,C These patients should not be given fibrinolysis.

7.1. Fibrinolytic therapy

I,A Fibrinolytic therapy (FT) has been shown to reduce mortality when given within the appropriate time frame.^{62,101} When given within 2 hours from time of onset of symptoms (the “golden hour”), it is most beneficial and has been shown to be able to abort the infarction and reduce mortality by up to 50%.^{62,87,102,103}

In the **golden hour**, when symptom duration is within 1 to 2 hours, **prompt FT** may provide clinical benefit compared with primary PCI and should be considered as a potentially preferable option.

I,A When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis. If it is diagnosed in prehospital settings by PHC in a well- equipped ambulance, fibrinolytic therapy should preferably be initiated pre-hospital while awaiting transfer to a hospital.^{43,87,104,105}

The DNT should be within 30 minutes.^{62,84} Strategies should be put in place to achieve this target. Fibrinolytic therapy should be made available in all hospitals and there should be protocols to initiate it in the emergency department.

I,A Pre-hospital fibrinolytic therapy has been shown to achieve faster reperfusion.^{86,87}

7.1.1 Indications

Fibrinolytic therapy should only be given to patients with STEMI. (Section 3.1 and 3.2 pg 45-49)

III,A It has no role and may even be detrimental in patients with NSTEMI.^{106,107}

7.1.2 Contraindications

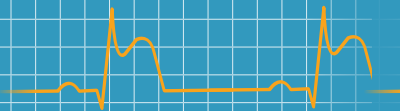
See section 7 (B), pg 63-64.

7.1.3 Choice of fibrinolytic agent

Presently the agents available in Malaysia are:

Streptokinase

IIa,A This is the most widely used agent. It is not fibrin specific and it results in a lower patency rate of the occluded vessel at 60 minutes than fibrin specific agents.¹⁰⁸⁻¹¹⁰ Despite having a lower risk of intracranial haemorrhage, the reduction in mortality is less than with fibrin specific agents.^{108,111}



Streptokinase is antigenic and promotes the production of antibodies. Thus the utilization of this agent for reinfarction is less effective if given between 3 days and 1 or even 4 years after the first administration.⁹⁵ Primary PCI or fibrin specific agents should then be considered.

Regimen:

1.5 mega units in 100 ml normal saline or 5% dextrose over 1 hour.

Fibrin Specific Agents

I,B A fibrin-specific agent such as tenecteplase (TNK-tPA) is recommended.^{112,113}

The benefit of using TNK-tPA is that it causes more rapid reperfusion of the occluded artery than streptokinase and is given as a single bolus dose.^{112,113}

This is a weight-based regimen and thus there is a risk of bleeding if the weight has been overestimated.

Regimen:

TNK-tPA

BODY WEIGHT	SINGLE IV BOLUS OVER 5 SECS	VOLUME TNK TO BE ADMINISTERED
< 60 kg	30 mg	6
60 to < 70 kg	35 mg	7
70 to < 80 kg	40 mg	8
80 to < 90 kg	45 mg	9
> 90 kg	50 mg	10

I,B In patients \geq 75 years of age, the dose should be reduced by 50%.¹¹³

Following administration of a fibrin specific agent, anticoagulant is recommended with:

- I,A** • Heparin;¹¹² or
- IIa,A** • Enoxaparin.^{113,114}

Either one of these agents should be given immediately after the completion of fibrinolysis and continued for at least 48 hours.

IIa,B Subcutaneous (s.c.) fondaparinux 2.5 mg daily may be given as an alternative for 8 days or until discharge.¹¹⁵

7.1.4 Fibrinolysis in Unstable Patients

Ideally, these patients should be transferred for primary PCI. If this cannot be done in a timely manner or the patient is too unstable for transfer, they should be considered for fibrinolysis and then transferred for early PCI when stable.

7.1.4.1 Presence of Hypotension at Presentation (SBP < 90mmHg)

Hypotension may be due to:

- Relative hypovolaemia.
- RV infarction.
- Acute LV failure.

These patients should be:

- Given IV fluids as necessary.
- Started on inotropes, preferably noradrenaline.¹¹⁶⁻¹¹⁸

Fibrinolytic therapy with a fibrin specific agent is preferred.

7.1.4.2 Hypotension during Fibrinolysis

If blood pressure drops during infusion of the fibrinolytic agent, administer fluids or start noradrenaline. When the SBP >90mmHg, fibrinolysis can be given concomitantly.

7.1.4.3 Presence of LV Failure

These patients should be treated with oxygen, non-invasive positive pressure ventilation, high flow nasal cannula or intubation and ventilation as necessary.

Diuretics should be given intravenously.

Fibrinolytic therapy with a fibrin specific agent should then be administered.

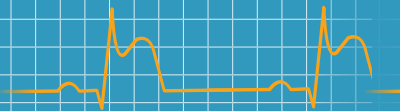
7.1.4.4 Presence of Cardiac Arrest

If the ECG shows STEMI, fibrinolysis with a fibrin specific agent may be considered.

7.1.5 Indicators of successful reperfusion

There is no sensitive bedside clinical method to reliably detect successful reperfusion. Some useful guides are:

- Resolution of chest pain (may be confounded by the use of narcotic analgesics).
- Early return of ST segment elevation to isoelectric line or a decrease in the height of the ST elevation by 50% (in the lead that records the highest ST elevation) within 60-90 minutes of initiation of fibrinolytic therapy.¹¹⁹
- Early peaking of CK and CK-MB levels.
- Restoration and/or maintenance of haemodynamic and/or electrical stability.



The occurrence of 'reperfusion arrhythmias' is not a reliable indicator of successful reperfusion. An exception is accelerated idioventricular rhythm and sudden sinus bradycardia which have been correlated with a patent infarct-related coronary artery after fibrinolytic therapy or primary PCI.¹¹⁹

7.1.6 Failed fibrinolysis

Failure of fibrinolytic agents to open the occluded infarct related artery (IRA) is manifested as continuing chest pain, persistent ST segment elevation and haemodynamic instability. These patients are more likely to develop complications such as heart failure and arrhythmias.

I,A The treatment of choice for these patients is rescue PCI.^{120,121}

III,B They should not be given a second dose of a fibrinolytic agent. This is because there has been no difference in event free survival demonstrated whether these patients are given a repeat dose of a fibrinolytic agent or are treated conservatively.¹²²

7.2 Percutaneous Coronary Intervention (PCI)

7.2.1 Primary PCI

I,A Primary PCI is the preferred reperfusion strategy in patients with ischaemic symptoms < 12 hours when it can be performed in a timely manner and promptly by experienced operators in centres performing a sufficient number of primary PCI procedures.^{49-51,89}

7.2.1.1 Transfer of patient

Transfer of patients with STEMI to PCI-capable centres should be considered in the following situations:

- I,A • Onset of ischaemic symptoms < 12 hours and fibrinolytic therapy is contraindicated irrespective of time delay from FMC.^{123,124}
- I,A • Cardiogenic shock irrespective of time delay.^{96,125}
- STEMI presenting with acute HF. These patients should be stabilised rapidly and ventilated if necessary. Options include:
 - I,C ♦ Transfer for primary PCI or
 - I,A ♦ Give fibrinolytic therapy and transfer the patient within 24 hours for a pharmacoinvasive strategy.^{90,91,113,114}
- I,A • When symptoms have been present between 3 and 12 hours and PCI can be performed within 120 minutes (preferably 90 minutes).^{59,89,126,127}
- I,C • When transferred from a non PCI-capable hospital to a PCI-capable hospital, the DIDO time should be < **30 minutes** and transfer time should be < **60 minutes**.
- I,A • Failed fibrinolytic therapy or re-occlusion post-fibrinolysis (see Failed Fibrinolysis, section 7.1.6, pg 68).^{89,120-122,128}

I,A

- As part of a pharmaco-invasive strategy in stable patients who have been given fibrinolytics and an elective PCI can be performed within 3 and 24 hours.^{90,91,113,114,129-132}

7.2.2 PCI post-fibrinolysis or patients who did not receive fibrinolysis

Following fibrinolysis, or in patients who did not receive fibrinolysis, early PCI, preferably during the index hospitalisation, should be considered in the following situations:

I,A

- Failed reperfusion or re-occlusion after fibrinolytic therapy.¹²⁰⁻¹²²

I,A

- Cardiogenic shock or acute pulmonary oedema that develops after initial presentation.^{96,97,125,133}

I,A

- Stable patients within 3-24 hours post-fibrinolysis as part of a pharmaco-invasive strategy.^{90,91,113,114,129-132}

I,C

- STEMI TIMI risk score of ≥ 6.0 at admission.⁸² (see Appendix III, pg 120)

I,C

- Spontaneous or easily provoked myocardial ischaemia such as recurrence of chest pains and/or dynamic ECG changes.^{134,135}

I,C

- If symptoms are completely relieved and ST segment completely normalises either spontaneously or after GTN or antiplatelet therapy.

Failed fibrinolytic therapy is manifested as one or more of the following:

- Ongoing chest pains.
- Persistent hyper-acute ECG changes ($< 50\%$ resolution of ST elevation in the lead showing the greatest degree of ST elevation at presentation).¹¹⁹
- Haemodynamic and electrical instability.

Rescue PCI is initiated very early (1 to 2 hours) after failed fibrinolytic therapy.

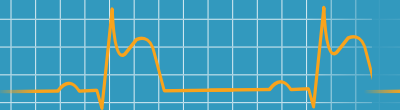
It is associated with a reduction in HF, reinfarction and a trend towards reduction in mortality but with increased risk of bleeding and stroke. Hence, these patients should be individually evaluated.^{121,122}

7.2.3 Facilitated PCI

This refers to a strategy of planned immediate PCI (< 1 hour) after an initial pharmacologic regimen consisting of a reduced dose of a fibrinolytic agent, glycoprotein (GP) IIb/IIIa inhibitor or a combination of these agents. The purpose of facilitated PCI was to achieve earlier reperfusion but retain the benefits of primary PCI.

III,A

This strategy was associated with increased mortality and major bleeding. It is thus **not recommended**.¹³⁶⁻¹³⁸



7.2.4 Routine angiography and PCI after thrombolysis (pharmacoinvasive therapy)

This refers to stable patients routinely undergoing angiography and PCI between 3-24 hours after fibrinolysis, irrespective of the absence or presence of ongoing myocardial ischaemia and reperfusion status.

I,A

Given the advances in PCI and antithrombotic therapy, recent studies show that routine angiography with the intent to perform PCI with stenting between 3 and 24 hours after fibrinolysis improved patient outcomes as compared to symptom or ischaemia guided delayed intervention. This strategy has resulted in a significant reduction in mortality and reinfarction rates without an increase in adverse events.^{114,126,139-141}

I,A

All patients who have been given fibrinolytic therapy should be considered for a strategy of early PCI between 3-24 hours after fibrinolysis wherever possible.^{90,91, 113,114,129-132,139-141}

7.2.5 Delayed Angiography and PCI -Symptom onset >12h

I,B

A primary PCI strategy is indicated in the presence of ongoing symptoms suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias.¹⁴²

III,A

In asymptomatic patients, routine PCI of an occluded IRA > 48h after onset of STEMI is not indicated.^{143,144}

7.2.6 Delayed selective angiography and PCI

Patients with STEMI who have not had coronary angiography within 24 hours should be considered for delayed selective angiography. This refers to a strategy of doing angiography and PCI only if there is spontaneous or inducible ischaemia.

Stable patients who are not at high risk (Section 7 (C); pg 64) and who did not undergo early (<24 hours) angiography should undergo non-invasive ischaemia testing.

I,A

If spontaneous or inducible ischaemia is present, then angiography and appropriate revascularization should be performed.^{134,135}

7.3. Technical considerations and pharmacotherapy during primary PCI

For a favourable outcome, it is important to obtain good TIMI 3 epicardial flow as well as optimum reperfusion of the myocardial microvasculature^{145,146} (TIMI myocardial perfusion grade – TMP) (Refer to the Malaysian CPG on the Management of Percutaneous Coronary intervention (PCI) ,1st Ed 2009).

7.3.1 Antiplatelet therapy to support primary PCI for STEMI

- I,A • Oral aspirin 300 mg should be given before primary PCI.
- I,A • In addition, a P2Y₁₂ receptor inhibitor should also be given:
 - I,B ♦ Clopidogrel 300-600 mg loading dose to be given as early as possible^{40,75,147}, **or**
 - I,B ♦ Prasugrel 60 mg loading dose to be given after the coronary angiogram has been performed¹⁴⁸ **or**
 - I,B ♦ Ticagrelor 180 mg loading dose to be given as early as possible.^{76,77}
- GP IIb/IIIa inhibitors may be considered in selected patients with IC thrombus:
 - IIa,B ♦ Abciximab.¹⁴⁹⁻¹⁵²
 - IIa,B ♦ Tirofiban.¹⁵³⁻¹⁵⁵

7.3.2 Antithrombotic therapy to support primary PCI for STEMI

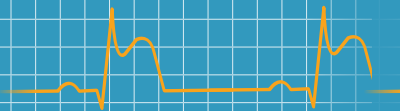
- IV unfractionated heparin (UFH) with additional bolus to maintain activated clotting time (ACT) above 275 secs.¹⁵⁶
- IV low molecular weight heparin (LMWH) – enoxaparin.¹⁵⁷
- IV fondaparinux is not recommended because of the risk of catheter thrombosis.¹¹⁵
- Bivalirudin infusion.

7.3.3 PCI access site

- I,A • Radial access is recommended over femoral access if performed by an experienced radial operator.¹⁵⁸⁻¹⁶⁴
- Radial access has the advantage of reducing bleeding complications. However, when larger devices are necessary and the use of intra-aortic balloon pump (IABP) is anticipated, femoral access may be preferable.
- A recent study, however, showed that bleeding rates and 30-day mortality following PCI for STEMI were no different between radial and femoral approaches.¹⁶⁵

7.3.4 Technical tips during procedure

- I,A • Primary PCI should be performed on the IRA.
- IIb,B • Complete revascularization should not be routinely attempted on critical lesions in non-culprit vessels in the same procedure when patient is in cardiogenic shock.¹⁶⁶⁻¹⁷⁶
- I,A • PCI is indicated in a non-infarct artery at a later time when there is evidence of myocardial ischaemia or Fractional Flow Reserve < 0.8.^{134,135,166}
- I,A • Stenting is recommended (over balloon angioplasty) for primary PCI.¹⁷⁶
- I,A • Stenting with new-generation DES is recommended over BMS for primary PCI.¹⁷⁷⁻¹⁸⁰ Despite higher total costs relative to BMS, DES appeared to be a cost-effective strategy.^{181,182}



7.3.5 Distal embolisation and the use of adjunctive devices and pharmacotherapy

Thrombus burden is usually large if the patient presents late or the IRA is ectatic. Predictors of slow flow and no-reflow (TIMI 0) of the IRA are:^{183,184}

- Vessel diameter ≥ 3.5 mm.
- Treatment of the right coronary artery.
- Higher TIMI thrombus score.
- Angiographic findings such as:
 - ◆ “Cut-off” sign (i.e. abrupt occlusion of the epicardial vessel) seen on the coronary angiogram.
 - ◆ Persistent contrast stasis just proximal and/or distal to the obstruction.
 - ◆ Longer lesions.
 - ◆ Thrombus of > 5 mm proximal to occlusion.
 - ◆ Floating thrombus.

