ACUTE CORONARY SINDROMES

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OBJECTIVES
Definition of ACS
Epidemiology
Etiologies
Pathophysiology
Clinical manifestations of the patient with ACSs:
Unstable angina(UA)
NSTEMI-AMI
STEMI-AMI
Assessement and Management
Treatment of Acute Coronary Syndromes
Conclusions
References

Definition Acute Coronary Syndromes describes a continuum of conditions that are associated with acute myocardial ischaemia as a result of interruption of the coronary blood supply. The syndrom represent a spectrum of disease ranging from unstable angina(UA) to non–ST-segment- elevation myocardial infarction(NSTEMI) and ST-segment- elevation myocardial infarction (STEMI)

Epidemiology of ACS. Significant changes in sosioeconomic status and life style in developing countries,and the rise in prevalence of major risk factors such as obesity, diabetes and advanced age, have led to a significant increase in the prevalence of cardiovascular disease; it is estimated to become the leading cause of death and disability woldwide.
Coronary heart disease(CHD) is a worldwide health epidemic, 30% of all deaths can be attributed to cardiovascular disease, of which more than half are caused by CHD.
The incidence of STEMI is dicreasing in many European countries; however, the incidence of NSTEMI – ACS is increasing.
Although in-hospital mortality from STEMI has been redused significantly by modern reperfusion therapy and improved secondary prophylaxis, the overoll 28- day mortality is virttually unchanged because about two thirds or those who die do so before hospital arrival, mostly from lethal arrhythmias triggered by ischemia. Acute coronary syndromes are the commonest cause of malignant arrhythmias leading to sudden cardiac death.The therapeutic goals are to treat acut life-threatening conditions,such as ventricular fibrillation(VF) or extreme bradycardia,and to preserve left ventricular function and prevent heart failure by minimising the extent of myocardial damage. Over 50 percent of these deths occur prior to arrival at the hospital. An acute coronary syndrome(ACS) due to a disrupted plaque is present in the majority of patients with adult cardiac arrest.More than half the patients with sudden cardiac death(SCD) have no prior symptoms; in 17% ,SCD is the first,last,and only symptom.
The best way of improving survival from an ischaemic attack is reducing the delay from symptom onset to first medical contact and targeted treatment started in the early out-of–hospital phase

Etiology of ACS.

Primary etiologies	Secondary etiologies
Coronary artery spasm **Disruption or erosion of atherosclerotic plaques** **Platelet aggregation or thrombus formation at the site of an atherosclerotic lesion**	**Increased myocardial oxygen demand** **Reduced myocardial blood flow** **Reduced myocardial oxygen delivery**

PATHOPHYSIOLOGY OF MYOCARDIAL ISCHEMIA

MAJOR DETERMINANTS OF MYOCARDIAL OXYGEN SUPPLAY AND DEMAND

SUPPLY:
Aortic diastolic presure
Coronary vascular resistance
Diastolic duration
DEMAND:
Heart rate
Wall tension:
Preload – left ventricular end diastolic pressure
Afterload – mean aortic pressure
Contractility

Myocardial ischemia results from imbalance between myocardial oxygen supply and demand.

Key points – pathophysiology

- The common underlying mechanism of acute coronary syndromes (ACS) is atherosclerotic plaque rupture or erosion, with differing degrees of superimposed thrombosis and distal embolization.
- Although atherosclerosis starts with the development of dysfunctional endothelium in the presence of cardiovascular risk factors early in life, the speed of progression is non-linear, unpredictable and varies markedly between individuals.
- A vulnerable plaque is prone to rupture or erosion and consists of a thin-capped fibroatheroma that is enriched in cholesterol debris, a large number of inflammatory cells (especially macrophages, some activated T cells), and smooth muscle cells.
- The major determinants of thrombus generation are those of the classic 'triad of Virchow': thrombogenicity of the exposed plaque material (plaque vulnerability), local flow disturbances (vessel vulnerability), and systemic thrombotic propensity (blood vulnerability).

- Mural platelet-rich 'white' thrombi most often incompletely block coronary blood flow and are present in unstable angina (UA) and non-ST-segment elevation myocardial infarction (NSTEMI).
- ST-segment elevation Ml (STEMI) is often characterized by the complete obstruction of coronary vessels by thrombi rich in red blood cells and fibrin, which overlay platelet-rich thrombi.

MORPHOLOGY of ATHEROTHROMBOSIS

Coronary atherosclerosis is a diffuse process with segmental lesions called coronary plaque that gradually enlarge and extend, causing variable degrees of coronary artery occlusion.
Coronary arteries are usually closed about 70% before they cause symptoms and are considered for percutaneous coronary intervention (PCI) or surgery.
Plaques can be classified as stable and unstable or vulnerable on the basis of their lipid content,thickness of the cap that covers and separates them from the arterial lumen,and the degree of inflammation in the plaque itself.(FIGURE 1)
Stable and Unstable Plaque A stable intracoronary plaque has a lipid core separated from the arterial lumen by a thick fibrous cap.Stable plaques have less lipid,and the thick cap makes them resistant to fissuring and formation of thrombi.

Over time the lumen of the vessel becomes progressively narrower, leading to flow limitations, supply-demand imbalance, and exertional angina. Stable plaques may progress to complete occlusion but do not usually cause STEMI because of the development over time of collateral supply to the myocardium at risk , thus preventing or limiting Ml.

Vulnerable Plaque(Unstable Plaque) A "vulnerable" intracoronary plaque has a lipid-rich core combined with an active inflammatory process that makes the plaque soft and prone to rupture. These plaques infrequently restrict blood flow enough to cause clinical angina.

3. Inflammation is often found in the plaque. Inflammatory processes are concentrated in the leading edge impacted by coronary blood flow. It is here that most plaque ruptures occur. A plaque that is inflamed and prone to rupture is called unstable.

