Coronary Heart Disease
Myocardial Infarction

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What is ischemic heart disease

Ischemic heart disease (IHD) = coronary artery disease (CAD) = coronary heart disease (CHD)

- It is the most significant health disorder in the industrialized world

CAD may present as
- Subclinical
- Silent (or unspecific such as new-onset breathlessness or fatigue)
- **Stable CAD** (stable angina pectoris – from the Latin words ‘angere’, meaning to choke or throttle, and ‘pectus’, meaning chest
- Unstable CAD = **acute coronary syndromes (ACS) = unstable angina pectoris + myocardial infarction** (STEMI or NSTEMI) = the most serious consequences of CAD
- Sudden cardiac death
What is ischemic heart disease

Ischemic heart dis. = coronary artery dis. = coronary heart dis.

Due to changes in the coronary arteries

Ischemia occurs: insufficient blood supply (and drain):

Demand vs. supply

Oxygen and nutrients and electrolytes

Cleavage of metabolic products and CO₂

Affects the heart

Characterized by etiology and pathophysiology: it is a disease, not a syndrome in contrast to ACS
Ischemic heart disease

- It is a condition in which blood flow within the coronary arteries is impaired => insufficient delivery of oxygen and nutrients to meet the demands of the myocardium
- In stable disease => particularly apparent on exertion

- Most common cause
  - **atheroma** – lipid-rich sub-intimal deposits in the coronary vasculature =>
    - narrowing of the vessel lumen (stenosis)
    - interruption of coronary blood flow
    - some degree of myocardial ischaemia as a result of inadequate oxygen supply to the heart muscle cells

- Rare causes
  - **vasospasm** (spasm in the small muscle fibres within the artery)
  - coronary artery **embolism** (material from another site, infected material or air, or a clot)
  - **vasculitis** (inflammation or infection of the vessel)
  - **aneurysm** (weakness in the vessel wall)
Underlying condition

In stable disease:
- A plaque partially blocks the vessel

In acute disease:
- The atheromatous plaque ruptures
- The coagulation cascade and platelets are activated
- Thrombus is formed
- Acute ischaemia onset => acute coronary syndromes (ACS), depending on the location and degree of obstruction:
  - from unstable angina
  - to transmural infarction (spanning the full thickness of the cardiac muscle)
General progress of atheromatous disease of the coronary arteries

- Foam cells
- Fatty streak
- Intermediate lesion
- Atheroma
- Fibrous plaque
- Complicated lesion/rupture

Endothelial dysfunction

- From first decade
- From third decade
- From fourth decade

Growth mainly by lipid accumulation

Smooth muscle and collagen

Thrombosis, haematoma
Endothelial dysfunction: Early start of atherosclerosis

Atherosclerosis
- Is the most common cause of CAD
- It is considered to be a chronic inflammatory disease\textsuperscript{11–13}

Atherogenesis (plaque formation)
- Is initiated by endothelial dysfunction

Endothelium
- The inner layer of a vessel wall in constant contact with the blood flow
- Regulates the blood flow
- It consists of endothelial cells

Endothelial dysfunction is supported by various factors, including:
- Shear stress resulting from hypertension (leading to intimal injury of the coronary endothelium)
- Hypercholesterolaemia
- Circulating vasoactive amines
- Advanced glycation end-products in T2DM\textsuperscript{11}
- Exposure to certain constituents of cigarette smoke\textsuperscript{13}
- Adipokines associated with central obesity
Normal blood vessel
**Atherosclerosis:**
Endothelial dysfunction, foam cells

**Endothelial dysfunction**
- facilitates entry of LDL into the vessel wall through the spaces between the cells of the endothelial layer, where it undergoes modification, in particular oxidation.
- modified LDL stimulates endothelial expression of adhesion molecules, such as VCAM–1, and production of chemokines by endothelial and smooth muscle cells
- this results in the adherence of leukocytes from circulating blood, including monocytes and T lymphocytes, to the luminal surface of the artery
- these cells can then migrate into the arterial wall