The following steps can be taken to prevent distal embolization:

III.A

- Aspiration catheter - Routine use of thrombus aspiration is not recommended.^{185,186}
- Distal embolic protection - meta-analysis showed that these devices had a neutral effect on mortality.¹⁸⁷
- GP IIb/IIIa inhibitors – abciximab and tirofiban therapy during primary PCI showed short term benefit especially in high-risk patients.^{149-155,188,189} The data on its effect on long-term survival is however conflicting.

7.3.6 Management of no reflow

No reflow (TIMI 0) or slow reflow (TIMI 1 and 2) may occur transiently or may persist after primary PCI.

No-reflow may occur as a consequence of:

- Microvascular dysfunction from vasospasm.
- Distal embolisation.
- Intimal dissection/intramural haematoma.

It is associated with poor recovery of LV function and a higher incidence of post-MI complications.

Management includes:

- IC GTN 100 - 200 μg boluses.
- IC verapamil 100 – 200 μg boluses.
- IC adenosine 100 – 200 μg boluses.
- IC nitroprusside 50 – 100 μg boluses.
- IV nicardipine 100-200 μg boluses

Key Recommendation 5:

- Primary PCI is superior to fibrinolysis for STEMI and should be performed in a timely manner at experienced centres. (see Flow Chart 2, pg 34)

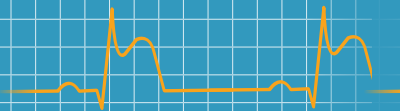
Key Message #7:

Primary PCI is superior to fibrinolysis for STEMI when performed in a timely manner at experienced centres. (see Flow Charts 1 & 2, pg 33 & 34)

- If the patient **presents at a PCI centre**, then the time from FMC (First Medical Contact) to wire crossing should be **≤ 90 minutes**.
- If transferred from **a centre with no PCI facilities**, the time from FMC to wire crossing should be **≤120 minutes** (including transfer delay). This is made up of:
 - ◆ door-in-door-out (DIDO) of non-PCI-capable hospital (spoke): ≤ 30 minutes.
 - ◆ Transport time to PCI -capable centre (hub): ≤ 60 minutes.
 - ◆ Door of PCI capable centre to wire crossing: ≤ 30 minutes.
 - ◆ If the time delay to primary PCI is >120 minutes, the best option is to give fibrinolytic therapy and make arrangements to transfer the patient to a PCI capable centre for a pharmaco-invasive strategy.

Key Recommendation 6:

- When fibrinolytic therapy is administered, the Door to Needle time (DNT) should be ≤ 30 minutes.
- Whenever possible, patients given fibrinolytic therapy should be considered for a pharmaco-invasive approach (elective angiogram within 3-24 hours post fibrinolysis).



8. Cardiac Care Unit (CCU) management

8.1 General measures

All STEMI patients should be admitted to a CCU or equivalent unit equipped with adequate monitoring facilities.

Following successful reperfusion, uncomplicated cases may be kept for a minimum of 24 hours before transfer to a step-down unit. They can sit out of bed and undertake self-care the next day. Patients with STEMI complicated by significant myocardial damage and arrhythmias need longer bed rest and may need to be kept in the CCU longer.

Sedatives may be useful. Titrated IV opioids may be administered to relieve pain.

Use of bedside commode and assisted bedside washing should be safe in most patients.

The Valsalva manoeuvre has been shown to precipitate dangerous haemodynamic and electrocardiographic changes.¹⁹⁰ Prevention of constipation with stool softeners is encouraged.

Early referral for cardiac rehabilitation is advisable.¹⁹¹

8.2 Monitoring

The general condition of the patient, vital signs, pulse oximetry and the cardiac rhythm should be continuously monitored following STEMI.

In general, systolic blood pressure should be > 90mmHg prior to starting ACE-I or β -blockers.

8.3 Concomitant therapy

8.3.1 Oxygen

- Oxygen, via nasal prongs, at 2-4 litres/minute is usually adequate. One should aim to maintain the oxygen saturation > 95%.⁷⁸⁻⁸⁰

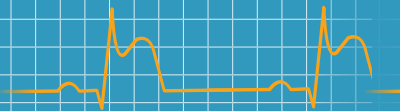
8.3.2 Antiplatelet agents

In STEMI, DAPT is indicated.^{40-42,75-77,192-196} This includes:

- A loading dose of aspirin 300 mg followed by low dose aspirin 75-100 mg daily which is indicated indefinitely after STEMI unless contraindicated.^{40-42,192}
- +
- A P2Y₁₂ inhibitor which could be:
 - ◆ Clopidogrel - **OR**
 - This is indicated as part of both a fibrinolytic as well as a primary PCI strategy.^{40-42,192,193}



- I,A
 - In patients 75 years of age or younger given fibrinolysis, a loading dose of 300 mg may be administered followed by a maintenance dose of 75 mg daily. In older patients, a loading dose of 75 mg may be adequate.^{42,194}
- IIa,B
 - In patients considered for primary PCI, a higher loading dose of 300-600 mg may be necessary.^{40,75,147}
- I,B
 - ◆ Prasugrel – **OR**
 - This has been investigated as part of a primary PCI strategy only.^{148,195,196}
 - The loading dose is 60 mg and it should be given after the coronary angiogram.^{148,195,196} The maintenance dose is 10 mg daily.^{148,195,196}
 - It is not recommended for patients > 75 years old, < 60 kg weight, have a history of TIA or stroke due to a higher risk of major bleeding.^{148,195,196}
- I,B
 - ◆ Ticagrelor
 - This has been investigated as part of a primary PCI strategy only.^{77,197}
 - The loading dose is 180 mg and given early after the diagnosis. The maintenance dose is 90 mg bd.^{77,197}
 - Potential drawback is dyspnoea and transient ventricular pauses during the first week. This was rarely associated with symptoms or need for a pacemaker. Caution should be exercised in patients with heart block.
- IIa,B
 - ◆ Ticlopidine
 - Ticlopidine has not been tested as part of either a fibrinolytic or primary PCI strategy.
 - It may be, however, be considered for secondary prevention.^{198,199}
 - The dose is 250 mg twice daily.
- I,C
 - The duration of DAPT will vary and depend on the patient's risk of future coronary thrombotic events and his bleeding risk.²⁰⁰⁻²⁰² Prolonged DAPT leads to an absolute decrease in stent thrombosis and ischaemic complications of ≈1 to 2% at the cost of an absolute increase in bleeding complications of ≈1%.^{201,202}
 - In East Asians (Japan, South Korea and China), the newer P2Y₁₂ inhibitors had similar efficacy as clopidogrel but at an increased risk of bleeding.²⁰³⁻²⁰⁵
 - Recommendations for duration of DAPT:
 - ◆ Post-fibrinolysis –
 - The duration of dual antiplatelet therapy (DAPT) should be between 1 month to 1 year, the duration being a balance between the ischaemic vs the bleeding risks.^{41,42,192,193}
 - ◆ Post PCI –
 - DAPT for up to a year depending on the thrombotic/ischaemic versus bleeding risks.²⁰²
 - In patients with high bleeding risks, a shorter period of DAPT of 6 months may be considered.²⁰⁰⁻²⁰²
 - Aspirin and ticagrelor 60 mg twice a day for >12 months may be considered for up to 3 years, in high risk patients who have tolerated DAPT without a bleeding complication.²⁰⁶



8.3.3 Antithrombotic therapy

These agents are administered to patients who received fibrinolytic therapy and did not undergo PCI.²⁰⁷⁻²¹⁰ They include: (Table 9, pg 78)

A) Heparin

I,B

- UFH²⁰⁷

I,A

- LMWH - enoxaparin^{207,208}

- ◆ In patients > 75 years of age and with renal impairment (serum creatinine (Scr) > 200 µmol/L in women and > 250 µmol/L in men), UFH is preferable to LMWH.²⁰⁸

B) subcutaneous Anti Xa inhibitors

- fondaparinux^{209,210}

IIa,B

- ◆ May be given to those patients treated medically including those not receiving fibrinolytic therapy.²¹⁰ In STEMI patients not undergoing primary PCI and not receiving fibrinolytic therapy, fondaparinux was shown to reduce mortality and reinfarction without increasing bleeding and stroke rates when compared to UFH or placebo.²¹⁰

III,A

- ◆ It is associated with an increase in catheter-related thrombus and coronary angiographic complications. Thus, fondaparinux is not recommended as the sole anti-coagulant during PCI.¹¹⁵

C) Oral Anticoagulants (OAC)

These include:

- Vitamin K antagonists - Warfarin
- Non-Vitamin K antagonists - Direct Oral Anticoagulants (DOAC)

OACs are prescribed for the following indications:

8.3.3.1. Atrial Fibrillation

8.3.3.2. LV thrombus

8.3.3.1 Atrial Fibrillation (Appendix 5, pg 123 for CHA₂DS₂- VASc SCORE)

IIa,B

In STEMI patients with AF who had undergone PCI, the use of DOAC with antiplatelet therapy is associated with a lower risk of bleeding than the standard triple therapy (DAPT + warfarin).²¹¹⁻²¹³

The following **regimens** may be considered:

1. Warfarin + DAPT

IIa,B

- Triple therapy with aspirin, clopidogrel and vitamin K antagonist (warfarin) may be given, with a target INR in the lower part of the recommended target range (INR: 2)^{214,215}
- The duration of triple therapy depends on the individual risk for ischaemic and bleeding events – between 1-6 months.²¹⁶

- The use of ticagrelor or prasugrel is not recommended as part of triple anti-thrombotic therapy with aspirin and OAC.²¹⁶

2. DOAC + DAPT

Ia,B

- Dabigatran 110 or 150mg twice daily + aspirin <100 mg daily + clopidogrel 75mg once daily for one to six months depending on bleeding risks followed by anti-platelet monotherapy and dabigatran 110 or 150 mg twice daily²¹¹ **or**

Ia,B

- Rivaroxaban 15mg once daily (10mg if CrCl 30-50ml/min) + aspirin + clopidogrel 75mg once daily for one to six months depending on bleeding risks followed by anti-platelet monotherapy and rivaroxaban 15mg once daily.²¹² **or**

Ia,B

- Rivaroxaban 2.5mg twice daily and aspirin 75-100mg once daily and clopidogrel 75mg once daily for one to 12 months.²¹² The duration of DAPT with this combination will depend on the risk of stent thrombosis versus bleeding risk. Rivaroxaban 2.5mg is yet to be registered in Malaysia.

Ia,B

- Apixaban 5 mg bid and clopidogrel 75 mg once daily for 6 months resulted in less bleeding and fewer hospitalisations without significant differences in the incidence of ischaemic events when compared to regimens that included warfarin, aspirin, or both.²¹³

In patients with AF who have undergone PCI, the risks of ischaemic complications (cardioembolic stroke, coronary ischaemic events) must be balanced against the risks of bleeding. In addition, the clinical setting (elderly, women, kidney disease etc) as well as the angiographic complexity of the PCI should also be considered in the choice of anti-thrombotic regimen.²¹⁷

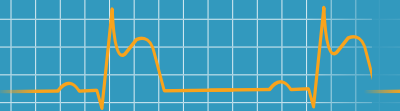
In patients with a low risk of thrombotic events or a high risk of bleeding, early omission of aspirin therapy and treatment with a DOAC plus clopidogrel is entirely warranted. However, in patients undergoing complex, multivessel, or high-risk PCI or in those presenting with high-risk STEMI, aspirin should probably not be routinely omitted for at least several weeks or longer, depending on bleeding risk.²¹⁷

Ia,B

In patients who have been stable (> 1-year post STEMI and post PCI/stent), warfarin or DOAC monotherapy should be used and concomitant anti-platelet therapy should not be prescribed on a routine basis.²¹⁶

Ib,B

Combination of OAC plus single anti-platelet therapy (preferably clopidogrel 75 mg once a day, or as an alternative, aspirin 75–100 mg once a day) may be sometimes continued in very selected cases, e.g. stenting of the left main, proximal left anterior descending, proximal bifurcation, recurrent MIs, etc.²¹⁶



8.3.3.2 LV Thrombus

In patients with LV thrombus demonstrated by echocardiography following a recent MI:

- Warfarin may be considered in addition to DAPT for at least 3 months in patients:
 - ◆ With non-ischaemic stroke or TIA²¹⁸
 - ◆ Without prior stroke or TIA
- In patients with high risk of bleeding, warfarin plus anti-platelet monotherapy may be considered.
- In patients with haemorrhagic stroke, warfarin and antiplatelet therapy are contraindicated.

I,C

IIa,C

IIb,C

III,C

Table 9: Recommended dosages of anti-thrombotics in STEMI

Heparin	Dosage	Duration of therapy
Enoxaparin	< 75 years: 30 mg IV bolus followed by sc 1.0 mg/kg bd	8 days or until hospital discharge
	≥ 75 years: No bolus, sc 0.75 mg/kg bd	
UFH	60 U/kg i.v. bolus (max 4000 U)	48 hours
	i.v. infusion 12 U/kg/h (max 1000 U/h) – to maintain an activated partial thromboplastin time (APTT) of 1.5 – 2.5 x control	
Fondaparinux	sc 2.5 mg once daily	8 days or until hospital discharge

sc: subcutaneous

8.3.4 β-blockers (Table 10, pg 79)

- The benefit of long-term treatment with β-blockers after STEMI is well established from clinical trials conducted in the pre-thrombolytic era.²¹⁹
- Initiation of a β-blocker immediately after STEMI, especially when it is associated with LV systolic dysfunction, reduces the rate of hospitalisation for HF and mortality.²²⁰
- Oral treatment with β-blockers is recommended in patients with heart failure and/or LV systolic dysfunction, unless contraindicated.²²⁰⁻²²⁴ β-blockers may be initiated when patients are haemodynamically stable.
- Routine oral treatment with β-blockers should be considered during hospitalisation and continued thereafter in all patients without contraindications.²²⁵⁻²²⁹

I,A

I,A

I,A

- Contraindications to β -blockers:
 - ◆ Bradycardia < 60 beats per minute.
 - ◆ SBP < 100 mmHg.
 - ◆ Pulmonary congestion with crepitations beyond the lung bases.
 - ◆ Signs of peripheral hypoperfusion.
 - ◆ Second or third degree atrio-ventricular (AV) block.