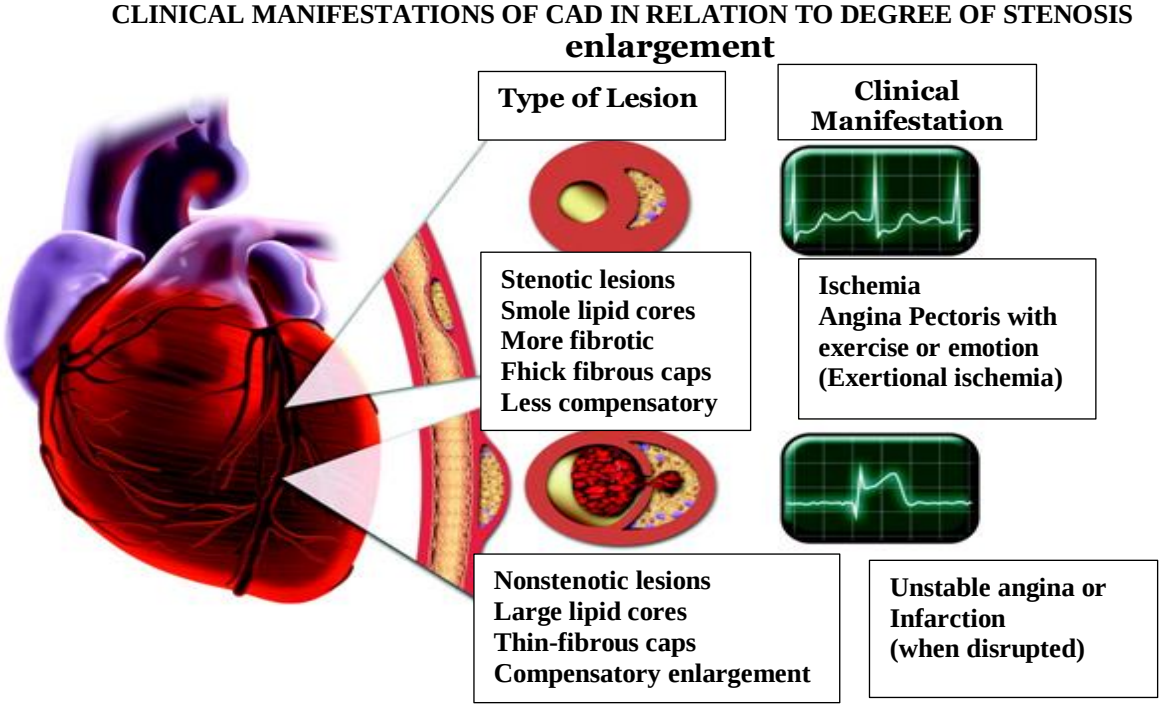


Fig. 1 Pathophiziology of coronary artery disease
Libby P, Theroux P. Circulation 2005; 111 (25): 3481-3488

The ACS were defined in an atempt to stratify patients with chest pain of cardiac origin in order to distinguish high – risk patients who require urgent intervention.
They comprise(Figure 2):
Non – ST –segment elevation MI (NSTEMI):
Unstable angina (UA):
ST – segment elevation(or new/presumed new left bundle branch block LBBB) MI (STEMI):