**endothelial dysfunction**
+ higher levels of LDL
+ increased oxidative load

= subendothelial inflammation
in the intima, the recruited monocytes mature into macrophages
by means of the scavenger receptor, macrophages internalise oxidised LDL by phagocytosis, resulting in the differentiation of the macrophage into a foam cell12
interactions among foam cells, Th1, and Th2 cells establish a chronic inflammatory process
secretion of cytokines and other inflammatory mediators by macrophages, T lymphocytes, and endothelial cells causes smooth muscle cells (SMCs) to migrate from the media to the luminal side of the intima
Atherosclerosis: Fibrous cap

- the SMC in the intima proliferate and produce extracellular matrix (in an inappropriate location)\(^\text{12}\)
- accumulation of lipids in the subintima ultimately results in the formation of multiple extracellular lipid deposits
- the deposits eventually develop into atherosclerotic plaques incorporating monocytes, macrophages, foam cells, SMCs and connective tissue.
Atherosclerosis: Plaque growth

- the progression of a plaque leads to thickening of the vessel wall
- the artery wall compensates up to a point by outward expansion/dilation (‘positive remodelling’)
- for a time the lumen remains unaltered, without stenosis
- if the plaque continues to develop unabated, at some point the artery will no longer be able to compensate with dilation => the plaque will begin to protrude into the lumen and cause stenosis, decreasing the flow of blood to the heart muscle cells downstream of that particular artery = stable CAD
- in most cases, the atherosclerotic plaque grows outward, and it is only in a minority of cases that intact plaque produces sufficient stenosis of a coronary artery to cause an acute coronary event (ACS, unstable CAD)\textsuperscript{14,15}
Atherosclerosis:
Fibrous cap, complicated lesion, plaque rupture

- within the plaque, apoptosis of macrophages and foam cells create a necrotic core that can be thought of as a waste deposit site.
- in advanced plaques, synthesis of extracellular matrix by SMCs (fibrin, proteoglycans, and fibrillar collagen, in particular) results in the formation of a fibrous cap, containing collagen and SMCs lying between the lipid core and the endothelium.
- formation of the fibrous cap can be viewed as a healing response to injury.2,11–13
Stenosis, or narrowing of the vessel lumen through which blood flows due to the presence of a plaque, can create an imbalance between myocardial oxygen demand and supply to the downstream cardiac muscle, resulting in myocardial ischaemia, and is the forerunner of CAD.

This can cause myocardial cells to switch from aerobic to anaerobic respiration, with loss of efficiency and other associated functional impairments.

The most common symptom of transient episodes of myocardial ischaemia is angina pectoris, a condition characterised by precordial discomfort or pressure.

It can be described as a precordial crushing feeling, rather than pain, and might be felt in the chest, left shoulder and arms, back, throat, jaws, and teeth.

Angina may be barely noticeable or severe, symptomatic, and disabling.

It is thought that during ischaemia, ATP is degraded to adenosine, which diffuses to the extracellular space and causes arteriolar dilation as well as anginal pain.

Patients with atherosclerotic lesions may experience angina if they are not able to match coronary blood flow to the increased myocardial metabolic demand that can be caused by exertion, hypertension, or stress.

With bigger plaques that cause more stenosis, patients may also experience angina at rest.

A decreased oxygen supply can also precipitate or aggravate angina in conditions such as anaemia or high altitude.
From stable disease to unstable disease

- As well as causing stenosis of an arterial vessel, an atherosclerotic plaque may become vulnerable to rupture.
- If it ruptures it leads to ACS.
- It is estimated that rupture of the fibrous cap with attendant thrombosis within the arterial lumen is responsible for over two thirds of all fatal coronary events, while superficial erosion of the cap, again with attendant thrombosis, is responsible for an additional 20%.
- Specific plaque characteristics contribute to vulnerability of rupture or erosion.\textsuperscript{11,16}

- Three histological features have been identified to contribute to plaque rupture and therefore most cases of ACS\textsuperscript{14,15}:
  - A large, eccentric lipid core
  - A thin fibrous cap
  - Heavy infiltration of the cap by macrophages and T cells
From plaque to plaque rupture

- Cap thickness and strength: result of the balance between the synthesis and catabolism of fibrillar collagen within the plaque.