Table 10: Recommended dosages of β -blockers in STEMI

TYPE	INITIATION DOSE	TARGET DOSE
Metoprolol	25 mg bd	100 mg bd
Carvedilol	3.125 mg bd	25 mg bd
Bisoprolol	1.25 mg od	10 mg od

8.3.5 ACE-Is and ARBs (Table 11, pg 80)

ACE-Is are indicated starting within the first 24 hours of STEMI in all patients especially the high-risk patients (LVEF \leq 40% or with evidence of heart failure, diabetes or an anterior infarct). In these high risk patients, it should be continued indefinitely if there are no contraindications.²³⁰⁻²³⁵

I,A

Contraindications to ACE-I and ARB therapy;

- SBP < 100 mmHg
- Established contraindications e.g. bilateral renal artery stenosis.

The dose of ACE-I/ARB should be reduced or stopped if there is:

- An increase in Scr of \geq 30% from baseline within 2 weeks after initiation.²³⁶
- Persistent hyperkalaemia (> 5.6 mmol/L).

I,B

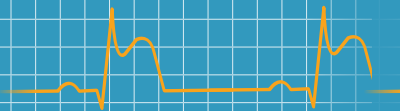
In ACE-I intolerant patients, an ARB may be used preferably valsartan.^{237,238}

8.3.6 Mineralocorticoid receptor antagonists

Mineralocorticoid antagonists, e.g. eplerenone should be considered in patients post MI with LVEF \leq 40% and HF in the absence of renal failure or hyperkalaemia.^{239,240}

I,B

Spironolactone has been mainly studied in patients with heart failure although there has been a small study in STEMI.²⁴¹ In this study in post STEMI patients, early spironolactone administration failed to show benefit.²⁴¹



8.3.7 Statins

I,A

- High-intensity statin therapy (atorvastatin 40-80mg daily or rosuvastatin 20-40mg daily) should be initiated as early as possible in patients with STEMI who do not have contraindications or history of intolerance, regardless of initial cholesterol values and continued indefinitely.²⁴²⁻²⁴⁵
- Target LDL-C should be <1.8mmol/L or a reduction of at least 50% from the baseline, the lower the better.^{243,246,247}
- Addition of non-statin therapy to reduce LDL-C should be considered in patients who remain at high risk with LDL-C \geq 1.8mmol/L despite the maximum tolerated statin dose.²⁴⁸⁻²⁵⁰
- High loading or re-loading dose of statins have been shown to be beneficial in preventing peri-procedural MI in ACS patients undergoing PCI.²⁵¹⁻²⁵⁵

I,A

I,A

I,A

Combination therapy consisting of aspirin, ACE-I, a β -blocker, and a statin is cost-effective therapy even in the absence of a poly pill.^{256,257}

Table 11: Recommended dosages of ACE-Is and ARBs in STEMI

TYPE	INITIATION DOSE	TARGET DOSE
Captopril	6.25 mg bd – tds	25 – 50 mg tds
Ramipril	2.5 mg bd	10 mg od
Enalapril	2.5 – 5 mg od	10 mg od
Lisinopril	5 mg od	10 mg od
Perindopril	2 mg od	8-10 mg od
Valsartan	40 mg – 80 mg od	160 mg bd

8.3.8. Nitrates (Table 12, pg 81)

III,C

I,C

- Oral nitrates are not routinely recommended.
- Nitrates can be considered in patients with:
 - ◆ Continuing chest pain and / or ischaemia.
 - ◆ HF
 - ◆ Hypertension
- In the acute stage, IV nitrates are recommended because of their rapid onset of action, ease of titration and potential for prompt termination in the event of side effects. After the first 48 hours, oral or topical nitrates may be continued in patients with persisting ischaemia and/or HF.
- Contraindications to nitrate therapy:
 - ◆ Hypotension (SBP < 90 mmHg).
 - ◆ RV infarction
 - ◆ History of phospho-diesterase 5 inhibitor ingestion depending upon the half-life of the agent.

IIa,B

- Oral nitrates have a role in improving symptoms and exercise tolerance in patients who continue to have angina. Despite this, it has not been shown to improve long term cardiac outcomes.²⁵⁸⁻²⁶¹

I,B

- In patients who continue to have angina, sublingual GTN as tablet or spray may be used as prophylaxis before engaging in activities known to cause angina.²⁵⁸⁻²⁶¹

Table 12: Recommended doses of nitrates

COMPOUND	ROUTE	DOSAGE	Time of Onset
Nitroglycerine, GTN	IV	5 – 200 µg/minute*	1 minute
	Sublingual GTN tablet	0.5 mg, can repeat up to 3 times at 5-minute intervals	2 minutes
	Sublingual GTN spray	1-2 sprays, more than 3 sprays at 15-minute intervals (400 mcg/dose)	2 minutes
	Transdermal patch	5-10 mg over 12 hours on, then 12 hours off	1 - 2 hours
Isosorbide dinitrate	IV	1.25 – 5 mg/hour	1 minute
	Transdermal patch	2.5 – 10 mg	3 - 4 minutes
	Oral	10 – 20 mg, bd/tds	30-60 minutes
Isosorbide mononitrate extended release	Oral	30-60 mg, od	60 minutes

*The dose of IV nitrates should be titrated every 5 - 10 minutes until symptoms and/or ischaemia is relieved and the desired haemodynamic response is obtained.

8.3.9. Calcium channel blockers (CCB)

IIb,B

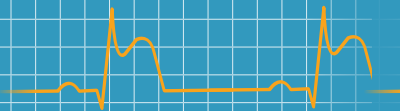
- There is no data to support the routine use of calcium channel blockers post-STEMI.²⁶²

IIa,B

- In patients who continue to have angina, CCBs in combination with β-blockers have been shown to be more effective than monotherapy in the relief of angina.²⁶²

IIa,B

- In those with contraindications to β-blockers, particularly in the presence of obstructive airway disease, CCBs such as verapamil or diltiazem may be considered.^{259,262}



- Despite providing symptom relief, CCBs have not been shown to improve long term cardiac outcomes.^{259,262}

8.3.10 Others

IIIa,B

- Trimetazidine (3-Ketoacyl CoA thiolase [KAT] inhibitor) and Ivabradine (If inhibitor) have been shown to be beneficial in patients post STEMI in registry data and in small studies.²⁶³⁻²⁶⁶

- Hormone replacement therapy (HRT) –

- ◆ Registry data showed that the risk of MI was highest in women with continuous regimens and in younger ages with longer duration of use.^{267,268}

- ◆ No certain conclusions can be drawn from the continued use of HRT after an MI.²⁶⁸

III,A

- ◆ It is not beneficial for secondary prevention.^{269,270}

III,A

- Vitamin E and antioxidants have no clinical benefit.²⁷¹⁻²⁷⁴

III,A

- Garlic, lecithin, Vitamin A and C are not beneficial.²⁷⁴

III,A

- Omega-3 fatty acids – The initial open label study indicated that these were beneficial but subsequent studies have been negative.²⁷⁵⁻²⁷⁷

Key Recommendation 7:

- All patients with STEMI receiving **fibrinolytic therapy** should receive:

- ◆ 300 mg aspirin

- + **(Plus) loading dose**

- 75 mg of clopidogrel (> 75 years of age) **or**

- 300 mg clopidogrel (≤ 75 years of age)

- ◆ followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily. The duration of dual antiplatelet therapy (DAPT) should be between 1 month to 1 year, the duration being a balance between the ischaemic vs the bleeding risks.

- All patients with STEMI undergoing **Primary PCI** should receive loading doses of:

- ◆ 300 mg aspirin

- + **(Plus)**

- 300-600 mg clopidogrel **or**

- 180 mg ticagrelor **or**

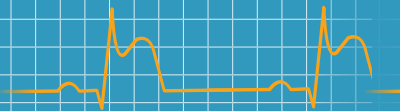
- 60 mg prasugrel (after the coronary angiogram)

- ◆ This is followed by a maintenance dose of 75-150 mg daily of aspirin long-term and 75 mg of clopidogrel daily or 90 mg twice daily ticagrelor or 10 mg prasugrel daily.

- ◆ Patients who underwent PCI require DAPT for up to a year depending on the thrombotic/ischaemic versus bleeding risks. In patients with high bleeding risks, a shorter period of DAPT of 6 months may be considered.

Key Recommendation 8:

- All patients with STEMI should receive medications that have been shown to improve survival if given early. These include:
 - ◆ ACE-Is
 - ◆ ARBs if ACE-I intolerant
 - ◆ β -blockers
 - ◆ Mineralocorticoid Receptor Antagonists (MRA)
 - ◆ High dose statins.



9. Complications of STEMI

These are:

- Arrhythmias.
- LV dysfunction and shock.
- Mechanical complications.
- RV infarction.
- Others e.g. pericarditis.

9.1 Arrhythmias

These include:

A. Tachyarrhythmias

• **Pulseless ventricular tachyarrhythmias**

This is either pulseless ventricular tachycardia (VT) or ventricular fibrillation (VF). Defibrillate immediately. Early VF occurs within the first 48 hours and is due to electrical instability. Late VF is associated with large infarcts and poor pump function and carries a poor prognosis (refer to algorithm 1, page 114).

• **Ventricular tachycardia (VT)**

VT in the setting of STEMI may arise from either ischaemia (usually within 48 hours) or from a myocardial scar due to the infarct (late onset). Treatment of ischaemia may result in the termination of the tachycardia (refer to algorithm 2, page 115).

• **Ventricular premature contractions (VPC)**

These are often benign and do not require treatment. Correct underlying ischaemia, hypoxia and electrolyte disturbances.

• **Accelerated idioventricular rhythm**

These do not require any treatment. This is a sign suggestive of successful reperfusion.

• **Atrial fibrillation (AF)**

This is more commonly seen in the elderly and is associated with large infarcts. It denotes a poorer prognosis and carries an increased risk of thromboembolism (refer to algorithm 3, page 116).

B. Bradyarrhythmias

These are:

• **Sinus bradycardia**

This does not require treatment unless associated with symptoms and/or hypotension.

- **Atrio-ventricular (AV) block**

- ◆ First degree and second degree type 1 (Mobitz 1) do not need treatment. Patients with second degree type 2 (Mobitz 2) and complete AV block may not require treatment if haemodynamically stable. If unstable, urgent temporary pacing is necessary. Atropine may be given in the interim (maximum 3 mg) (refer to algorithm 4, page 117).
- ◆ Patients with anterior infarcts who develop second degree (Mobitz 2) and complete AV block carry a worse prognosis. Even if haemodynamically stable, these patients require temporary pacing.
- ◆ In inferior MI, the inferior wall of the RV may be friable. Insertion of a temporary wire may lead to RV perforation. Thus, extra care is required to prevent this complication.

- **Asystole and pulseless electrical activity (PEA)**

Rhythms which require defibrillation (pulseless VT/VF) are called shockable rhythms while asystole and PEA are non-shockable rhythms.

For the management of asystole and PEA, refer to algorithm 1, page 114.

9.2 LV dysfunction and cardiogenic shock

LV dysfunction is the single strongest predictor of mortality following STEMI. The mechanisms responsible for acute LV dysfunction include myocardial necrosis, myocardial stunning, atrial and ventricular arrhythmias or mechanical causes such as acute septal rupture and valvular dysfunction (pre-existing and/or new).

Co-morbidities such as infection, pulmonary disease, renal dysfunction, diabetes, anaemia and drugs may aggravate HF.

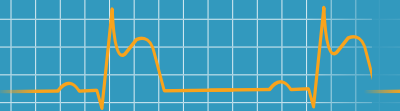
9.2.1 Presentation

The clinical manifestation of LV dysfunction varies from asymptomatic to cardiogenic shock. An important prognostic indicator is LVEF which can be assessed objectively using echocardiography.

A useful clinical classification of LV dysfunction is the Killip's Classification.²⁷⁸ (Table 13, page 86)

9.2.2 Investigations

Echocardiography is an essential tool and needs to be performed early to assess LV function and volumes, valvular function, extent of myocardial damage and to detect mechanical complications.



Other investigations that may be helpful in the management include:

- Chest radiograph (to assess extent of pulmonary congestion).
- ECG (for the detection of arrhythmias, ischaemia or reinfarction).
- Arterial blood gases.

Table 13: Prognosis Post Fibrinolysis and Post Primary PCI according to Killip's Classification

KILLIP CLASS	CLINICAL FEATURES	Post Fibrinolytics	Post Primary PCI		
		21-day mortality ⁹³	In-hospital ²⁷⁸	6 months ²⁷⁹	5 years ²⁸⁰
I	No signs of LV failure	7%	2.4%	4%	17.7%
II	S3 gallop, bibasal crackles, Elevated JVP	18%	7%	10%	27.3%
III	Acute pulmonary oedema	36%	9%	28%	30.4%
IV	Cardiogenic shock	70%			48.8%

9.2.3 Management

A. Acute Heart Failure

Acute management includes the following:

- Oxygen – by nasal prongs/face mask to maintain oxygen saturation above 95%. Consider non-invasive ventilation [bi-level positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP)] early if oxygen saturation cannot be maintained with high flow face mask or high nasal cannula.
- Diuretics – IV frusemide.
- IV nitrates.
- Inotropes if hypotensive.
 - ◆ Noradrenaline should be the agent of first choice. It is started at the lowest dose and titrated until the SBP is more than 90mmHG and the mean arterial pressure is at least 65 mmHg.²⁸¹
 - ◆ Dopamine should be avoided as it has been associated with a higher mortality when used in patients with cardiogenic shock.^{116,117,281}
 - ◆ Adrenaline has been associated with a higher incidence of refractory shock compared to noradrenaline and is best avoided.¹¹⁸

- In patients who are hypoxic or exhausted and are unable to achieve satisfactory oxygen saturation despite non-invasive ventilation, endotracheal intubation and ventilatory support may be required.