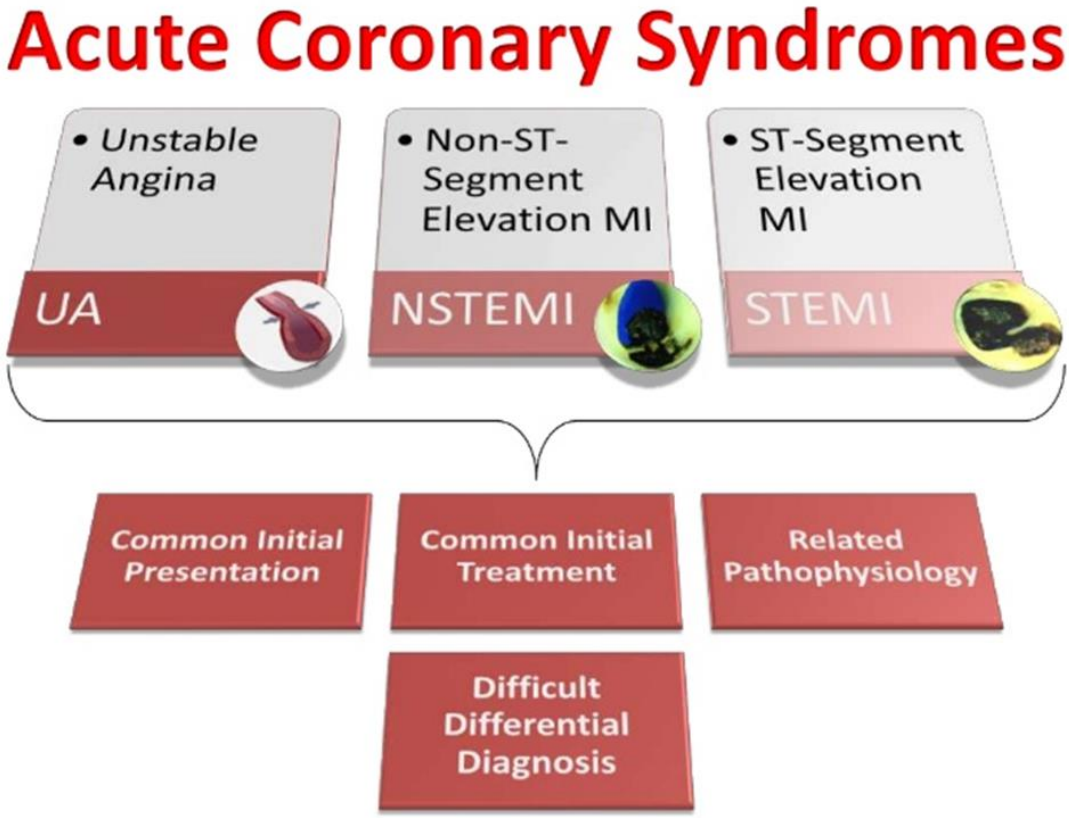


Fig.2.ACUTE CORONARY SYNDROME

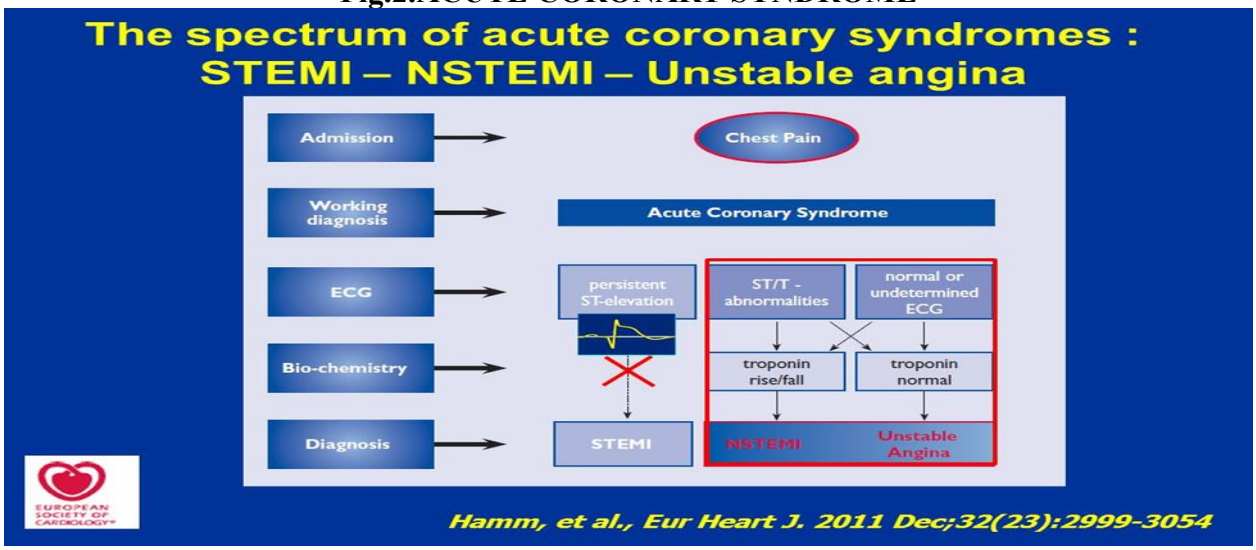


Fig. 3.The spectrum of acute coronary syndromes

Classification of ACS

Canadian Cardiovascular Society
Functional Classification of Angina

Class	Characteristics
Class I	No angina with ordinary activity.Angina with strenuous activity
Class II	Angina during ordinary activity ,e.g. walking up hills,walking rapidly upstairs,with mild limitation of activities
Class III	Angina with low levels of activity,e.g. walking 50-100 yards on the flat, walking up one flight of stairs, with marked restriction of activities.
Class IV	Angina at rest or with any level of exercise

Unstable Angina(UA)

New-Onset Angina	New-onset angina of at least CCS Class III severity.
Increasing (crescendo) Angina	Previously diagnosed angina that has become distinctly more frequent,longer in duration,or lower in threshold(i.e.increased by≥1 CCS class to at least CCS Class III severity).
Postinfarction Angina	Patients with recent myocardial infarction(within 2 wk) in whom biomarkers of myocardial necrosis have returned within normal range
Prinzmetal (Variant) angina	Atypical ischemic coronary syndrome characterized by sudden onset angina occurring almost exclusively at rest, particularly in the first hours of the day, associated with ST-segment elevation on the ECG caused by a focal spasm of a coronary artery.
Rest angina	Anginal symptoms present at rest>20min

WILLIAM HEBERDEN ON ANGINA PECTORIS, 1772

"But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it and the sense of strangling and anxiety with which it is attended, may make it not improperly be called angina pectoris. Those who are afflicted with it, are seized while they are walking (more especially if it be uphill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life if it were to increase or to continue; but the moment they stand still, all this uneasiness vanishes. In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated in the upper part, sometimes in the middle, sometimes in the bottom of the os. sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxism. Males are more liable to this disorder, especially such as have past their fiftieth year. After it has continued a year or more, it will not cease so instantaneously upon standing still; and it will come on not only when the

persons are walking, but when they are lying down, especially if they lie on the left side and oblige them to rise out of their beds. In some inveterate cases it has been brought on by the motion of a horse, or a carriage, and even by swallowing, coughing, going to stool or speaking, or any disturbance of mind.

Such is the most usual appearance of this disease; but some varieties may be met with. Some have been seized while they were standing still, or sitting, also upon first waking out of sleep; and the pain sometimes reaches to the right arm, as well as to the left and even down to the hands, but this is uncommon; in a very few instances the arm has at the same time been numbed and swelled. In one or two persons the pain has lasted some hours or even days; but this happened when the complaint has been of long standing, and thoroughly rooted in the constitution; once only the very first attack continued the whole night.

I have seen nearly a hundred people under this disorder, of which number there have been three women and one boy twelve years old. All the rest were men near or past the fiftieth year of their age…

The termination of the angina pectoris is remarkable. For if no accident interferes, but the disease goes on to its height, the patients all suddenly fall down, and perish almost immediately. Of which indeed their frequent faintness and sensations as if all the powers of life were failing, afford no obscure intimation."

ACC/AHA/ACP-ASIM CLINICAL CLASSIFICATION OF CHEST PAIN

Type	Definition
Typical angina **Atipical angina (probable)** **Noncardiac chest pain**	**1.Substernal chest discomfort with characteristic quality and duration** **2.Provoked by exertion or emotional stress** **3.Relieved by rest or sub-lingual nitrates** **Pain with≥2 of above features** **One or none of the typical anginal characteristics**

ACC-American College of Cardiology; AHA – American Heart Association;
ACP – American College of Physicians;ASIM – American Society of Internal Medicine.

Clinical presentation and history The most important factors to consider when taking the patient's history are the nature of the angina symptoms, a history of coronary artery disease (CAD) (in up to 80% of patients), male gender, older age and a number of traditional cardiovascular risk factors such as smoking, family history, hyperlipidemia, diabetes and hypertension.

Chest pain

The hallmark symptom of ACS is pain in the center (substernal) or left of the chest, with radiation to the left shoulder and arm, neck and jaw ; pain in the arm is usually on the inner (ulnar) aspect. Most often, pain in the chest feels like a pressure or heaviness lasting for more than 20 minutes. It may or may not be severe. Chest pain in the setting of ST-segment elevation myocardial infarction usually occurs at rest, while in the setting of unstable angina/non-ST-segment elevation MI chest pain often occurs during activity and stops at rest.

COMMON SITES FOR ANGINAL DICOMFORT

A. Upper part of chest.

B. Beneath the sternum radiating to neck and jaw.
C. Beneath the sternum radiating down left arm.
D.Epigastric.
E. Epigastric radiating to the neck,jaw,and arms.
F. Neck and jaw(common in women).
G. Left shoulder and arm(common in older adults and women).
H. Interscapular(common in older adult and women).