- Collagen synthesis by the SMCs is regulated by T-lymphocytes:
  - Transforming growth factor (TGF) β and platelet-derived growth factor (PDGF)
  - Interferon (IFN) -γ

- Collagen degradation is also regulated by T-lymphocytes:
  - produce CD40 ligand, which stimulates the production of MMPs by the macrophages
  - MMP–1, MMP–8, and MMP–13 cause initial proteolysis of collagen
  - MMP-9 and other gelatinases cause additional collagen degradation.

Plaque is made vulnerable by:
- ongoing inflammation
- Impaired endothelium-dependent vasodilation leading to vasospasm
- specific geometry of a plaque
- local shear stress16
From plaque rupture to thrombogenesis

- Rupture of a vulnerable atherosclerotic plaque exposes its highly thrombogenic interior to flowing blood.
- Tissue factor (TF), released from plaque macrophages and present in the plaque’s lipid core, activates the extrinsic coagulation pathway, which in turn leads to platelet adherence, activation, and recruitment.
- Initiation of the coagulation cascade can occur via multiple stimuli, that all ultimately activate thrombin (Factor IIa).
- Finally thrombin causes clot formation in two ways:
  - Activates platelets, which aggregate to form a platelet plug within the vessel lumen
  - Catalyses the conversion of soluble fibrinogen to insoluble fibrin strands, which then cross-link to strengthen and stabilise the platelet plug.
Coagulation in the thrombogenesis

- TF released from plaque macrophages activates Factor VII to Factor VIIa, leading to the formation of the TF-VIIa complex.
- The TF-VIIa complex then initiates coagulation by activating Factor X to Factor Xa and Factor IX to Factor IXa (the latter causing activation of even more Factor X).
- Factor Xa is therefore common to any initiation mechanism.
- At this crucial point in the coagulation cascade, Factor Xa combines with Factor Va, calcium, and phospholipids, creating the prothrombinase complex, which exerts its pivotal effect of catalysing the conversion of prothrombin to thrombin and beginning the propagation phase, when other clotting factors (V, VIII, and XI) further promote thrombin production.
- Amplification of the original signal for coagulation results in the 'thrombin burst' – massive production of thrombin on the surface of activated platelets.
- Fibrin generated by the conversion of fibrinogen by thrombin, stabilises the platelet plug that forms as a result of the exposure of subendothelial connective tissue.
- Thrombin produced by local activation of the coagulation cascade is also a powerful platelet agonist.
The coagulation cascade

Extrinsic system
- Initiation: VII
- TF+Ca\(^{2+}\)
  - Amplification/propagation: TF/Ca\(^{2+}/VIIa\)
  - X
  - IX
  - Plues Ca\(^{2+}\)+Va+
  - Xa
  - AT III

Intrinsic system
- XII
  - Collagen, kininogen, calicreine
  - Collagen, kininogen, calicreine
  - Plues Ca\(^{2+}\)+Va+
  - Xa
  - AT III

Thrombin activity
- II
  - Ila (Thrombin)
  - Fibrinogen
  - Fibrin

Regulation of the coagulation cascade

The coagulation cascade involves a complex series of enzymatic reactions, and clotting 'factors' (mediators or enzymes) that have a dual role in amplifying or subduing the process of coagulation.

These include TF pathway inhibitor (TFPI), antithrombin (AT), and proteins C and S:
- TFPI is the physiological inhibitor of the TF/Factor VII complex.
- AT inactivates Factor Xa; such inactivation is accelerated endogenously by heparin sulfate, a proteoglycan localised on the surface of healthy endothelial and other cells. Heparins and heparin-like drugs, when used therapeutically, affect anticoagulation primarily by enhancing the activity of AT.
- Activated protein C, together with its cofactor protein S, inactivates Factors V and VIII. Protein S is activated by thrombin in conjunction with thrombomodulin, a cell-surface Proteoglycan.\textsuperscript{22,23}
Platelet aggregation

Platelets adhere to areas of denuded (damaged) endothelium, forming a monolayer – neointima:

- GP Ia/IIa receptor binds subendothelial collagen
- GP Ib/IX receptor binds von Willebrand factor\textsuperscript{19}

Following adhesion to the site of injury, platelets become activated and secrete chemical mediators:

- ADP
- Thromboxane A\textsubscript{2}
- Serotonin

These serve to activate and recruit other platelets from the bloodstream.