B. Cardiogenic shock

This condition occurs in 6–10% of all cases of STEMI and remains a leading cause of death, with hospital mortality rates approaching 70%.²⁸² With timely reperfusion using primary PCI, mortality rates have decreased to about 50%.²⁸³

Criteria for the diagnosis of cardiogenic shock includes:²⁸¹

- systolic blood pressure less than 90 mmHg for 30 minutes or mean arterial pressure less than 65 mmHg for 30 minutes or vasopressors required to achieve a systolic blood pressure \geq 90 mmHg;
- pulmonary congestion or elevated left-ventricular filling pressures;
- signs of impaired organ perfusion with at least one of the following criteria:
 - ◆ altered mental status.
 - ◆ cold, clammy skin.
 - ◆ oliguria.
 - ◆ increased serum lactate.

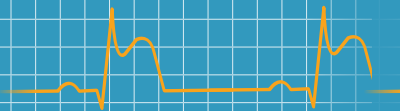
Cardiogenic shock may not be present at admission but may develop in the first 48 hours following admission.²⁸³

Emergency PCI may be life-saving and should be considered early irrespective of the time delay from onset of MI.²⁸¹ If primary PCI cannot be performed within 2 hours, a pharmaco-invasive strategy with immediate fibrinolysis and transfer to a PCI-capable centre is advised.

In management:

- A. Inotropes – the inotrope of choice is noradrenaline titrated to maintain a mean arterial pressure of at least 65 mmHg.^{116-118, 281}
- B. Insertion of a pulmonary artery catheter may be helpful in the diagnosis and management of these patients.
- C. The use of IABP has not shown a definite benefit and its use should be individualised.^{284,285}
- D. extracorporeal membrane oxygenation (ECMO) circuit and LV assist device may be considered for patients who do not respond to conventional therapies.

When cardiogenic shock is due to a mechanical defect, urgent surgical repair is indicated. Concomitant CABG surgery in these patients remains an issue of debate. The decision must be individualised.



9.3 Mechanical complications

These include the following:

- Free wall rupture - it is usually fatal and presents with sudden cardiovascular collapse and haemopericardium.
- Ventricular septal rupture.
- Mitral regurgitation.

The diagnosis should be suspected in patients with sudden clinical deterioration and suggested by the presence of new murmurs or diminished heart sounds. The diagnosis can be confirmed by echocardiography. In these patients, early surgery should be considered.

Ventricular septal rupture requires urgent surgical or percutaneous closure, but there is no agreement on the optimal timing for surgery.

9.4 Right Ventricular (RV) Infarct

Patients with RV infarct may have varying clinical presentation, from asymptomatic to cardiogenic shock.^{17,286-288} Haemodynamically significant RV infarct complicates approximately 5-10% of all STEMI. It occurs in 30 – 50% of patients with infero-basal (formerly known as infero-posterior) MI and is associated with a significantly higher mortality.^{15,285} RV infarct can also occur in patients with anterior STEMI.¹⁷

9.4.1 Clinical diagnosis

The presence of RVI should be sought in all patients with inferior STEMI. The clinical triad of hypotension, clear lung fields and elevated jugular venous pressure in the setting of inferior STEMI is suggestive of RV infarct.

ST elevation in the right praecordial leads (V4R) is the most specific finding in diagnosing RV infarct.¹⁸ However, this ECG finding may be transient, often resolving within 8-10 hours.

9.4.2 Management

Treatment strategies depend on the severity of peripheral hypoperfusion and the degree of co-existing LV dysfunction. Drugs that reduce the preload, such as nitrates and diuretics should be avoided.

Management includes:

- Optimisation of IV fluids (saline or colloids) is the key therapy to correct the hypotension.
- Inotropes.

Failure to respond to these measures usually indicates concomitant LV dysfunction. These patients require more aggressive management with afterload reducing agents such as nitroprusside and IABP.

9.5 Others

9.5.1 Chest pain post-STEMI

Chest pain post-STEMI may be due to reinfarction, recurrent MI, ischaemia or pericarditis. Non-cardiac causes must also be considered.

9.5.1.1 Reinfarction /Recurrent MI

In-hospital reinfarction occurred in about 3-4% of patients who had undergone fibrinolytic therapy and received aspirin.^{289,290} Even in contemporary practice, with primary PCI and DAPT, the incidence of reinfarction/recurrent MI is not infrequent -1.8% at 30 days and 4% at 1 year.²⁹¹ Reinfarction/Recurrent MI is associated with a poor prognosis especially if it is due to stent thrombosis.²⁹¹

Reinfarction may be diagnosed by:

- Recurrence of ischaemic type chest pain.
- Recurrence of ST segment elevation of at least 1mm in at least two contiguous leads and/or
- Re - elevation of serum cardiac biomarkers - CK-MB or troponins ($\geq 20\%$ increase in the value from the last sample).^{30,31}

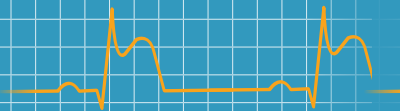
Death, severe HF and arrhythmias are more common in these patients. They should be considered for rescue PCI.

9.5.1.2 Post-infarct angina

After successful reperfusion with fibrinolytic therapy, early recurrent angina may occur in up to 20% of patients at 30 days.²⁹² Among patients undergoing primary PCI, 30% of patients reported angina at 6 weeks²⁹³ and about 10-20% continued to have angina at 12-months.²⁹³⁻²⁹⁶

These patients have a higher risk of recurrent MI and mortality especially when there are accompanying ECG and haemodynamic changes during the episodes of angina.²⁹² These patients should be:

- Sent for early coronary angiography with a view to revascularization.
- Treated optimally medically with anti-platelets, statins and anti-anginal medications.



9.5.1.3 Pericarditis

Pericarditis used to occur in about 20% of patients post STEMI and was associated with a worse prognosis.²⁹⁷ In the contemporary era, however, it is an uncommon complication (about 1.2%) and there was no difference in survival at 30 days, 1 and 5 years.²⁹⁸ It is usually associated with delayed presentations and bigger infarct size.^{298,299}

Pericarditis may produce pain as early as the first day and as late as 6 weeks.²⁹⁷ The pain classically becomes worse on deep inspiration and may be relieved when the patient sits up and leans forward. A pericardial rub may be detected.

Dressler's syndrome (post-MI syndrome) usually occurs 2-10 weeks after STEMI. This is immunologically mediated and used to occur in 3% to 4% of patients post STEMI.²⁹⁹ In the contemporary era, it is seen in much fewer patients.³⁰⁰

Management includes:

- Aspirin 600 mg 3-4 times a day
- Acetaminophen or narcotic analgesics may be reasonable if aspirin, even in higher doses, is not effective.
- Colchicine has been shown to reduce recurrences.^{300,301} However, there is insufficient data on its use in the treatment of Dressler's syndrome.³⁰⁰
- Glucocorticoids may be given if there are contraindications for aspirin and NSAIDs or in the case of refractory symptoms.^{300,301}

Only after stable remission with symptom resolution and normalisation of CRP should the doses of aspirin, NSAIDs or glucocorticoids be tapered down slowly.^{301,302}

9.5.2 LV thrombus and arterial embolism

The prevalence of LV mural thrombus has reduced from 20% to 2.7% in the era of primary PCI.^{303,304} The majority of these occur following anterior or large infarcts where the prevalence can be as high as 15%.³⁰⁵

The timing of LV thrombus assessment is important as too early an assessment after the MI may not be able to detect the thrombus. Although two-thirds of the LV thrombi were detected within the first week, an additional third were seen within the first 3 months.³⁰⁵

Anti-coagulation therapy is recommended for 3-6 months or until the LV thrombus disappears or organises on echocardiography.

9.5.3 Deep venous thrombosis (DVT)

In high-risk patients (prolonged bed rest, HF, unable to mobilise), prophylactic anti-coagulation therapy (s.c. heparin 5000 units bd, LMWH – e.g. enoxaparin 40 mg od) may be considered until the patient is ambulant.

Key Messages #9:

- Important complications following STEMI are arrhythmias and HF.
- HF may be due to extensive myocardial damage or mechanical complications.
- Chest pain post STEMI may be due to:
 - ◆ Reinfarction/Recurrent MI
 - ◆ Post infarct angina
 - ◆ Pericarditis

10. URGENT/EMERGENT CABG SURGERY

Urgent/emergent CABG surgery should be considered in the following situations:

- patients with a patent IRA but with unsuitable anatomy for PCI and either a large myocardial area at jeopardy or with cardiogenic shock.⁹⁶
- At the time of surgical repair of post-infarction ventricular septal rupture or mitral valve regurgitation.
- Patients with failed reperfusion whose coronary anatomy and clinical profile are suitable.

In general, CABG surgery in this group of patients carries a very high in-hospital mortality rate.

11. RISK STRATIFICATION POST STEMI

Risk stratification of patients post-STEMI serves to prognosticate and identify appropriate treatment strategies. It starts from admission and is a continuing process. It is especially important in patients treated medically and those with multivessel disease who underwent PCI of the IRA only.

11.1 Short-Term Risk

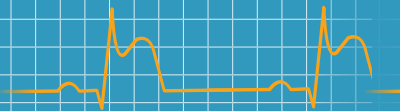
All patients with STEMI should have an early assessment of short-term risk. This can be done using the STEMI TIMI or GRACE risk scores (Appendix III & IV, pg 120-122).^{82,83}

In evaluating risk, the following are important considerations;

- an evaluation of the extent of myocardial damage,
- the occurrence of successful reperfusion, and
- the presence of clinical markers predictive of high risk of further CV events.

Assessment takes into consideration:

- older age,
- tachycardia,
- hypotension,



- Killip class >I,
- anterior MI,
- previous MI,
- elevated initial serum creatinine,
- history of heart failure
- peripheral arterial disease.

The GRACE score can also be used to predict both in-hospital and 6-month mortality.^{306,307}(Appendix IV, pg 121-122)

11.2 Long-Term Risk

All patients should also have an evaluation of long-term risk by assessing:

- LVEF – usually by ECHO
- residual ischaemia – usually by stress-testing,
- occurrence of complications during hospitalisation (eg: heart failure, malignant arrhythmias, mitral incompetence, septal rupture, LV aneurysms), and
- CV risk factors including:
 - ◆ Lipid profile- As LDL-C levels tend to decrease during the first few days after MI, they should be measured as soon as possible after admission.
 - ◆ Plasma glucose
 - ◆ Renal function.

I,C

Ideally, all patients with poor prognostic indicators (STEMI TIMI risk score ≥ 6.0) who did not undergo primary PCI should have a coronary angiogram during the index hospitalisation.⁸²

All other patients who did not undergo coronary angiography should be risk stratified early. This may be done by assessing:

- LV function by one or a combination of the following:
 - ◆ Clinical examination,
 - ◆ Chest X-ray,
 - ◆ Echocardiogram,
 - ◆ Radionuclide studies or
 - ◆ Cardiac MRI
- Presence of myocardial ischaemia by one or a combination of the following:
 - ◆ Clinical (recurrent angina).
 - ◆ Exercise stress testing in asymptomatic patients- This may be done pre-discharge post-STEMI (sub-maximal stress test with a target heart rate of 70% of maximum predicted heart rate) up to 6 weeks post-STEMI (maximal with a target heart rate of 90% of maximum predicted heart rate for age or symptom limited). If the pre-discharge sub-maximal stress test is negative, the patient

should be subjected to a maximal or symptom limited stress test within 6 weeks after discharge.

- ◆ For those who cannot exercise, consider:
 - Dobutamine stress echocardiogram, or;
 - Radionuclide perfusion studies, or;
 - Cardiac MRI
- Presence of malignant ventricular arrhythmias.

I,C

STEMI patients who present initially to non PCI-capable hospitals should be referred for early coronary angiography with a view to revascularization in the presence of any of the following:

- Post-infarct angina,¹³⁴
- Inducible ischaemia¹³⁴
- Late ventricular arrhythmias
- In the presence of a depressed LV function (LVEF < 35%) and significant regional wall motion abnormalities³⁰⁸
- STEMI TIMI risk score > 6.0⁸² (Appendix III, pg 120)

In patients with poor LV function, myocardial viability studies (dobutamine stress echocardiogram, radionuclide perfusion studies or cardiac MRI) can help to differentiate scarred from viable ischaemic myocardium.

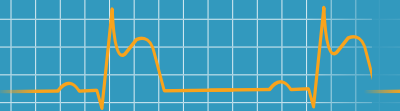
11.3 Sudden Cardiac Death

Patients with palpitations, near faints and syncope require comprehensive evaluation to determine the cause of their symptoms and risk of sudden cardiac death. This includes:

- Serum electrolytes.
- Resting ECG.
- 24-hour ambulatory ECG recording.
- Evaluation of LV function.
- Assessment for reversible myocardial ischaemia.
- Coronary angiography.

In these patients, reversible causes should be corrected.

In patients with ischemic cardiomyopathy, CABG has been shown to reduce CV death and in particular sudden death.³⁰⁸



The following medications have been shown to reduce the incidence of sudden death:

- I,A • β -blockers.^{309,310}
- I,A • ACE-I³¹¹
- I,B • MRA²³⁹
- IIb,B • Statins.^{312,313}

In addition, the following patients should be considered for an implantable cardioverter-defibrillator (ICD):

- I,A • Secondary prevention in patients with resuscitated sudden cardiac death.³¹⁴⁻³¹⁶
- IIa,A • Primary prevention in patients with LV dysfunction [ejection fraction (EF) < 30%]. ICD may be considered 40 days post-STEMI and 3 months post-revascularization.³¹⁷⁻³¹⁹

Key Recommendation 9:

- All patients post-STEMI should be risk-stratified either clinically or by using the STEMI TIMI and/or GRACE risk scores.
- STEMI patients who present initially to non PCI-capable hospitals should be referred for early coronary angiography with a view to revascularization in the presence of any of the following:
 - ◆ Post-infarct angina
 - ◆ Inducible ischaemia
 - ◆ Late ventricular arrhythmias
 - ◆ In the presence of a depressed LV function (LVEF \leq 35%) and significant regional wall motion abnormalities
 - ◆ STEMI TIMI risk score \geq 6.0 (Appendix III, pg 120)

12. DURATION OF HOSPITALISATION

The duration of hospital stay following STEMI will depend on the patient's cardiac risk, extent of myocardial damage, presence of complications, comorbidities and social support.

Early (same day) transfer to the referring centres may be considered in selected low-risk uncomplicated patients after successful primary PCI.³²⁰

Asymptomatic, low risk patients with uncomplicated STEMI may be discharged on day 2 or day 3 after successful primary PCI and complete revascularization.³²¹⁻³²⁷

Patients with significant LV dysfunction or other complications may require a longer hospital stay.

13. SECONDARY PREVENTION

13.1 Non-Pharmacological Measures

Important lifestyle interventions include:

- cessation of smoking,
- dietary modification,
- weight control and
- physical activity.