Common Terms Patients Use to Describe Angina

Described as sensation of

A band across my chest
A vise tightening around my chest
A weight in the center of my chest
Burning
Bursting
Constricting
Crushing
Cramping,
Grip – like
Heaviness
tightness,
Pressing
Aching
Squeezing
Strangling
Suffocating

Other typical symptoms(anginal equivalents) of myocardial ischemia:

- Isolated dyspnea
- Difficulty breathing
- Dizzines
- Dysrhythmias
- Fatigue
- Isolated arm or jaw pain
- Palpitations
- Syncope or near - syncope
- Weakness
- Diaphoresis
- Unexplained nausea or vomiting

ATYPICAL ST- ELEVATION MYOCARDIAL INFARCTION SIGNS AND SYMPTOMS

Acute indigestion
Atypical location of the pain
Central nervous system manifestations, resembling those of stroke as a result of a sharp reduction in cardiac output in a patient with cerebral arteriosclerosis
Classic angina pectoris without a particularly severe or prolonged episode.
Heart failure
Overwhelming weakness
Peripheral embolization
Sudden mania

Syncope

OLDER ADULTS, DIABETIC INDIVIDUALS , WOMEN,PATIENTS WITH PRIOR CARDIAC SURGERY AND DURING THE IMMEDIATE POSTOPERATIVE PERIOD MAY HAVE ATYPICAL SYMPTOMS

Older Adults

Dispnea

Shoulder or back pain
Weakness
Fatigue
Syncope
A change in mental status
Unexplained nausea,and abdominal or epigastric discomfort
More severe preexisting conditions,such as hypertension,heart failure,or a previous acute MI.

DIABETIC INDIVIDUALS

Generalized weakness
Syncope
Lightheadedness
Change in mental status.

WOMEN

Prodromal chest dyscomfort,dizziness or fainting
Unusual fatigue,sweating,arm or shoulder pain,and weakness
Sleep disturbances
Dyspnea
Nausea or vomiting,indigestion

MYOCARDIAL INFARCTION - CLASSIFICATION

Anatomic classification	Description	
Transmural	Ischemic necrosis of the full thickness of the affected muscle segment(s) extending from the endocardium through the miocardium	
Nontransmural	Area of ischemic necrosis is limited to the endocardium or endocardium and myocardium,it does not extend through the full thickness of myocardial wall segment(s).	
Classification by Size - Description		
Microscopic	Focal necrosis	
Small	Less than 10% of the left ventricular(LV) myocardium	
Moderate	10% to30% of the left ventricular myocardium	
Large	More than 30% of the left ventricular miocardium	
Pathological Classification	Time frame	Description
Evolving	Less than 6 hours	Minimal or no polymorphonuclear leukocytes may be seen
Acute	6 hours to 7 days	Presence of polymorphonuclear leukocytes

Healing	**7 to28 days**	**Presence of mononuclear cells and fibroblasts, absence of polymorphonuclear leukocytes**
Healed	**29 days or more**	**Scar tissue without cellular infiltration**
Classification by Location		
Anterior	**Inferior**	**Septal**
Lateral	**Inferobazal (posterior)**	**Right ventricular**

Killip Classification for Patients with ST – Segment Elevation Myocardial Infarction

	Clinical presentation	Mortalitate	Mortalitatea la 30 de zile (GUSTO-1) (%)
Killip I	**No congestive heart failure, rales**	**8.4%**	**5,1**
Killip II	**Mild congestive heart failure, rales over <50%of lung fields, congestion on chest radiography**	**30,5%**	**13,6**
Killip III	**Pulmonary edema, rales over >50% of lung fields, congestion on chest radiography**	**44%**	**32,2**
Killip IV	**Cardiogenic Shock**	**88-100%**	**57,8**

Subendocardial injury occurs within 20 to 40 minutes.Death of subendocardial tissue occurs in about 30 minutes and necrosis extends to about half of the myocardial wall by 2 hours.By 6 hours,necrosis involves about 90% of the myocardial wall and is complete by 24 hours.Healing begins within 24 to 72 hours.Within 2 to 8 weeks of the infarction,the necrotic tissue has been replaced by fibrous tissue.

The ACC/AHA guidelines list the following as pain descriptions that are not characteristic of myocardial ischemia

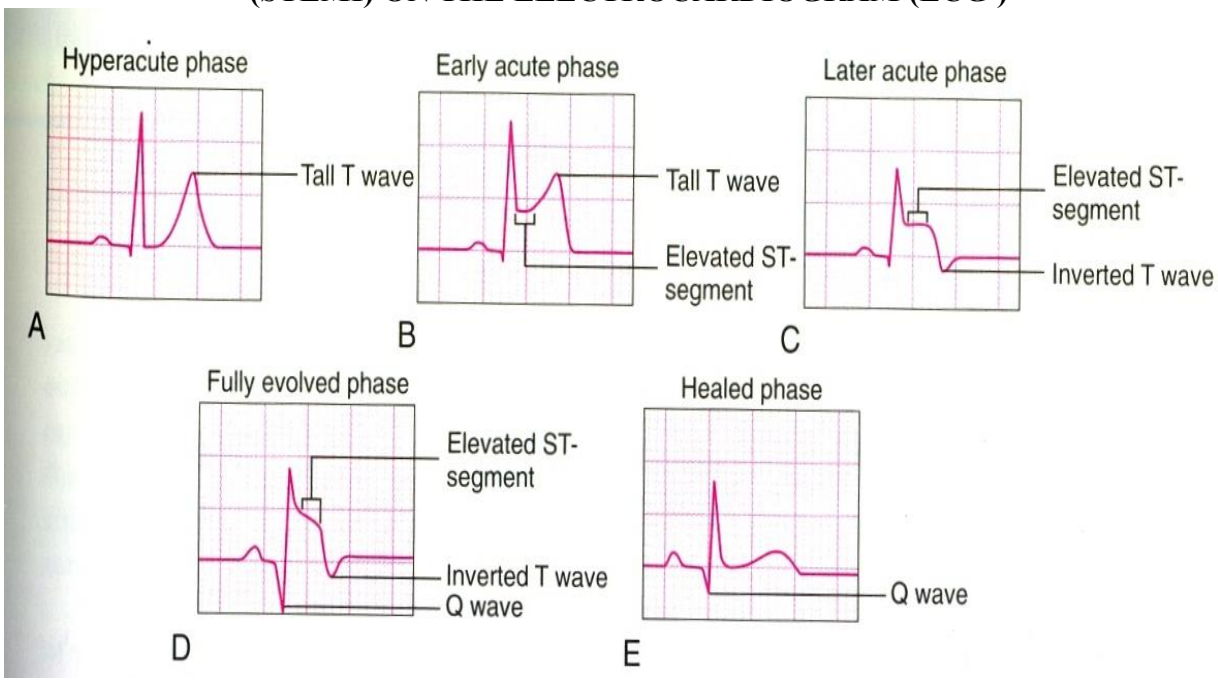
Pleuritic pain(i.e. sharp pain brought on by respiratory movements or cough)
Primary or sole location of discomfort in the middle or lower abdominal region
Pain that may be localized at the tip of one finger,particularly over the left ventricular apex
Pain reproduced with movement or palpation of the chest wall or arms
Constant pain that persists for many hours
Very brief episodes of pain that last a few seconds or less
Pain that radiates into the lower extremities