GP IIb/IIIa receptor (upon activation undergoes conformational change) binds fibrinogen \(\Rightarrow\) aggregation
IHD: variable disease

Varying degrees of plaque disruption produce varying degrees of thrombosis:
- intramural thrombi (within the vessel wall)
- Intraluminal thrombi occluding the arterial lumen to varying extents (or not at all)

Symptoms will vary depending on the degrees of occlusion and collateral circulation, or may be absent.

The thrombogenicity of plaque contents also varies due to different:
- TF concentrations
- Circulating levels of procoagulant proteins
- Hypercoagulable state (activated protein C deficiency, for example)
IHD: Complete evolution

- Normal
- Fatty streak
- Plaque
- Increasing plaque
- Obstructive atherosclerotic plaque
- Plaque fissure or erosion results in thrombosis

- Unstable angina
- Acute myocardial infarction
- Death from coronary disease

- Endothelial dysfunction
- Positive remodeling
- Exertional angina

- Inflammatory markers (e.g., C-reactive protein)

- Clinically silent
- Clinically apparent
Acute ischemia

Clot formation as a result of plaque rupture may result in acute ischaemia. Consequences of acute ischaemia = ACS:
- Unstable angina
- Non-ST-segment elevation myocardial infarction (NSTEMI)
- ST-segment elevation myocardial infarction (STEMI)

STEMI is myocardial necrosis caused by a prolonged period of reduced blood supply to the myocardium, affecting a large area of the heart muscle. This necrosis causes a ST-segment elevation on the ECG trace that is not quickly reversed by nitroglycerin (a medication administered to dilate the coronary vessels)

Patients with ACS who lack ST-elevation on the ECG (NSTE ACS) may or may not go on to have a full MI, but may still have some myocardial damage or necrosis. NSTE ACS includes:
- Unstable angina (no infarction)
- NSTEMI (myocardial necrosis without acute ST-segment elevation).

The Global Registry of Acute Coronary Events (GRACE) study found that 38% of ACS patients have STEMI, whereas the second Euro Heart Survey on ACS (EHS-ACS-II) reported that 47% of patients with ACS have STEMI

ACS signs and symptoms:
Same in STEMI and NSTEMI

The clinical presentation of ACS is variable and dependent on:

- The extent
- The duration
- The location of coronary vessel obstruction
- The volume of myocardium affected
- Patients may present with their first episode of pain or because of a change in pattern of severity of symptoms.

Unfortunately, some patients do not survive the onset of pain.
ACS signs and symptoms:
Same in STEMI and NSTEMI

Symptoms of unstable angina may include:
- New-onset chest pain
- Increasing symptoms of pre-existing angina pectoris (i.e. more frequent/intense/longer-lasting/precipitated by low levels of exertion/occurs spontaneously at rest/crescendo (increasing in frequency))
- Rest angina lasting more than 20 minutes

Unstable angina may spontaneously reverse or be relieved with medications, but may progress to an MI and is considered a medical emergency.
ACS signs and symptoms:
Same in STEMI and NSTEMI

„If you see a man with pain in his left arm, in his heart sided chest, in his stomach or in his jaw, dead is coming soon.“

„Ebers Papyrus“ 2600 years BC
DESCRIPTORS OF MYOCARDIAL ISCHEMIA

A. “LIKE AN ELEPHANT SITTING ON MY CHEST”

B. “A BURNING SENSATION”

C. “A CHOKING FEELING IN MY THROAT”

D. “LIKE A TOOTHACHE”

E. “MY BRA IS TOO TIGHT”
ACS signs and symptoms: Same in STEMI and NSTEMI

Prodromal (early warning) symptoms in days/weeks up to event in two-thirds of patients:
- Shortness of breath
- Fatigue
- Brief episodes of chest tightness
- Unstable angina