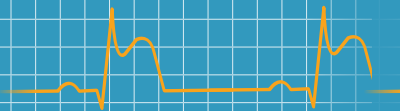
Often, lifetime habits are not easily changed and team work between cardiologists and general practitioners, rehabilitative physicians, pharmacists, dieticians, physiotherapists and occupational therapists is needed for implementation and follow-up.

13.1.1. Cessation of Smoking

Smoking cessation has been consistently associated with a mortality benefit and it is one of the cornerstones of secondary prevention.^{328,329}

In a cohort of patients with ACS on optimal secondary prevention therapy, those who continued to smoke had an 80% risk of lower survival at a mean follow-up of 3.9 years while those who quit had comparable survival to lifelong non-smokers.³³⁰ Persistent smokers at 30 days post-PCI experienced an almost twofold increase in long-term mortality.³³⁰

This underscores the importance of smoking cessation in secondary prevention despite the improvement in management of ACS with PCI and pharmacotherapy. This also emphasises the malignant pathophysiological effects of smoking, namely



endothelial dysfunction, thrombogenicity and coronary vasoconstriction, which predispose to ACS.³³¹

13.1.1.1 Smoking Cessation Interventions

Smoking cessation is difficult, even after life-threatening ACS. The Melbourne Registry showed that only 54% of patients stopped smoking by 30 days.³³⁰ Almost 23% of those who quit smoking at 30 days had relapsed at 12 months highlighting the difficulty of long-term abstinence.^{330,332}

Hospitalisation for an acute cardiovascular event provides a unique window of opportunity to encourage patients to quit smoking. A study has shown that the majority of successful quitters at 1 year stopped immediately after their ACS.³³³

However, smoking-cessation therapy in hospitalised patients offers challenges. The duration of hospitalisation for acute myocardial infarction is usually brief and hospital stay is busy, making it difficult to gain the patient's full attention for smoking-cessation counselling. Nevertheless, effective counselling in the hospital should be provided for all smokers, and not just the minority who are ready to quit.³³⁴ Effective transition from inpatient to outpatient smoking cessation treatment should take place, with a minimum of 1-month follow-up.³³⁴ MQuit (Quit smoking) Services is currently available in all health clinics (Klinik Kesihatan) throughout the country.

13.1.1.2 Pharmacotherapy

Post-STEMI patients usually have been chronic smokers and most of them would have high degree of nicotine dependency. Thus, they should be given personalised smoking cessation medication intended to relieve withdrawal symptoms and to support long-term cessation.

However, very low rates of these medications are prescribed post-MI, and this rate has declined over time.³³⁵ Some clinicians are hesitant to add a smoking-cessation medication on top of a number of other medications that have been initiated or continued. All smoking cessation interventions (nicotine replacement therapy, varenicline and bupropion) have been shown to be safe in cardiac patients.^{336,337}

For further details of smoking cessation, please refer to the Malaysian Clinical Practice Guidelines on Primary and Secondary Prevention of Cardiovascular Disease, 1st Ed, 2017.³³⁸

13.1.2 Diet and Weight Control

Current guidelines on secondary CV prevention recommend:^{338,339}

- A diet similar to the Mediterranean diet, which includes a maximum of 10% of total energy intake from saturated fat, replacing it wherever possible with

polyunsaturated fatty acids and to consume as little as possible of trans fatty acids;

- Salt intake of < 5 g per day;
- 30–45 g fibre per day;
- ≥ 200 g fruits and 200 g vegetables per day;
- Fish 1–2 times per week (especially oily varieties);
- 30 g unsalted nuts daily;
- Limited alcohol intake [maximum of 2 glasses (20 g of alcohol) daily for men and 1 for women];
- Discouraging sugar-sweetened drinks.

Overweight and obesity is associated with higher all-cause mortality compared with a healthy weight.³⁴⁰

Thus, maintaining a healthy weight or losing weight is recommended for all subjects including patients with STEMI.³⁴⁰ However, it has not been established that weight reduction per se reduces mortality.

I,B

13.1.3 Regular Exercise

There is increasing evidence that, when adequately prescribed and supervised, regular exercise after an MI can prevent future complications and increase the quality of life and longevity of these patients^{338,341,342}

I,A

Any amount of physical activity (PA) is better than none; adults engaging in any form and amount of PA gain some form of health benefits in both primary and secondary prevention.^{338,342}

Following an acute cardiac event or post cardiac surgery, patients should be referred to a cardiac rehabilitative physician for exercise prescription.

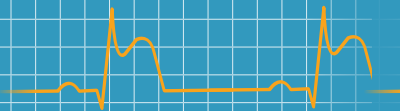
For a more detailed discussion on physical activity and exercise prescription, refer to the Malaysian Clinical Practice Guidelines on Primary and Secondary Prevention of Cardiovascular Disease, 1st Ed, 2017.³³⁸

13.2 Control of CV Risk Factors

13.2.1 Control of hypertension

The prognosis is affected by both the pre-existing and the subsequent BP. The higher the pre-existing BP, the higher the fatality rate.³⁴³

After ACS, the target BP is 110 to < 140/ < 90mmHg (using standard, routine clinician office measurements).^{344,345}



Drugs of choice include β -blockers, ACE-Is and ARB (if ACE-I intolerant).³⁴⁶⁻³⁴⁸

I,A In addition, lifestyle modification (reduced salt intake, increased physical activity and weight loss) usually help achieve these goals.³⁴⁹⁻³⁵¹

Please refer to Malaysian CPG on Primary and Secondary prevention of Cardiovascular Disease, 1st Ed, 2017 and Malaysian CPG on Hypertension, 4th Ed, 2018.^{338,344}

13.2.2. Good glycaemic control (see also Section 14.2, pg 103)

IIa,B After STEMI, diabetic patients have a high risk of subsequent CVD events, including another MI, stroke, and death. While it is imperative to achieve good blood glucose control, glycaemic control should be individualised.^{352,353}

Those with long duration of diabetes, known history of severe hypoglycaemia, advanced atherosclerosis, or advanced age/frailty may benefit from less aggressive targets. However, in type 2 diabetes, there is evidence that more intensive treatment of glycaemia (without causing hypoglycaemia) in newly diagnosed patients may reduce long-term CVD rates.

Table 14: Individualised A1c Targets and Patients' Profile*

A1c TARGETS	PATIENT'S PROFILE
Tight (6.0–6.5%):	<ul style="list-style-type: none"> Newly diagnosed Younger age Healthier (long life expectancy, no CVD complications) Low risk of hypoglycaemia
6.6–7.0%	<ul style="list-style-type: none"> All others
Less tight (7.1–8.0%)	<ul style="list-style-type: none"> Comorbidities (coronary disease, heart failure, renal failure, liver dysfunction) Short life expectancy Prone to hypoglycaemia

*Modified from: Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E et al. Management of Hyperglycaemia in Type 2 Diabetes: A Patient-Centered Approach: A Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), Diabetes Care 2012 Jun; 35(6): 1364-1379

13.3 Pharmacotherapy for Secondary Prevention (see also Section 8.3, pg 74-83)

Medications that have been proven to improve CV outcomes long term post STEMI include:

A. **Anti-platelet agents:**

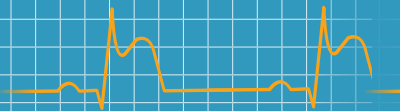
- I,A • Aspirin - low dose aspirin 75-100 mg daily indefinitely^{38,39}
- A P2Y₁₂ inhibitor –
 - I,A ♦ Clopidogrel
 - A component of DAPT in patients who underwent a:
 - ~ Fibrinolytic strategy^{41,42}
 - ~ Primary PCI strategy^{40,192}
 - As an alternative in aspirin intolerant individuals³⁵⁴
 - ♦ Ticlopidine- As an alternative to aspirin intolerant individuals^{198,199}
 - ♦ Ticagrelor-
 - A component of DAPT in patients who:
 - ~ underwent a primary PCI strategy^{76,77,197}
 - ~ are at high risk for recurrent ischemic events. The dose of ticagrelor was 60 mg twice daily and it was given for up to 3 years.²⁰⁶ The benefit was partially offset by a small increased risk of bleeding.²⁰⁶
 - ♦ Prasugrel- A component of DAPT in patients who underwent a primary PCI strategy.^{148,195}

B. **Statins**

- I,A • Statins have been shown to improve prognosis in patients with stable CAD, the lower the low-density lipoprotein cholesterol (LDL-C) achieved, the better the CV outcome.²⁴²⁻²⁴⁵
- I,A • There appears to be a dose-dependent reduction in CVD with LDL-C lowering; the greater the LDL-C reduction, the greater the CV risk reduction.
- The target LDL-C < 1.8 mmol/l- the lower the better.^{242,243,245}
- I,A • If LDL-C levels cannot be achieved, the additional use of other non-statin therapy (e.g. ezetimibe, PCSK-9 inhibitors) may be considered.²⁴⁸⁻²⁵⁰
- I,A • In patients who have achieved LDL-C but the TG remains elevated (1.52-5.63mmol/l) the use of a TG lowering agent, icosapent ethyl 2 g twice daily, was superior to placebo in reducing TGs, CV events, and CV death.³⁵⁵

C. **β -blockers**

- I,A • Oral treatment with β -blockers is indicated in all patients post STEMI especially in those with HF or LV dysfunction.^{220,226,227}
- Evidence supporting the use of β -blockers > 1- year post STEMI for the treatment of stable CAD is less well established.^{228,229,356,357}



D. ACE-Is and ARBs

I,A

- ACE-Is/ARBs are indicated starting within the first 24 hours of STEMI in high-risk patients (LVEF \leq 40% or who have experienced HF in the early phase, DM or an anterior infarct) and should be continued indefinitely if there are no contraindications.^{230-234,237,238}

- ACEi/ARB do not have any additional benefits in reducing CV events and death in patients with Stable CAD and preserved LV function.³⁵⁸⁻³⁶¹

IIb,B

- Thus routine use of ACEi/ARB > 1 year post-STEMI is not recommended.³⁵⁸⁻³⁶¹

E. MRA

I,B

- Mineralocorticoid antagonists, e.g. eplerenone should be considered in patients with LVEF \leq 40% and HF in the absence of renal failure or renal impairment.²³⁹

F. DOAC

IIa,B

- The use of rivaroxaban 2.5 mg twice daily in combination with aspirin 100 mg daily in high risk post-MI patients, significantly reduced the risk of major CV events at a mean follow up of 2 years (the composite of CV death, stroke, or MI) compared to aspirin alone but the risk of major bleeding was also significantly higher.³⁶²

G. Anti-ischaemic Therapy

In patients who continue to have angina post revascularization, the following may be considered:³⁶³

IIa,B

- β -blockers and/or CCBs should be prescribed as first-line treatment to reduce angina because it is widely available.

IIa,B

- Ivabradine, trimetazidine, long-acting nitrates and ranolazine are recommended as add-on therapy in patients who remain symptomatic.

Key Recommendation 10:

- Post STEMI, all patients should receive secondary prevention interventions that have been shown to reduce mortality and cardiovascular event rate. These include:
 - ◆ smoking cessation and other lifestyle changes
 - ◆ regular exercise
 - ◆ control of CV risk factors- hypertension, diabetes, smoking, dyslipidaemia
 - ◆ drug therapy;
 - anti-platelet agents
 - statins therapy
 - β -blockers:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%
 - ACE-I/ARB:
 - ◇ < 1 year in all patients
 - ◇ > 1 year in the presence of LVEF \leq 40%, anterior infarct and diabetes

14. SPECIAL GROUPS

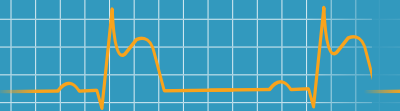
14.1 STEMI in Older Individuals

Patients above the age of 75 years have much higher in-hospital as well as 1-year mortality.³⁶⁴⁻³⁶⁷ This may be explained by their atypical and delayed presentations, multiple co-morbidities and under-utilisation of reperfusion strategies.^{368,369} Diagnosis may be delayed because of:

- Atypical symptoms such as dyspnoea, syncope and acute delirium and confusion in the presence of pre-existing cognitive impairment.^{365,366}
- Non-diagnostic and difficult to interpret ECGs complicated by an abnormal baseline.
- Non-diagnostic cardiac biomarkers. The baseline troponin levels may be elevated in as many as 22% of the elderly without an MI because of pre-existing cardiac and renal disease.^{370,371} Thus, a high index of suspicion must be present to make a diagnosis of ACS in older individuals. The trend of a rise and fall cardiac biomarker levels is critical to the diagnosis.

Management

Evidence for risk benefit ratio for interventions in older patients is scarce as they were largely excluded from most of the large trials and data is mainly derived from post-hoc analysis.^{365,372} In determining the appropriate management for this group, one should consider the heterogeneity of this population and consider the biological



age rather than the chronological age of the patient. Therefore, the risk-benefit ratio of each intervention should be individualised so that these patients are not excluded from interventions.³⁷³ It is important to assess frailty, general health and functional status, co-morbidities as well as the particular wishes of the patient and family.

In addition, age related differences in physiology can affect disease manifestation, bleeding risks, drug metabolism and management. Most MI's in older patients are NSTEMI rather than STEMI.³⁷⁴ Older patients are more likely to develop left ventricular failure (more than 50% of those aged > 75 years of age) and more than >10% develop cardiogenic shock.^{374,375} This is due to their more extensive disease, late presentation, and age-related changes in cardiac physiology or decreased vascular compliance, ventricular hypertrophy and remodeling.^{375,376}

CKD is common in these patients and may increase the risk of bleeding.^{375,376} Most drugs are excreted by the kidneys and doses need to be adjusted. Creatinine clearance (CrCL) should be estimated using the Cockcroft-Gault and the estimated glomerular filtration rate (eGFR) by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations or Modification of Diet in Renal Disease (MDRD) equations. (Appendix VI, pg 124).