ECG findings in ACS

I Lateral	aVR	V1 Septal	V4 Anterior
II Inferior	aVL Lateral	V2 Septal	V5 Lateral
III Inferior	aVF Inferior	V3 Anterior	V6 Lateral

SITE	FACING	RECIPROCAL
SEPTAL	V1, V2	NONE
ANTERIOR	V3, V4	NONE
ANTEROSEPTAL	V1, V2, V3, V4	NONE
LATERAL	I, aVL, V5, V6	II, III, aVF
ANTEROLATERAL	I, aVL, V3, V4, V5, V6	II, III, aVF
INFERIOR	II, III, aVF	I, aVL
POSTERIOR	NONE	V1, V2, V3, V4

THE EVOLVING PATTERN of ST-ELEVATION MYOCARDIAL INFARCTION (STEMI) ON THE ELECTROCARDIOGRAM (ECG)



CARDIAC MARKER FOR ACUT MYOCARDIAL INFARCTION

Cardiac Marker	Initial Appearance (hr.)	Mean Time to Peak	Return to Normal Range
Myoglobin	1 - 4	6 – 7h	24h
MB – CK tissue isoform	2-6	18h	Unknown
Cardiac Troponin I (cTnI)	3-12	24h	5-10 d
CardiacTroponina T (cTnT)	3-12	12h-48h	5-14d
MM – CK tissue isoform	1-6	12h	38h
Creatine-kinase-MB(CK-MB)	3 – 12	24h	48-72h
Lactate dehydrogenase	8-12	24-48h	10-12d

Cardiac biomarkers:

- **Troponin:**
  - **Myocardial troponin I (TnI) and troponin T (TnT) are elevated as early as 3 hours, but may stay elevated for up to 10-14 days.**

Creatine kinase (CK):

- **CK-MB is myocardial specific, usually elevated as early as 3 hours and peaking within 24 hours; it normalizes 2-3 days after injury.**
- **Myoglobin:**
- **Myocardial myoglobin is not distinguishable from skeletal muscle myoglobin and thus is not a useful marker in ACS.**
- **• Initially rises 1-2 hours post event, peaks at 5-7 hours, and normalizes by 24 hours.**

STEMI Chain of Survival

The STEMI Chain of Survival described by the AHA is similar to the Chain of Survival for sudden cardiac arrest. It links actions to be taken by patients, family members, and healthcare providers, to maximize STEMI recovery.

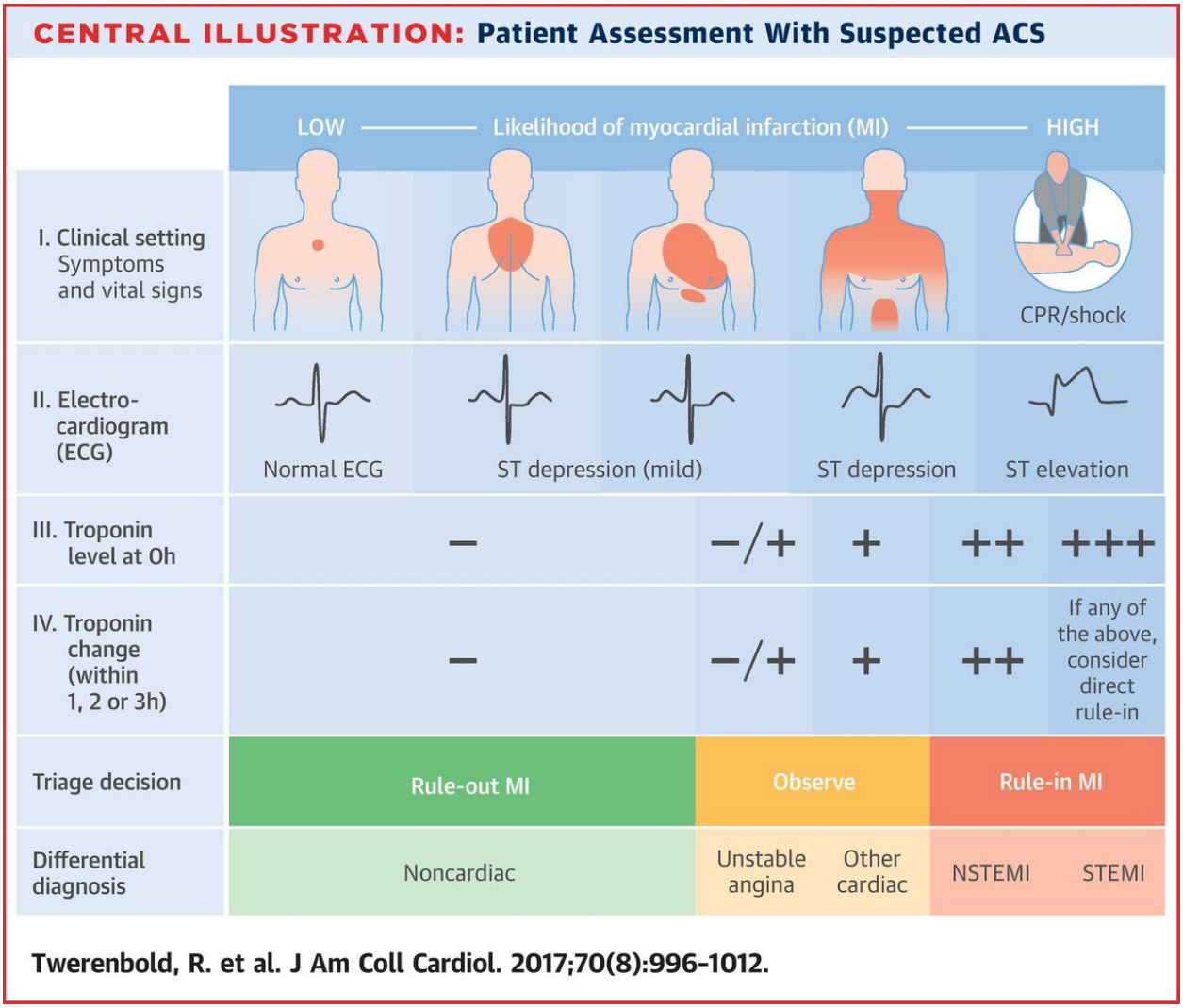
Rapid recognition and reaction to STEMI warning signs	**Rapid EMS dispatch and rapid EMS system transport and prearrival notification to the receiving hospital**	**Rapid assessment and diagnosis in the ED (or cath. lab)**	**Rapid treatment**

Unless allergies or contraindications exist, 4 agents may be considered in patients with ischemic-type chest discomfort:

- Oxygen if hypoxemic (O_2 % less than 90%) or signs of heart failure
- Aspirin
- Nitroglycerin
- Opiate (eg, morphine if ongoing discomfort or no response to nitrates)

Because these agents may have been given out of hospital, administer initial or supplementary doses as indicated. (See the discussion of these drugs in the previous section, EMS Assessment, Care, and Hospital Preparation.)