Symptoms of the acute event:
- Pain similar to angina, but more severe and long-lasting, can be described as substernal aching or pressure that may radiate to the arms (typically the left arm), shoulders, back, or jaw
- Often accompanied by dyspnoea (breathlessness), nausea and vomiting, syncope (blackout), palpitations (irregular or inappropriately fast or strong heartbeats), and decreased exercise tolerance (not relieved by rest or nitroglycerin)
- Patients may feel restless
- Patients may appear pale with diaphoresis and/or cyanosis
- Pulse may be weak and patients may have high or low blood pressure

Up to two-thirds of ischaemic episodes in patients with stable angina are silent (only mild discomfort), this is thought to be more common in:
- Elderly
- Diabetic patients
- Women are more likely to suffer an MI with atypical chest discomfort
When a patient presents with chest pain, ACS should be considered, particularly in:

- Women over 40 years old
- Men over 30 years old
- Younger ages in individuals with diabetes or lipid disorders such as familial hypercholesterolaemia
Acute coronary syndrome:
Working diagnosis

A working diagnosis of ACS is confirmed by:
- Initial ECG
- Subsequent confirmation of elevated biomarkers of cardiac injury in addition to ECG allows a reliable diagnosis

ACS may be distinguished from conditions that may cause physical symptoms similar to those of ACS:
- Pneumonia
- Rib fracture
- Oesophageal or peptic ulcer disease
- Pulmonary embolism
- Aortic dissection (tear)
- Pericarditis (viral inflammation of the lining of the heart)

By initial and serial ECGs, and serial measurement of cardiac biomarkers by immunoassay.
ECG in ACS

ECG is an effective and low-cost investigation for initial diagnosis of ACS. There are several key indicators of ACS in an ECG reading:

- ST-segment elevation
- ST-segment depression
- T-wave inversion

Initial ECG should be performed within 10 minutes of a patient presenting, and is the most important of the diagnostic tests.

Initial ECG is critical in the decision pathway for proper use of thrombolysis, as ST-segment elevation is strongly correlated with acute occlusive obstruction of an epicardial vessel and usually indicates that a patient has STEMI\(^{24}\) – in which reperfusion with fibrinolytic (‘clot-busting’) drugs or with immediate angioplasty can benefit the patient – as distinct from NSTEMI patients, in whom fibrinolytics may increase risk of harm by worsening the plaque rupture.

Absence of ST-segment elevation does not exclude complete epicardial occlusion, but the benefit of fibrinolysis has not been demonstrated among these patients. A normal ECG when a patient is pain free does not rule out unstable angina, though a normal ECG taken during pain indicates the pain is less likely to be due to ischaemia.
ECG in ACS

A QT interval is measured from the beginning of the QRS complex to the end of the T wave. The QRS complex is a recording of a single heartbeat on the ECG that corresponds to the depolarisation of the right and left ventricles. The ST segment connects the QRS complex and the T wave.
ECG

- Classical: ST elevation, later (days) + deep Q, later (weeks) + negative T - ST elevation, later (months) - negative T

- Variants:
  - Non-STEMI
  - Non-Q
  - Persistent STE
Regular action, heart rate 66/min, sinus rhythm, P waves of borderline duration, biphasic in V1 preceding each QRS complex, PR interval 160 ms, QRS complexes are narrow, normally configured, electrical axis 50°, Sokolow index 50 mm, diffuse changes repolarization.

LVH with overload and hypertrophy of the LA
Action irregularly irregular, heart rate 150/min, no sinus rhythm, no P waves, uncoordinated atrial activity, QRS complexes are narrow, of normal configuration, electrical axis -30°, Sokolow index 50 mm, negative T in V4-6.

**Atrial fibrillation with fast ventricular response, LVH with overload**
LV overload: Heart rate
Action regularly irregular, heart rate 80/min, no sinus rhythm, normally configured P waves are preceding only narrow QRS complexes, which are followed by broad, deformed QRS complexes without P waves followed by complete recovery pause. In sinus complexes PR interval 160 ms, QRS electrical axis 25°, without signs of LVH, ST elevations in II, III, aVF with reciprocal changes in I a aVL.