In the management of STEMI in older patients:

- **Primary PCI** - this is the preferred reperfusion strategy if facilities are available and the patient is eligible for PCI.³⁷⁶⁻³⁸¹ Procedural success is highly variable. Older patients are more likely to have PCI related complications especially bleeding.³⁸²
- **Fibrinolytic therapy** - there is an increased risk of intracranial haemorrhage in older patients and the risks of bleeding have to be carefully considered in those older than 75 years.³⁸³⁻³⁸⁶ The dose of tenecteplase is 50% of the recommended dose in those \geq 75 years of age.³⁸⁷
- **Adjunctive therapy** - when compared with younger patients, older patients have a greater absolute reduction with most evidence based medications.³⁶⁵ It is important to balance the risks of polypharmacy and the risks of drug interactions with the benefit of not withholding guideline-directed medications, proven to be of benefit in these older individuals. While in-hospital mortality and complication rates increased with advancing age, those receiving more recommended therapies had lower mortality than those who did not receive these medications.³⁸⁸
 - ◆ Aspirin - at a dose of 75 to 150 mg in the absence of contraindications.^{365,389,390}
 - ◆ Clopidogrel - the absolute benefits of clopidogrel are similar, but relative benefits are less in older patients.^{192,365} Patients undergoing PCI with higher STEMI TIMI risk scores or prior revascularization are more likely to benefit.³⁹¹ A loading dose when compared to a conventional dose of clopidogrel did not result in an increased bleeding risk in older patients.¹⁹⁴ The need for a loading

dose needs however, to be individualised. When given as part of a fibrinolytic strategy, the loading dose in patients > 75 years is 75 mg.⁴²

- ◆ Ticagrelor – ticagrelor has a similar efficacy as clopidogrel in patients aged ≥ 75 years of age and those < 75 years of age. There was no increased risk of bleeding.⁷⁷
- ◆ Prasugrel - should be avoided in patients > 75 years of age.^{195,196}
- ◆ Enoxaparin was found to be more effective than UFH, the absolute risk reductions for the composite end points of death and non-fatal MI at 30 days was the same in both younger and older patients.²⁰⁸ The risk of bleeding was higher in those > 75 years even with the reduced dose.²⁰⁸ (Table 9, pg 78)
- **Secondary prevention** - the benefit associated with the use of β-blockers, ACE-Is and statins is similar to, and often greater than, that observed in younger patients.³⁹²⁻³⁹⁹
- **Cardiac rehabilitation**- Older patients benefit from cardiac rehabilitation and exercise training.⁴⁰⁰⁻⁴⁰⁵ It is a combination of secondary preventive efforts and improving their functional capacity.
- **Risk stratification** - this needs to be individualised and patient preferences are important in determining further management. The presence of on-going ischaemia, symptomatic malignant arrhythmias and a depressed LV function are poor prognostic indicators and would generally necessitate a more aggressive approach. Both PCI and CABG, when indicated, can be carried out in older patients with acceptable morbidity and mortality by experienced operators. The risks are however higher than in younger patients.

14.2 STEMI in diabetics

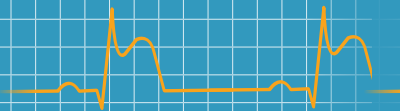
In patients with STEMI, the blood glucose level was associated with adverse outcomes independent of prior diabetic status.^{406,407} Following an ACS, patients with diabetes unlike those without diabetes, do not have similar reductions in CV mortality despite receiving modern therapies.⁴⁰⁸⁻⁴¹⁰ The rate of successful reperfusion of the infarct related vessel treated with fibrinolytic regimens is similar in both diabetics and non-diabetics. Despite this, diabetics have a worse prognosis and they require almost 50% more time to achieve satisfactory ST-segment elevation recovery.⁴¹¹ Local NCVd registry data indicate that diabetics with STEMI did worse than would be expected from their STEMI TIMI risk score.⁸¹

Patients with diabetes may have atypical presentations and this may contribute to their late presentation. They also tend to have more diffuse atherosclerotic disease.

Management

Diabetic patients should be treated in a similar manner as non-diabetics.

- Primary PCI is the reperfusion strategy of choice in these high-risk patients.⁴¹²
- Adjunctive therapy includes:



- ◆ Anti-platelet agents – aspirin and clopidogrel or prasugrel or ticagrelor.^{38,39,40,76,148}
- ◆ Prasugrel has been found to be more effective in diabetics.¹⁴⁸

Diabetes is a well-recognised risk factor for contrast induced nephropathy (CIN).⁴¹³ In the setting of STEMI, an elevated pre-procedural glucose level is associated with a greater risk for CIN even in patients without known diabetes.⁴¹³

There is still a lack of consensus on the optimal management of blood sugars during the acute event.⁴¹⁴⁻⁴¹⁶ Intensive insulin therapy to achieve normoglycaemia in the acute setting has not been shown to reduce mortality and is associated with an increase in the episodes of hypoglycaemia. A low blood sugar level (< 4.0 mmol/L) has also been associated with adverse outcomes.

A general consensus is to keep blood sugars between 6-10 mmol/L in the acute setting and then aim for optimal control following discharge.^{417,418}

- In the pharmacotherapy of diabetic patients with CAD:
 - ◆ Both the SGLT2i and the GLP-1 agonists have been shown to be associated with a reduction in the risk of CV composite end-points.⁴¹⁹⁻⁴²³
 - ◆ The SGLT2i have been shown to reduce the risk of heart failure.^{419,422,423}
 - ◆ In a meta-analysis, the SGLT2i and GLP-1 agonists have been associated with a reduction in all cause mortality.⁴²⁴
 - ◆ thiazolidinediones are associated with an increase in the incidence of heart failure and should be avoided in those in NYHA Functional class 3 & 4.⁴²⁵⁻⁴²⁷
 - ◆ Saxagliptin, a DPP-4i, was also shown to be associated with an increase in hospitalization for heart failure.⁴²⁷ However this is not seen with the other agents of the same class.⁴²⁸
 - ◆ Sulphonylureas, biguanides like metformin and alpha-glucosidase inhibitors like acarbose are generally safe.

14.3 STEMI in women

Women have a higher mortality following STEMI.⁴²⁹⁻⁴⁴⁰ They are generally about 10 years older when they develop CHD and have more comorbidities. They were also less likely to undergo angiography, reperfusion and receive less medical treatment.^{430,439}

This gender difference in 30-day mortality was not seen if the analysis was adjusted for both baseline characteristics and treatment especially for Primary PCI. Women below 60 years however, had a higher mortality despite multivariable adjustment for both comorbidities and treatment effects.^{430,440} Women are more likely to present with cardiogenic shock.^{433,434}

Women tend to have atypical symptoms and generally do not present with classical ischaemic-type chest pain.⁴³¹ They are more likely to have fatigue, neck pain, syncope, nausea, right arm pain, dizziness and jaw pain.⁴³¹ Subjective reports of sleep disturbance preceding MI seem to be common in women.⁴³² Thus a high degree of clinical suspicion is necessary to diagnose MI in women.

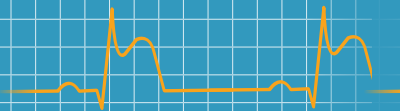
Management

In general, women should be treated the same as men taking into consideration the following:^{389,390,441}

- Primary PCI is the preferred reperfusion strategy. Women however, have higher early all-cause and cardiac mortality after primary PCI and they also have higher bleeding risk.⁴³⁴ Women are less likely to undergo coronary angiography and reperfusion and those who underwent primary PCI tend to have longer DBT.⁴³⁴
- Women given fibrinolytics [recombinant tissue plasminogen activators (r-TPA)] had a higher incidence but lower mortality from bleeding than men.⁴⁴²
- Adjunctive therapy is similar in both gender.⁴⁴³⁻⁴⁴⁵ Women however have higher bleeding risk.
- Cardiac rehabilitation – women, especially older women, are under-referred for cardiac rehabilitation.^{446,447} Efforts should be initiated to overcome these barriers.⁴⁴⁸
- Continuing HRT after STEMI does not confer a benefit nor pose a worrisome increase in risk. When considering the need for HRT for menopausal symptoms, clinical judgement is necessary.^{449,450}

Key messages #12:

- Diagnosis of STEMI in the elderly, diabetics and women is difficult and a high index of suspicion is important.
- Treatment is the same although the elderly and women tend to have higher bleeding risk.



14.4 STEMI in renal disease

Patients with all grades of Chronic Kidney Disease (CKD) (Appendix VI, pg 124) have a worse prognosis after an MI compared to those with normal renal function; those on dialysis may have as high as 74% mortality at 2 years.^{81,451-457} The serum creatinine (Scr) at admission predicts long-term mortality even after successful primary PCI.⁴⁵¹ One in 6 survivors develop worsening renal function during the admission and this is also associated with increased mortality even in patients with normal renal function at baseline.⁴⁵⁷

Patients with CKD tend to:⁴⁵⁸⁻⁴⁶¹

- be older.
- have more comorbidities such as diabetes.
- be on more cardio-protective medications.
- have more extensive coronary atherosclerosis with a higher plaque burden.
- have culprit lesions which are more proximal and threatening a larger myocardial volume.
- be more likely to present without chest pain.
- be in Killip Class III or IV.
- present as NSTEMI.

Troponins may be elevated in patients with CKD even in the absence of ACS.⁴⁶² A rise and fall in cardiac biomarkers is essential to make a diagnosis of MI. Small studies seem to indicate that Troponin I may be more specific for myocardial necrosis than Troponin T in CKD.⁴⁶³

Management

Reperfusion Strategy:

The optimal mode of reperfusion in patients with CKD presenting with STEMI has not been addressed in large prospective trials. The best strategy in patients with severe CKD and those on dialysis is still unclear.⁴⁶⁴⁻⁴⁶⁸ Registry data seem to indicate that the benefits of reperfusion is uncertain in this population.⁴⁶⁴⁻⁴⁶⁹

In patients receiving fibrinolytics, there are no dose adjustment recommendations for the use of streptokinase, alteplase, reteplase, or tenecteplase in patients with CKD. However, the risk of intracranial haemorrhage is increased.⁴⁷⁰

The success rate of emergency PCI in patients with CKD is generally lower and can result in worsening renal function due to haemodynamic instability and CIN.⁴⁷¹ Patients with CKD tend to have more extensive atherosclerosis and more complex calcified lesions.⁴⁷¹ In some patients with multivessel coronary involvement and haemodynamic instability, complete revascularization by CABG may be superior to PCI.

CIN is higher among patients undergoing primary PCI as compared to elective procedures. It occurs in as high as 20-30% of cases and is associated with adverse 1- year mortality.⁴⁷² Half of these patients may go on to develop persistent renal failure.⁴⁷³ Recent studies have shown high-dose statin therapy to reduce the incidence of CIN but more studies are needed to confirm these findings.⁴⁷⁴⁻⁴⁷⁶

Adjunctive therapy:

Patients with CKD were excluded from most clinical trials and most of the available data is derived from post-hoc analyses. These patients have higher rates of bleeding and the doses of antithrombotic agents need to be adjusted accordingly.⁴⁷⁷ (Table 15, pg 108)

The Cockcroft -Gault (CG) equation has traditionally been used for drug dosing based on CrCL. In recent practice, the CKD-EPI Creatinine (CKD-EPI) has been used for drug dosing based on eGFR especially for newer generation drugs. Drug dosing adjustment, however, should be done according to the United States Food and Drug Administration or the European Medicine Agency approved drug labelling.

- Anti-platelet therapy:
 - ◆ Standard care: aspirin 75-100 mg^{478,479} and clopidogrel 75 mg.⁴⁷⁸ In patients on dialysis, aspirin did not result in an increase in bleeding risk.^{480,481}
 - ◆ In patients with mild to moderate CKD who underwent primary PCI, a 600 mg loading dose of clopidogrel was not found to be beneficial.⁴⁸²⁻⁴⁸⁴ This dose however did not increase the in-hospital major bleeding rate.⁴⁸²⁻⁴⁸⁴
 - ◆ Both ticagrelor and prasugrel were shown to be more effective than clopidogrel in patients with normal and reduced renal function without an increased risk of major bleeding.^{195,485}
- Anti-thrombotic therapy:
 - ◆ Enoxaparin was found to more effective than UFH in patients with mild to moderate CKD.^{486,487} In patients with CrCL < 30 ml/minute, enoxaparin has been associated with an increased risk of bleeding.⁴⁷⁷
 - ◆ Fondaparinux - in patients with mild to moderate CKD, fondaparinux was more effective than enoxaparin largely explained by the lower rates of bleeding.⁴⁸⁸ However, it should be avoided in patients with CrCL < 30 ml/minute.
- β -blocker, ACE- I and statin therapy:
 - ◆ In patients with mild to moderate CKD, meta-analyses and post-hoc analyses of studies have noted benefits.^{477,489-493} In patients on ACE-I, renal function and potassium should be monitored.
 - ◆ In patients on dialysis, there is a lack of evidence concerning the cardiovascular benefits of statins.⁴⁹³ Aspirin, β -blockers and ACE-Is however, remain beneficial.⁴⁹⁴

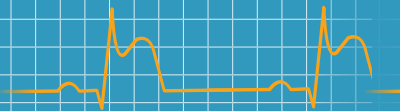


Table 15: Dosages of Anti-thrombotics in CKD⁴⁴⁷

	LOADING DOSE	MAINTENANCE DOSE
UFH	No change	No change
Enoxaparin (Following fibrinolytic therapy)	< 75 years :30 mg IV plus a 1-mg/kg SC dose	<75 years : 1 mg/kg administered SC once daily
	≥ 75 years: no loading dose	≥ 75 y :1 mg/kg administered SC once daily
	Not recommended in dialysis patients	
Fondaparinux	Avoid if CrCL < 30 ml/minute	
Tirofiban	25 µg/kg IV over 3 minutes followed	CrCL ≤60 mL/minute: infusion of 0.075 µg/kg/ minute for up to 18 h post- PCI

Key messages #12:

- Treatment of STEMI in patients with CKD should be individualised.
- Primary PCI is the preferred reperfusion strategy but morbidity and mortality are high.
- In view of bleeding risks, the dosages of anti-platelet agents and anti-thrombotics need to be adjusted accordingly.
- Aspirin, β- blockers, ACE-I and statins are beneficial in patients with mild to moderate CKD. In patients on dialysis, only aspirin, β- blockers and ACE-I remain beneficial.

15. CARDIAC REHABILITATION

Cardiac Rehabilitation Programme (CRP) consists of coordinated, multifaceted interventions designed to optimise a cardiac patient's physical, psychological, and social functioning.⁴⁹⁵⁻⁴⁹⁷ It is a comprehensive, long-term program involving:

- medical evaluation,
- exercise prescriptions,
- cardiac risk-factor modification,
- education and counseling

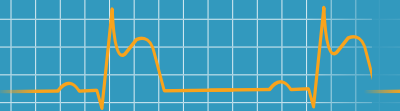
The core components of CRP are:^{496,497}

- Healthy behaviour changes and education
- Lifestyle risk factor management
- Physical activity and exercise
- Diet
- Smoking cessation
- Psychosocial health
- Medical risk factor management
- Long-term management
- Audit and evaluation

CRP can be initiated once the patient is stable and out of the critical care unit and before discharge from hospital.