Treatment of ACS involves the initial use of drugs to relieve ischemic discomfort, dissolve clots, and inhibit thrombin and platelets.



Twerenbold, R. et al. J Am Coll Cardiol. 2017;70(8):996-1012.

Adjunctive Treatments

Other drugs are useful when indicated in addition to oxygen, sublingual or spray nitroglycerin, aspirin, morphine, and fibrinolytic therapy. These include

- Unfractionated or low-molecular-weight heparin
- Bivalirudin
- $P2Y_{12}$ inhibitors
- IV nitroglycerin
- ß-Blockers
- Glycoprotein IIb/IIIa inhibitors

Oxygen EMS providers should administer oxygen if the patient is dyspneic, is hypoxemic, has obvious signs of heart failure, has an arterial oxygen saturation less than 90%, or the oxygen saturation is unknown. Providers should titrate oxygen therapy to a noninvasively monitored oxyhemoglobin saturation 94-98% or greater.

Aspirin A dose of 160 to 325 mg of non-enteric-coated aspirin causes immediate and near-total inhibition of thromboxane A, production by inhibiting platelet cyclooxygenase (COX-1). Platelets are one of the principal and earliest participants in thrombus formation. This rapid inhibition also reduces coronary reocclusion and other recurrent events independently and after fibrinolytic therapy.

If the patient has not taken *aspirin* and has no history of true aspirin allergy and no evidence of recent Gl bleeding, give the patient aspirin (160 to 325 mg) to chew. In the initial hours of an ACS. aspirin is absorbed better when chewed than when swallowed, particularly if morphine has been given.

Nitroglycerin Nitroglycerin is a venodilator and needs to be used cautiously or not at all in patients with inadequate ventricular preload. These situations include:

1. Inferior wall Ml and RV infarction. RV infarction may complicate an inferior wall Ml. Patients with acute RV infarction are very dependent on RV filling pressures to maintain cardiac output and blood pressure. If RV infarction cannot be ruled out, providers must use caution in administering nitrates to patients with inferior STEMI. If RV infarction is confirmed by right-sided precordial leads or clinical findings by an experienced provider, nitroglycerin and other vasodilators (morphine) or volume-depleting drugs (diuretics) are contraindicated as well.
2. Hypotension, bradycardia, or tachycardia. Avoid use of nitroglycerin in patients with hypotension (SBP less than 90 mm Hg), marked bradycardia (less than 50/min), or tachycardia.
3. Recent phosphodiesterase inhibitor use. Avoid the use of nitroglycerin if it is suspected or known that the patient has taken sildenafil or vardenafil within the previous 24 hours or tadalafil within 48 hours. These agents are generally used for erectile dysfunction or in cases of pulmonary hypertension and in combination with nitrates may cause severe hypotension refractory to vasopressor agents.

Indications for intiation of IV nitroglycerin in STEMI are:
Recurrent or continuing chest discomfort unresponsive to sublingual or spray nitroglycerin
Pulmonary edema complicating STEMI

Hypertension complicating STEMI .

Opiates Give morphine for chest discomfort unresponsive to sublingual or spray nitroglycerin if authorized by protocol or medical control. Morphine is indicated in STEMI when chest discomfort is unresponsive to nitrates. Use morphine with caution in NSTE-ACS because of an association with increased mortality.

Morphine may be utilized in the management of ACS because it

Produces central nervous system analgesia, which reduces the adverse effects of neurohumoral activation, catecholamine release, and heightened myocardial oxygen demand

Produces venodilation, which reduces LV preload and oxygen requirements

Decreases systemic vascular resistance, thereby reducing LV afterload

Helps redistribute blood volume in patients with acute pulmonary edema

Remember, morphine is a venodilator. Like nitroglycerin, use smaller doses and carefully monitor physiologic response before administering additional doses in patients who may be preload dependent. If hypotension develops, administer fluids as a first line of therapy. Unless contraindicated, initial therapy with oxygen if needed, aspirin, nitrates, and, if indicated, morphine is recommended for all patients suspected of having ischemic chest discomfort.

The major contraindication to nitroglycerin and morphine is hypotension, including hypotenston from an RV infarction. The major contraindications to aspirin are true aspirin allergy and active or recent Gl bleeding.

Review the initial 12-lead ECG and classify patients into 1 of the 3 following clinical groups.

The First 10 Minutes in ED

Assessment and stabilization of the patient in the first 10 minutes should include the following:

- Check vital signs and evaluate oxygen saturation.
- Establish IV access.
- Take a brief focused history and perform a physical examination.
- Complete the fibrinolytic checklist and check for contraindications, if indicated.
- Obtain a blood sample to evaluate initial cardiac marker levels, electrolytes, and coagulation.
- Obtain and review portable chest x-ray (less than 30 minutes after the patient's arrival in the ED). This should not delay fibrinolytic therapy for STEMI or activation of the PCI team for STEMI.

Note: The results of cardiac markers, chest x-ray, and laboratory studies should not delay reperfusion therapy unless clinically necessary, eg, suspected aortic dissection or coagulopathy.