**Ventricular bigeminia, inferior AMI**
Action regular, heart rate 50/min, sinus rhythm, normally configured P waves preceding each QRS complex, PR interval 160 ms, QRS complexes normally configured, narrow, electrical axis 50°, without signs of LVH, ST elevations in II, III, aVF with reciprocal changes I and aVL.

Acute inferior MI
Regular action, heart rate 66/min, sinus rhythm, P waves normally configured preceding each QRS complex, PR interval 160 ms, QRS complexes normally configured, narrow, electrical axis 80°, without signs of LVH, ST elevations in I, aVL, V2-4, reciprocal changes in III and aVF.

Acute anterior MI
Irregularly irregular action, heart rate 72/min, no sinus rhythm, no P waves, irregular atrial activity, normally configured QRS complexes, narrow, electrical axis 45°, without signs of LVH, deep broad Q in II and III and aVF.

Previous inferior MI, atrial fibrillation with normal ventricular response
Biomarkers in ACS

Different Cardiac Biomarkers Are Useful for Different Aspects of ACS Diagnosis.
After myocyte necrosis (damage to the cardiac muscle cells), cardiac enzymes and cell contents are released into the blood, and thus the presence or absence of these biomarkers can be used to indicate or exclude cardiac ischaemia or infarction.

Different cardiac biomarkers increase at different times after injury, to different extents, and decrease at different rates.

These proteins include:
- Lactate dehydrogenase (LD)
- Creatine kinase (CK) isoenzymes (CK-MM, CK-BB and CK-MB)
- Troponin – a complex of three regulatory proteins (Tn-C, Tn-T, and Tn-I) that is integral to non-smooth muscle contraction in muscles

Being evaluated:
- Heart fatty acid-binding proteins
- Myoglobin
Biochemistry

- AST: early myocardial infarction (days)
- CK: early myocardial infarction (days)
- LDH: earlier myocardial infarction (week)
- Troponin I: hours - 9 days
- Troponin T: hours - 2 weeks
Biomarkers in ACS

![Graph showing the multiple of cut-off level over days after symptom onset for different biomarkers (Troponin without reperfusion, Troponin with reperfusion, CK-MB without reperfusion, CK-MB with reperfusion). The x-axis represents days after symptom onset, and the y-axis represents the multiple of cut-off level. The graph includes a cut-off level marked below the x-axis.](image)
CK in ACS

CK is expressed in a number of tissues, and catalyses the conversion of creatinine to phosphocreatine, degrading ATP to ADP.

CK lacks specificity for cardiac damage, though determination of the MB fraction and proportion is prognostic of cardiac damage.

A two-fold increase of CK with a simultaneous increase in CK-MB is diagnostic of MI.

CK and CK-MB levels begin to rise approximately 4–6 hours after the onset of infarction, and usually return to baseline by 36 hours. CK activity peaks at 18–24 hours, and CK-MB peaks at around 12 hours.

CK-MB levels can be useful for indication of reinfarction, if levels normalise and then increase again.

False positives can occur with diagnostic measurement of CK/CK-MB, in situations such as skeletal muscle injury, CNS damage such as stroke, or blunt chest trauma, among others, and prognostic value is therefore limited.
Troponins in ACS

Troponins are more specific than CK for myocardial necrosis, but can’t be used for diagnosis of reinfarction

- Troponins are not detectable in the blood of healthy patients, unless they have undergone extreme exercise or other cardiac stress, and are highly specific for cardiac myocyte injury.
- Tn-I has the greatest cardiac specificity as it is not found in tissues outside the heart.

Tn-I levels are more sensitive than CK-MB for myocardial necrosis, and are therefore more useful for the early detection of small MIs. Levels rise approximately 6 hours after the onset of infarction and may remain elevated for as long as 2 weeks following an infarction – for this reason troponins cannot be used to diagnose reinfarction, but are useful for the retrospective diagnosis of MI. A direct correlation between troponin elevation and risk of death in ACS patients has been observed.