There are 4 Phases using the Wenger Model:⁴⁹⁸

- Acute phase (Phase I):
 - ◆ This is the in-hospital period immediately following the MI and leading up to discharge.
 - ◆ It involves early mobilization of the patient.
 - ◆ It can be started after 48 hours of hospitalisation in stable patients.
- Convalescent phase (Phase II):
 - ◆ This is at home/convalescent hospital.
 - ◆ This continues the program started in phase I until the myocardial scar has matured.
- Training phase (Phase III):
 - ◆ This is initiated after healing is complete (about 4 to 6 weeks) and the patient is safe for aerobic exercise.
- Maintenance (Phase IV):
 - ◆ This is home-based regular exercise to maintain aerobic conditioning gains made in phase III.



Exercise training programs include warm-up, resistance training, endurance training, and cool-down. Examples:

1. Warm-up: stretching, warm-up exercise, low-intensity (slow) walking
2. Main exercises: aerobic exercise and resistance training at prescribed intensity
3. Cool-down: low-intensity (slow) walking, stretching, cooling-down exercise

For patients at High Risk during Cardiac Rehabilitation and contraindications to exercise training see Tables 17 & 18, pg 111-112.

Sexual counselling is advisable.⁴⁹⁹ In general, sexual activity may be resumed one week after uncomplicated STEMI in the absence of cardiac symptoms after mild to moderate physical activity.⁵⁰⁰ In the presence of complications, it should be individualised.

There is no unanimous consensus as when to resume driving after STEMI. In general, for:⁵⁰¹⁻⁵⁰³

- Private drivers:
 - ◆ After one month if no complications and LVEF >35%.
 - ◆ In those with complications such as LVEF <35%, acute decompensated heart failure, arrhythmias etc- it may be longer.
 - Commercial drivers:
 - ◆ should be assessed at 3 months post-STEMI for fitness to resume duties.⁵⁰⁴
- Criteria include:
- Stress test (exercise tolerance of greater than 9 minutes (stage 3) on the Bruce Treadmill Test
 - Less than 2 mm ST segment depression on an exercise ECG (stress test)
 - LVEF must be > 40%.

For fitness for commercial air travel, see Table 16, pg 111.

Table 16: Fitness for commercial air Travel Post STEMI⁵⁰⁵

FUNCTIONAL STATUS	GUIDANCE
Low risk: age < 65 years, first event, successful reperfusion, LVEF > 45%, no complications, no planned investigations or interventions	Fly after 3 days
Medium risk: EF > 40%, no symptoms of heart failure, no evidence of inducible ischaemia or arrhythmia, no planned investigations or interventions	Fly after 10 days
High risk: EF < 40%, signs and symptoms of heart failure, those pending further investigation, revascularization or device therapy	Defer until condition is stable

Table 17: Patients at High Risk during Cardiac Rehabilitation

Patients at High Risk during Cardiac Rehabilitation

- Ischemic risk
 - ◆ Postoperative angina
 - ◆ LVEF < 35%
 - ◆ CHF- NYHA grade III or IV
 - ◆ Ventricular tachycardia or fibrillation in the postoperative period
 - ◆ SBP drop of 10 points or more with exercise
 - ◆ Excessive ventricular ectopy with exercise
 - ◆ Incapable of self-monitoring
 - ◆ Myocardial ischaemia with exercise
- Arrhythmic risk
 - ◆ Acute infarction within 6 weeks
 - ◆ Active ischaemia by angina or exercise testing
 - ◆ Significant left ventricular dysfunction (LVEF < 30%)
 - ◆ History of sustained ventricular tachycardia
 - ◆ History of sustained life-threatening supraventricular arrhythmia
 - ◆ History of sudden death, not yet stabilized on medical therapy
 - ◆ Initial therapy of patients with automatic implantable cardioverter defibrillator
 - ◆ Initial therapy of a patient with a rate adaptive cardiac pacemaker

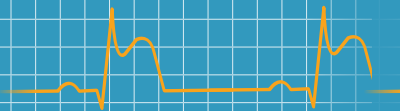


Table 18: Contraindications to Exercise Training

Contraindications to Exercise Training

- Unstable angina
- Uncontrolled hypertension, that is, resting systolic blood pressure (SBP) >180 mmHg, or resting diastolic blood pressure (DBP) > 110 mmHg
- Orthostatic blood pressure drop of > 20 mmHg with symptoms
- Significant aortic stenosis (aortic valve area < 1.0 cm²)
- Acute systemic illness or fever
- Uncontrolled atrial or ventricular arrhythmias
- Uncontrolled sinus tachycardia (HR > 120 bpm)
- Acute pericarditis or myocarditis
- Uncompensated HF
- Third degree (complete) atrioventricular (AV) block without pacemaker
- Recent embolism
- Acute thrombophlebitis
- Resting ST segment displacement (> 2 mm)
- Uncontrolled diabetes mellitus
- Severe orthopaedic conditions that would prohibit exercise
- Other metabolic conditions, such as acute thyroiditis, hypokalaemia, hyperkalaemia or hypovolaemia (until adequately treated)

16. CHECKLISTS FOR FOLLOW-UP VISITS

The following should be assessed at each follow-up visit:

- Assess the presence or absence of cardiac symptoms and determine the functional class of the patient.
- Evaluate patients' psychosocial (anxiety & depression) status and the social integration and support network.
- Review pre-discharge risk assessment and evaluate:
 - ◆ Presence of residual ischaemia.
 - ◆ LV function.
 - ◆ Current medications and optimize their doses.
- Treat to target.
 - ◆ BP: < 140/90 mmHg.
 - ◆ Lipids: LDL-C < 1.8 mmol/L, the lower the better.
 - ◆ Diabetic control: targets should be individualised.
 - ◆ Achieve and maintain ideal body weight and waist circumference.

17. PERFORMANCE MEASURES

Performance measures should be used with the goal of improving the quality of care.⁵⁰⁶

Process performance measures focus on the aspects of care that are delivered to a patient, while outcome measures focus on the end-points such as mortality or repeat hospitalisation.

Table 19: Performance Measures

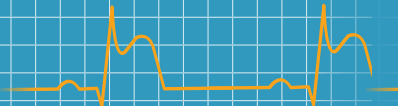
INDICATORS FOR STEMI AT PRESENTATION	TARGETS
ECG done within 10 minutes of FMC	90%
FMC to Device time ≤ 90 minutes if in same hospital	60%
FMC to Device time ≤ 120 minutes if transferred from another hospital	60%
FMC to needle time < 30 minutes	75%
Medications at discharge: <ul style="list-style-type: none"> • Aspirin • P2 Y₁₂ inhibitors • High intensity statins 	90% 90% 90%
If LVEF < 40% <ul style="list-style-type: none"> • ACE-I/ARB • β - blocker • MRA 	70% 70% 70%
Cardiac rehabilitation	50%

Outcome Measures indicators include:

- In hospital mortality < 10%
- 30-day mortality < 14%
- 1-year mortality < 18%

Key Recommendation 11:

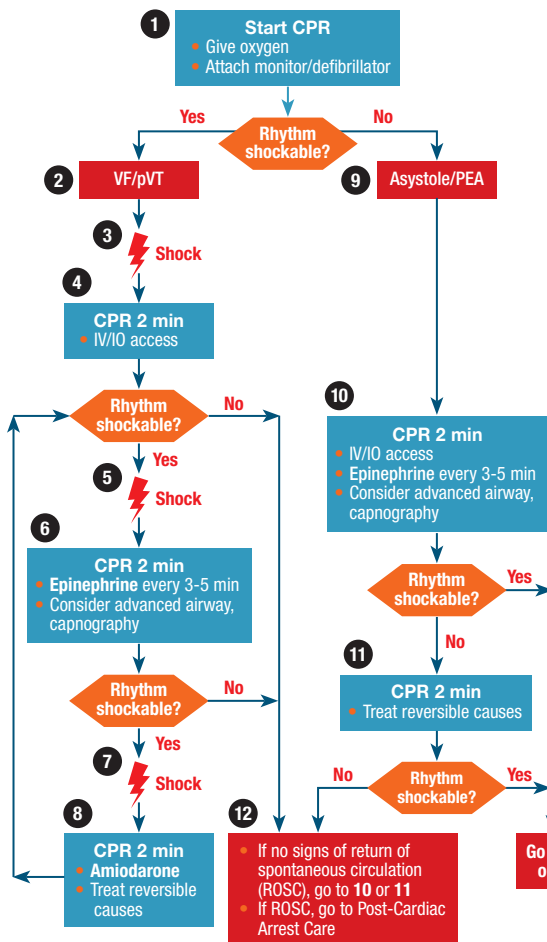
- Regular audit of performance measures (Table 19, pg 113) and outcomes measures are important to monitor and improve quality of care.



ALGORITHMS

ALGORITHM 1: PULSELESS ARRHYTHMIAS

ADULT CARDIAC ARREST ALGORITHM 2015 UPDATE

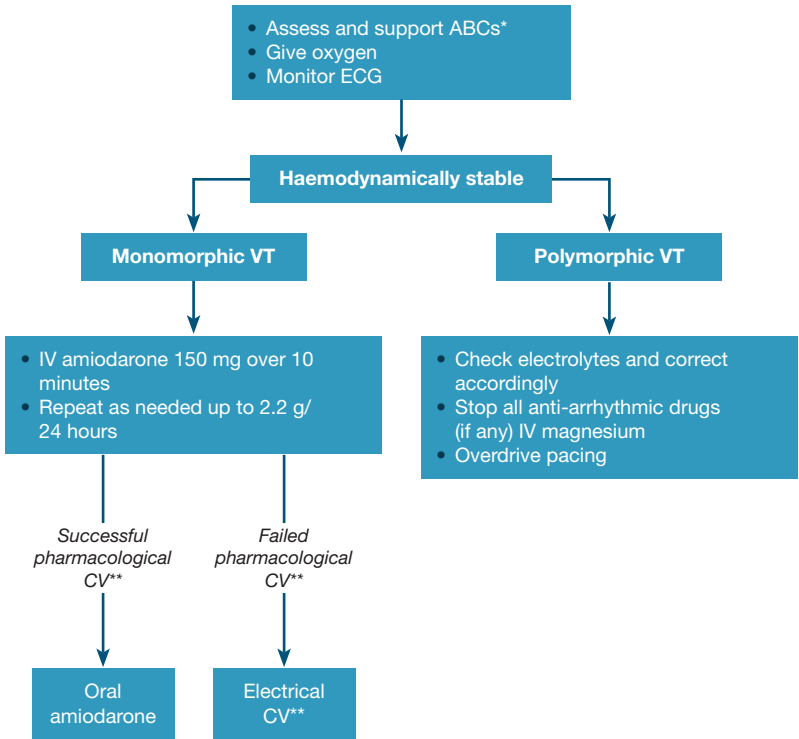


CPR Quality
<ul style="list-style-type: none"> • Push hard (at least 2 inches [5 cm]) and fast (100-120/min) and allow complete chest recoil. • Minimize interruptions in compressions. • Avoid excessive ventilation. • Rotate compressor every 2 minutes, or sooner if fatigued. • If no advanced airway, 30:2 compression - ventilation ratio. • Quantitative waveform capnography <ul style="list-style-type: none"> - If PETCO₂ < 10 mm Hg, attempt to improve CPR quality. - Intra-arterial pressure - If relaxation phase (diastolic) pressure < 20 mm Hg, attempt to improve CPR quality.
Shock Energy for Defibrillation
<ul style="list-style-type: none"> • Biphasic: Manufacturer recommendation (eg, initial dose of 120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered. • Monophasic: 360 J
Drug Therapy
<ul style="list-style-type: none"> • Epinephrine IV/IO dose: 1 mg every 3-5 minutes • Amiodarone IV/IO dose: First dose: 300 mg bolus. Second dose: 150 mg.
Advance Airway
<ul style="list-style-type: none"> • Endotracheal intubation or supraglottic advanced airway • Waveform capnography or capnometry to confirm and monitor ET tube placement • Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions
Return of Spontaneous Circulation (ROSC)
<ul style="list-style-type: none"> • Pulse and blood pressure • Abrupt sustained increase in PETCO₂ (typically > 40 mm Hg) • Spontaneous arterial pressure waves with intra-arterial monitoring
Reversible Causes
<ul style="list-style-type: none"> • Hypovolemia • Hypoxia • Hydrogen ion (acidosis) • Hypo-/hyperkalemia • Hypothermia • Tension pneumothorax • Tamponade, cardiac • Toxins • Thrombosis, pulmonary • Thrombosis, coronary

From: Guidelines for resuscitation training for Ministry of Health Malaysia, March 2016

ALGORITHM 2: STABLE VENTRICULAR TACHYCARDIA

(if unstable for immediate synchronised cardioversion)

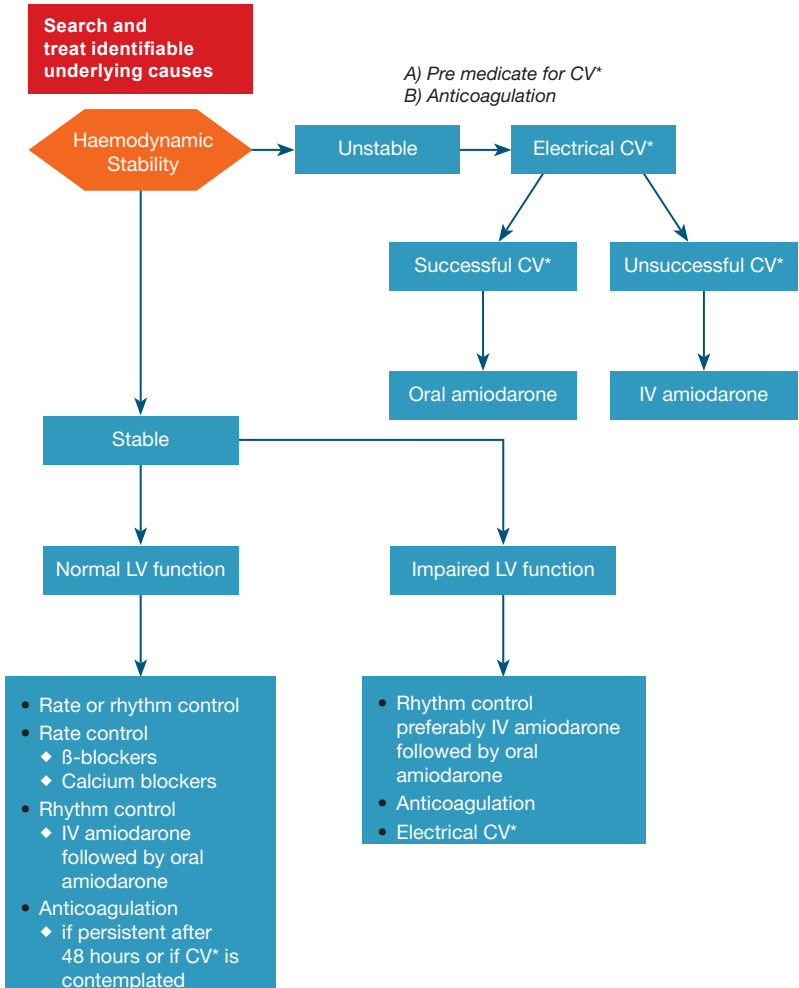


*ABC: airway, breathing, circulation

** CV: cardioversion



ALGORITHM 3: ATRIAL FIBRILLATION



*CV: cardioversion

ALGORITHM 4: BRADYCARDIA

- Slow (absolute bradycardia ≤ 50 bpm)
- or
- Relatively slow (rate less than expected relative to the underlying condition/cause)

- Assess ABC
- Vital signs monitoring
- Search for underlying reversible causes (e.g. electrolytes, drugs) and treat accordingly

Serious symptoms due to bradycardia?