Antiplatelet agents:

Antiplatelet Agents

Oral Antiplatelet Therapy	
Aspirin	Initial dose of 162–325 mg nonenteric formulation followed by 75–162 mg/day of an enteric or a nonenteric formulation
Clopidogrel	Loading dose of 300-600 mg followed by 75 mg/day
Prasugrel	Pre-PCI: Loading dose 60 mg followed by 10 mg/day

Intravenous Antiplatelet Therapy	
Abciximab	0.25 mg/kg bolus followed by infusion of 0.125µ g/kg per min (maximum 10µ g/min) for 12 to 24 hour
Eptifibatide	180µ g/kg bolus followed by infusion of 2.0µ g/kg per min for 72 to 96 hour
Tirofiban	0.4µ g/kg per min for 30 min followed by infusion of 0.1µ g/kg per min for 48 to 96 hour

Anticoagulant:

Anticoagulants

Drug	Indication	Adverse Side Effects	Monitoring
Unfractionated Heparin	STEMI, NSTE ACS, PCI ** For UA/ NSTEMI give for at least 48 hours if conservative management chosen	Bleeding, HIT	aPTT until target or change in dose. CBC , HIT if indicated
Enoxaparin		Bleeding, HIT Avoid if severe bleeding risk	CBC and Scr, HIT if indicated. Avoid if CrCl<15
Fondaparinux	STEMI, NSTEMI (Not well studied in pts with PCI)	Bleeding	CBC and Scr
Bivalirudin	NSTE ACS, PCI	Bleeding	Direct thrombin inhibition (DTI), CBC and Scr
GP IIb \ IIIa inhibitors: Abciximab Tirofiban Eptifibitide	With PCI: Abciximab ACS: Epitifibitide Tirofiban	Bleeding, Acute profound thrombocytopenia	Baseline Scr and daily (for eptifibitide and tirofiban) Daily CBC (with emphasis on Plt count) 4hrs after initiation
For all above: Monitoring for clinical signs of bleeding			

Beta blockers:

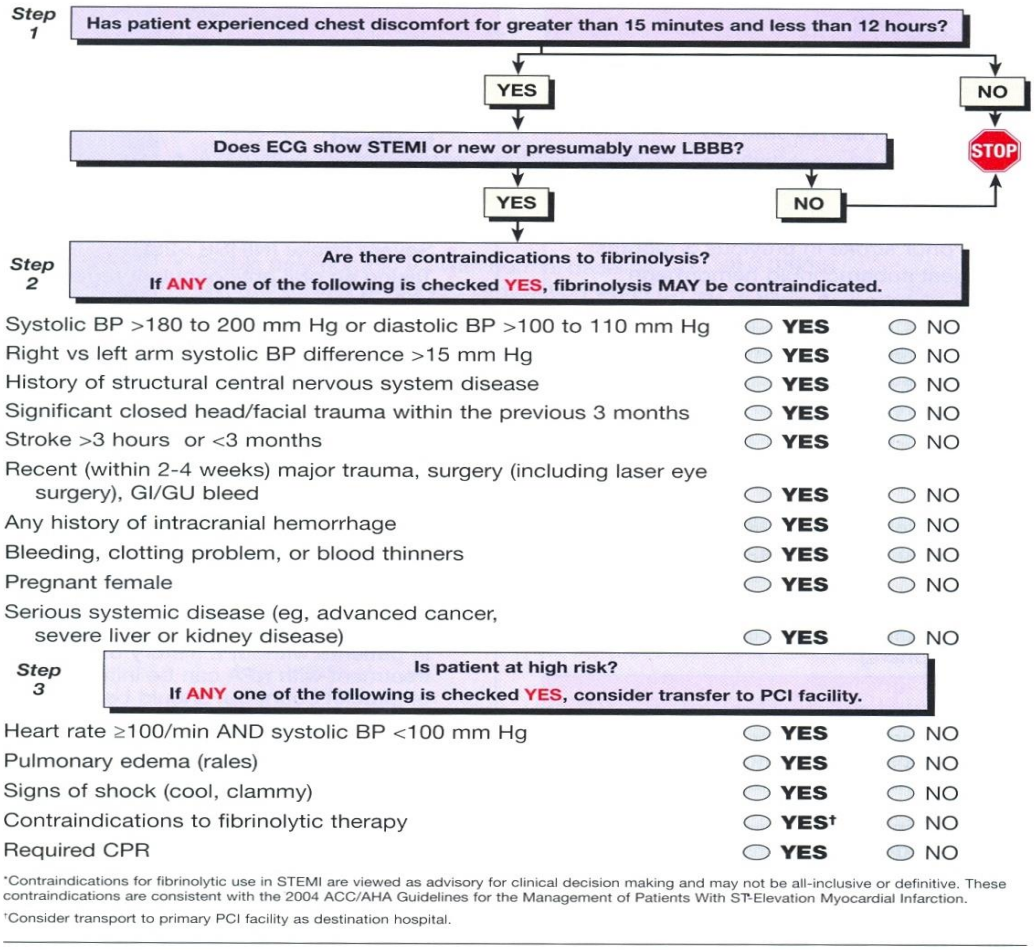
Indications for beta blockers

- Angina pectoris
- Atrial fibrillation
- Cardiac arrhythmia
- Congestive heart failure
- Essential tremor
- Glaucoma
- Hypertension
- Migraine prophylaxis
- Mitral valve prolapse
- Myocardial infarction
- Phaeochromocytoma, in conjunction with α-blocker
- Symptomatic control (tachycardia, tremor) in anxiety and hyperthyroidism

Table 1. Medications for the Treatment of Acute Coronary Syndrome *(continued)*

Therapy	*Recommendations for STEMI*	*Recommendations for NSTE-ACS**
Beta blockers		
Carvedilol, oral (Coreg)	6.25 mg twice daily, titrate up to 25 mg as tolerated	Same dosing and contraindications as for STEMI with all beta blockers
Metoprolol, IV	5 mg every five minutes as tolerated, up to three doses	
Metoprolol, oral (Lopressor)	25 to 50 mg every six to 12 hours, eventually transitioning to twice daily or daily	
	Contraindications to beta-blocker therapy include signs of heart failure, low output state, and risk of cardiogenic shock	

Acute Coronary Syndromes: Fibrinolytic Checklist for STEMI*



Early Reperfusion Therapy

Rapidly identify patients with STEMI and quickly screen them for indications and contraindications to fibrinolytic therapy by using a fibrinolytic checklist if appropriate. The first qualified physician who encounters a patient with STEMI should interpret or confirm the 12-lead ECG. determine the risk/benefit of reperfusion therapy, and direct administration of fibrinolytic therapy or activation of the PCI team. Early activation of PCI may occur with established protocols. The following time frames are recommended:

- For ***PCI,*** this goal for ED door-to-balloon inflation time is 90 minutes. In patients presenting to a non-PCI-capable hospital, time from first medical contact to device should be less than 120 minutes when primary PCI is considered.
- If fibrinolysis is the intended reperfusion. an ED door-to-needle time (needle time is the beginning of infusion of a fibrinolytic agent) of 30 minutes is the medical system goal that is considered the longest time acceptable. Systems should strive, to achieve the shortest time possible.

- Patients who are ineligible for fibrinolytic therapy should be considered for transfer to a PCI facility regardless of delay. The system should prepare for a door-to-departure time of 30 minutes when a transfer decision is made.

Adjunctive treatments may also be indicated.

Use of PCI

The most commonly used form of PCI is coronary intervention with stent placement.

Optimally performed primary PCI is the preferred reperfusion strategy over fibrinolytic administration. Rescue PCI is used early after fibrinolytics in patients who may have persistent occlusion of the infarct artery (failure to reperfuse with fibrinolytics), although this term has been recently replaced and included by the term pharmacoinvasive strategy. P has been shown to be superior to fibrinolysis in the combined end points of death, stroke and reinfarction in many studies for patients presenting between 3 and 12 hours after onset. However, these results have been achieved in experienced medical settings with skilled providers (performing more than 75 PCIs per year) at a skilled PCI facility (performing more than 200 PCIs for STEMI with cardiac surgery capabilities).

Considerations for the use of PCI include the following:

- PCI is the treatment of choice for the management of STEMI when it can be performed effectively with a door-to-balloon time of less than 90 minutes from first medical contact by a skilled provider at a skilled PCI facility.
- Primary PCI may also be offered to patients presenting to non-PCI-capable centers if PCI can be initiated promptly within 120 minutes from first medical contact. The TRANSFER AMI (Trial of Routine Angioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction) trial supports the transfer of high-risk patients who receive fibrinolysis in a non-PCI center within 12 hours of symptom onset to a PCI center within 6 hours of fibrinolytic administration to receive routine early coronary angiography and PCI if indicated.
- For patients admitted to a hospital without PCI capabilities, there may be some benefit associated with transfer for PCI versus administration of on-site fibrinolytics in terms of reinfarction, stroke, and a trend to lower mortality when PCI can be performed within 120 minutes of first medical contact. •
- PCI is also preferred in patients with contraindications to fibrinolytics and is indicated in patients with cardiogenic shock or heart failure complicating

Use of Fibrinolytic Therapy

A fibrinolytic agent or "clot-buster" is administered to patients with J-point ST-segment elevation greater than 2 mm (0.2 mV) in leads V_2 and V_3 and 1 mm or more in all other leads or by new or presumed new LBBB (eg, leads III, aVF; leads V_3, V_4; leads I and aVL) without contraindications. Fibrin-specific agents are effective in achieving normal flow in about 50% of patients given these drugs. Examples of fibrin-specific drugs are rtPA, reteplase, and tenecteplase. Streptokinase was the first fibrinolytic used widely, but it is not fibrin specific.

Considerations for the use of fibrinolytic therapy are as follows:

- In the absence of contraindications and in the presence of a favorable risk-benefit ratio, fibrinolytic therapy is one option for reperfusion in patients with STEMI and onset of symptoms within 12 hours of presentation with qualifying ECG findings and if PCI is not available within 90 minutes' of first medical contact.
- In the absence of contraindications, it is also reasonable to give fibrinolytics to patients with onset of symptoms within the prior 12 hours and ECG findings consistent with true posterior Ml. Experienced providers will recognize this as a condition where ST-segment depression in the early precordial leads is equivalent to ST-segment elevation in others. When these changes are associated with other ECG findings, it is suggestive of a "STEMI" on the posterior wall of the heart.
- Fibrinolytics are generally not recommended for patients presenting more than 12 hours after onset of symptoms. But they may be considered if ischemic chest discomfort continues with persistent ST-segment elevation.
- Do not give fibrinolytics to patients who present more than 24 hours after the onset of symptoms or patients with ST-segment depression unless a true posterior MI is suspected.

Fibrinolytic agents Used in ST elevation MI	
Streptokinase	1.5 million intravenous over 30-60 mins
Alteplase (tPA)	a 15-mg bolus, then 0.75 mg/kg (up to 50 mg) IV over the initial 30 minutes, and 0.5 mg/kg (up to 35 mg) over the next 60 minutes
Reteplase (rPA)	two 10-U boluses 30 minutes apart
Tenecteplase (TNK-tPA)	IV Bolus adjusted for weight (30mg if < 60 kg; 35mg if 60-70 kg; 40 mg if 70-80 kg, 45mg if 80-90 kg; 50mg if > 90 kg)

CONCLUSIONS

- Acute coronary syndrome occurs as a spectrum of diseases that includes unstable angina pectoris, non-ST- segment elevation myocardial infarction, and ST-segment elevation myocardial infarction.
- The common underlying mechanism of acute coronary syndromes (ACS) is atherosclerotic plaque rupture or erosion, with differing degrees of superimposed thrombosis and distal embolization.
- ACS is classically manifested as chest tightness or pressure with associated dyspnea, nausea,and diaphoresis.
- ACS is diagnosed through a careful history and analysis of the 12-lead ECG and cardiac biomarkers.
- A 12-lead ECG is the key investigation for assessment of an ACS. Myocardial distress is manifest in the ST- segments of the ECG; ST- segment depression indicates myocardial ischemia whereas ST- segment elevation (STF.) indicates acute myocardial infarction (>1 mm in two contiguous standard limb leads or >2 mm in two contiguous precordial leads).
- Cardiac biomarkers: Myocardial troponin I (TnI) and troponin T (TnT) are elevated as early as 3 hours, but may stay elevated for up to 10-14 days.
- Creatine kinase (CK):CK-MB is myocardial specific, usually elevated as early as 3 hours and peaking within 24 hours; it normalizes 2-3 days after injury.
- .Immediate complications of ACS include congestive heart failure, cardiogenic shock, and rhythm disturbances, both tachyarrhythmias and bradyarrhythmias.
- Risk assessment scores and clinical prediction algorithms using clinical history,phisical examination, ECG, and cardiac troponins have been developed to help identify patients with ACS at increased risk of adverse outcomeGRACE and TIMI risk scores are the most commonly used.
- Treatment of the spectrum of ACS involves oxygen, aspirin, beta-lockers,nitrates and anticoagulants,and also benefit from clopidogrel and glycoprotein IIb/IIIa receptor inhibitors.
- Patients with ST-segment elevation myocardial infarction require early revascularization therapy with either fibrinolysis or primary percutaneous coronaryintervention.

- The best way of improving survival from an ischaemic attack is reducing the delay from symptom onset to first medical contact and targeted treatment started in the early out-of–hospital phase

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