No

Yes

Type II second degree AV block
or
Third degree AV block?

Intervention sequence:

- Atropine 0.5 to 1 mg, max 3 mg
- Dopamine 2 to 10 mcg/kg/minute
- Epinephrine 2 to 10 mcg/minute
- Transcutaneous pacing if available

No

Yes

Haemodynamically stable

Yes

Anterior MI

No

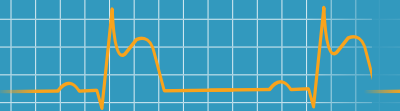
Yes

No

Observe

Transvenous pacing

*ABC: airway, breathing and circulation



APPENDICES

APPENDIX I: DIFFICULTIES IN ECG DIAGNOSIS OF MI

The following conditions may cause ECG changes that may be confused with that of STEMI:

- Prior MI with Q-waves and/or persistent ST elevation.
- Early repolarisation.
- LBBB.
- Right ventricular pacing.
- Pre-excitation.
- Peri-/myocarditis.
- Pulmonary embolism.
- Subarachnoid haemorrhage.
- Metabolic disturbances such as hyperkalaemia.
- Cardiomyopathy.
- Cholecystitis.
- Tricyclic antidepressants or phenothiazines.
- J point elevation syndromes, e.g. Brugada syndrome.

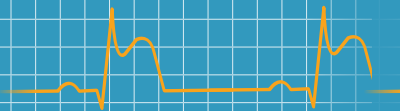
In these difficult situations where the ECG is non-diagnostic, cardiac imaging techniques such as echocardiogram looking for presumed new wall motion abnormalities or elevation of cardiac biomarkers will help in making the diagnosis.

Adapted from Thygesen K et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60(16): 1581-98.

APPENDIX II: ELEVATIONS OF CARDIAC TROPONIN IN THE ABSENCE OF OVERT ISCHAEMIC HEART DISEASE.

DAMAGE RELATED TO SECONDARY MYOCARDIAL ISCHAEMIA (MI TYPE 2)
Tachy- or bradyarrhythmias
Aortic dissection and severe aortic valve disease
Hypo- or hypertension, e.g. haemorrhagic shock, hypertensive emergency
Acute and chronic HF without significant concomitant CAD
Hypertrophic cardiomyopathy
Coronary vasculitis, e.g. systemic lupus erythaematosus, Kawasaki syndrome
Coronary endothelial dysfunction without significant CAD e.g. cocaine abuse
DAMAGE NOT RELATED TO MYOCARDIAL ISCHAEMIA
Cardiac contusion
Cardiac incisions with surgery
Radiofrequency or cryoablation therapy
Rhabdomyolysis with cardiac involvement
Myocarditis
Cardiotoxic agents, e.g. anthracyclines, herceptin , carbon monoxide poisoning
Severe burns affecting > 30% of body surface
INDETERMINANT OR MULTIFACTORIAL GROUP
Apical ballooning syndrome
Severe pulmonary embolism or pulmonary hypertension
Peripartum cardiomyopathy
Renal failure
Severe acute neurological disease e.g. stroke, trauma
Infiltrative disease e.g. amyloidosis, sarcoidosis
Extreme exertion
Sepsis
Acute respiratory failure
Frequent defibrillator shocks

Adapted from Thygesen K et al. Recommendations for the use of cardiac troponin measurement in acute cardiac care. Eur Heart J 2010; 31:2197-2204.



APPENDIX III: STEMI TIMI RISK SCORE FOR PREDICTING 30 DAY MORTALITY⁸²

CATEGORIES	Options	Points
Age (years)	<input type="checkbox"/> < 65	0
	<input type="checkbox"/> 65 - 74	2
	<input type="checkbox"/> ≥ 75	3
Weight < 67 kg	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
SBP < 100 mmHg	<input type="checkbox"/> Yes	3
	<input type="checkbox"/> No	0
Heart rate > 100 bpm	<input type="checkbox"/> Yes	2
	<input type="checkbox"/> No	0
Killip Class II-IV	<input type="checkbox"/> Yes	2
	<input type="checkbox"/> No	0
Anterior ST segment elevation or LBBB	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
Diabetes, history of hypertension, history of angina	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
Time to treatment > 4 hours	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0

Note:

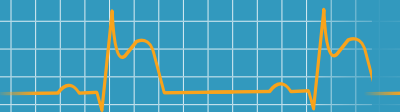
TIMI Risk Score: 0 – 14 plausible points

- Low and moderate risk: 5 points and below (< 12%)
- High-risk: 6 points and above (16-36.0%)

APPENDIX IV: GRACE ACS RISK MODEL⁸³

• **At Admission (in-hospital/to 6 months)**

CATEGORIES	Options
Age (years)	<input type="checkbox"/> <30 <input type="checkbox"/> 60 – 69 <input type="checkbox"/> 30 – 39 <input type="checkbox"/> 70 – 79 <input type="checkbox"/> 40 – 49 <input type="checkbox"/> 80 – 89 <input type="checkbox"/> 50 – 59 <input type="checkbox"/> 90 – 100
Heart rate (bpm)	<input type="checkbox"/> 0 < 50 <input type="checkbox"/> 110 – 149 <input type="checkbox"/> 50 – 69 <input type="checkbox"/> 150 – 199 <input type="checkbox"/> 70 – 89 <input type="checkbox"/> ≥ 200 <input type="checkbox"/> 90 – 109
SBP(mmHg)	<input type="checkbox"/> <80 <input type="checkbox"/> 140 – 159 <input type="checkbox"/> 80 – 99 <input type="checkbox"/> 160 – 199 <input type="checkbox"/> 100 – 119 <input type="checkbox"/> ≥ 200 <input type="checkbox"/> 120 – 139
Creatinine (mg/dL)	<input type="checkbox"/> 0 – 0.39 <input type="checkbox"/> 1.6 – 1.99 <input type="checkbox"/> 0.4 – 0.79 <input type="checkbox"/> 2.0 – 3.99 <input type="checkbox"/> 0.8 – 1.19 <input type="checkbox"/> ≥ 4 <input type="checkbox"/> 1.2 – 1.59
CHF (Killip Class)	<input type="checkbox"/> I (No CHF) <input type="checkbox"/> II (Rales and/or jugular venous distention) <input type="checkbox"/> III (Pulmonary oedema) <input type="checkbox"/> IV (Cardiogenic shock)
Cardiac arrest at admission	<input type="checkbox"/> Yes <input type="checkbox"/> No
ST segment deviation	<input type="checkbox"/> Yes <input type="checkbox"/> No
Elevated cardiac enzymes/markers	<input type="checkbox"/> Yes <input type="checkbox"/> No



• At Discharge (to 6 months)⁸³

CATEGORIES	Options
Age (years)	<input type="checkbox"/> <30 <input type="checkbox"/> 60 – 69 <input type="checkbox"/> 30 – 39 <input type="checkbox"/> 70 – 79 <input type="checkbox"/> 40 – 49 <input type="checkbox"/> 80 – 89 <input type="checkbox"/> 50 – 59 <input type="checkbox"/> 90 – 100
Heart rate (bpm)	<input type="checkbox"/> 0 < 50 <input type="checkbox"/> 110 – 149 <input type="checkbox"/> 50 – 69 <input type="checkbox"/> 150 – 199 <input type="checkbox"/> 70 – 89 <input type="checkbox"/> ≥ 200 <input type="checkbox"/> 90 – 109
SBP(mmHg)	<input type="checkbox"/> <80 <input type="checkbox"/> 140 – 159 <input type="checkbox"/> 80 – 99 <input type="checkbox"/> 160 – 199 <input type="checkbox"/> 100 – 119 <input type="checkbox"/> ≥ 200 <input type="checkbox"/> 120 – 139
Creatinine (mg/dL)	<input type="checkbox"/> 0 – 0.39 <input type="checkbox"/> 1.6 – 1.99 <input type="checkbox"/> 0.4 – 0.79 <input type="checkbox"/> 2.0 – 3.99 <input type="checkbox"/> 0.8 – 1.19 <input type="checkbox"/> ≥ 4 <input type="checkbox"/> 1.2 – 1.59
CHF (Killip Class)	<input type="checkbox"/> I (No CHF) <input type="checkbox"/> II (Rales and/or jugular venous distention) <input type="checkbox"/> III (Pulmonary oedema) <input type="checkbox"/> IV (Cardiogenic shock)
Congestive HF	<input type="checkbox"/> Yes <input type="checkbox"/> No
In-hospital PCI	<input type="checkbox"/> Yes <input type="checkbox"/> No
In-hospital CABG	<input type="checkbox"/> Yes <input type="checkbox"/> No
Past history of MI	<input type="checkbox"/> Yes <input type="checkbox"/> No
ST segment depression	<input type="checkbox"/> Yes <input type="checkbox"/> No
Elevated cardiac enzymes/markers	<input type="checkbox"/> Yes <input type="checkbox"/> No

APPENDIX V: CHA₂DS₂ - VASc SCORE

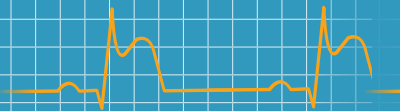
CATEGORIES	Options	Points
Age (years)	<input type="checkbox"/> < 65	0
	<input type="checkbox"/> 65 - 74	1
	<input type="checkbox"/> ≥ 75	2
Sex	<input type="checkbox"/> Male	0
	<input type="checkbox"/> Female	1
Congestive Heart Failure	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
Hypertension	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
Stroke/TIA	<input type="checkbox"/> Yes	2
	<input type="checkbox"/> No	0
History of Vascular disease	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0
Diabetes Mellitus	<input type="checkbox"/> Yes	1
	<input type="checkbox"/> No	0

Score:

- CHA₂DS₂ - VASc score 0 in men or 1 in women: low -risk – reasonable to omit anti-coagulation
- CHA₂DS₂ - VASc score 1 in men or 2 in women: moderate -risk – antiplatelet or anti-coagulation
- CHA₂DS₂ - VASc score ≥ 2 in men and ≥ 3 in women: moderate to high-risk and should be anti-coagulated.

Adapted from:

January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE et al 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. <https://doi.org/10.1016/j.hrthm.2019.01.024>



APPENDIX VI: Calculation of Creatine Clearance and GFR for drug dosing adjustments

Creatinine clearance (Cr Cl) is determined by the Cockcroft -Gault (CG) Equation whereas eGFR can be derived from various equations including most commonly, the CKD-EPI Creatinine (CKD -EPI) and Modification of Diet in Renal Disease Study (MDRD) Equations.

In a local population, CKD-EPI performs just as well as CKD-MDRD for GFR 60-89ml/min and better at the other GFR levels.⁵⁰⁷

Equations for Estimation of Renal Function

i. 2009 CKD-EPI creatinine equation =

$141 \times \min(\text{Scr}/k, 1)^\alpha \times \max(\text{Scr}/k, 1)^{-1.209} \times 0.993^{\text{Age}}$ [x 1.018 if female] [x 1.159 if black], where Scr is serum creatinine (in mg/dl), k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1

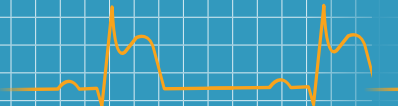
ii. Cockcroft -Gault Creatinine Clearance =

$\text{CrCl (ml/min/1.73 m}^2) = (140 - \text{age (yrs)}) \times \text{body weight (kg)}/\text{SCr (umol/l)} \times \text{Constant}$ where the constant is 1.23 in male or 1.04 in female

Available at: https://www.kidney.org/professionals/KDOQI/gfr_calculatorCoc

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25th November 2018.

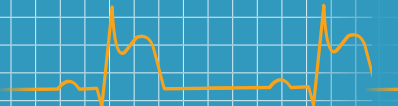
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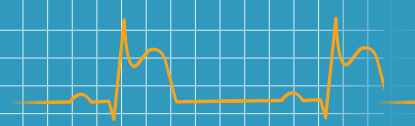
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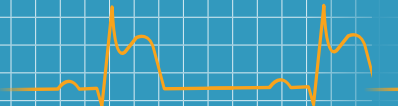
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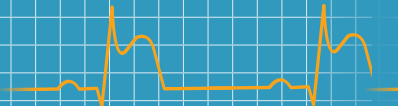
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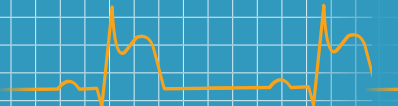
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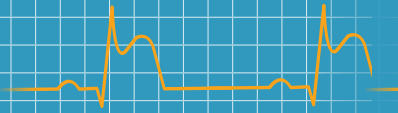
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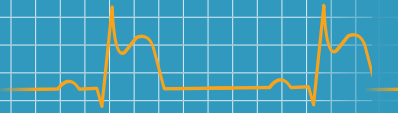
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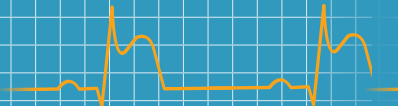
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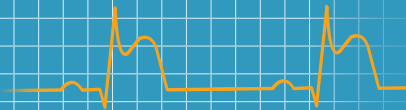
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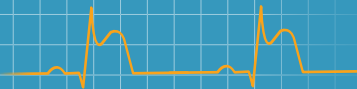
National Heart Association of Malaysia

D-13A-06, Menara SUEZCAP 1, KL Gateway
No.2 Jalan Kerinchi, Gerbang Kerinchi Lestari
59200 Kuala Lumpur

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