Because several physiological causes besides ACS can result in elevated biomarkers, the ACC/AHA task force state that clinical evidence of MI in addition to biochemical evidence is necessary for a diagnosis of ACS.24
# Troponins vs. CK

<table>
<thead>
<tr>
<th></th>
<th>Creatine kinase (CK)</th>
<th>Troponins (TnC, TnT, and TnI)</th>
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<tbody>
<tr>
<td></td>
<td>(isoenzymes CK-MM, CK-BB, CK-MB)</td>
<td></td>
</tr>
<tr>
<td><strong>Physiological function</strong></td>
<td>Catalyses conversion of creatinine to phosphocreatine, degrading ATP to ADP</td>
<td>Integral to non-smooth muscle contraction in muscles</td>
</tr>
<tr>
<td><strong>Presence in the body</strong></td>
<td>Expressed in a number of tissues</td>
<td>Not detectable in blood of healthy patients (unless they have undergone extreme exercise or other cardiac stress)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>Non-specific for cardiac damage, though determination of the MB isoenzyme fraction and proportion is prognostic of cardiac damage</td>
<td>Highly specific for cardiac myocyte injury – Tn-I has greatest cardiac specificity as it is not found in tissues outside the heart</td>
</tr>
<tr>
<td><strong>Diagnostic cut-off for MI</strong></td>
<td>Measurement exceeding 99th percentile of a normal reference population</td>
<td>Measurement exceeding 99th percentile of a normal reference population</td>
</tr>
<tr>
<td><strong>Time to increase after onset of infarction</strong></td>
<td>Approximately 4–6 hours</td>
<td>Approximately 6 hours</td>
</tr>
<tr>
<td><strong>Time to return to baseline level following infarction</strong></td>
<td>Usually by 36 hours</td>
<td>May remain elevated for as long as 2 weeks</td>
</tr>
<tr>
<td><strong>Use in MI diagnosis</strong></td>
<td>CK-MB levels can be useful for indication of reinfarction, if levels normalise and then increase again</td>
<td>Useful for retrospective diagnosis. Cannot be used to diagnose reinfarction because of long duration of elevation</td>
</tr>
<tr>
<td><strong>False positives?</strong></td>
<td>Skeletal myopathies, CNS damage such as stroke, blunt chest trauma, among others</td>
<td>Skeletal myopathies, chronic renal failure</td>
</tr>
</tbody>
</table>
STEMI: Biomarker confirmation is not decisive in therapy initiation

Although troponins can be detected in blood as early as 2–4 h after the onset of symptoms, elevation can be delayed for up to 8–12 h.

For patients with ST elevation on the 12-lead ECG and symptoms of STEMI, reperfusion therapy should be initiated as soon as possible and is not contingent on a biomarker assay.


Post MI remodeling

- Acute infarction, hours
- Acute infarction, hours to days
- Acute infarction, days to months
Modifiable Risk Factors

Hypercholesterolaemia
- high blood levels of low-density lipoprotein (LDL) cholesterol and lipoprotein(a)/low blood levels of high-density lipoprotein (HDL) cholesterol are associated with CAD²

Obesity (centripetal or waist)
- being overweight (BMI >25) or obese (BMI >30) increases CAD risk³
- high waist circumference is particularly associated with the development of CAD⁴

Smoking status
- habitual smokers have twice the risk of developing CAD as non-smokers⁵
- smoking may be a stronger predictor of CAD risk in women⁶

Hypertension (partially modifiable)
- hypertension is the most common cause of CAD
- systolic blood pressure (SBP) of more than 160 mmHg and/or diastolic BP of more than 95 mmHg is associated with a CAD risk 5x that of subjects with normal BP⁷

Physical inactivity
- regular exercise helps protect against the onset of CAD and is known to increase levels of cardioprotective HDL⁵
- sedentary patients have around twice the risk of developing CAD as active patients⁸
Non-modifiable Risk Factors

Advanced age
- approximately 70% of CAD deaths occur in patients over 75 years old(4)
- MI risk increases with age, although the process of atherosclerosis may begin while a patient is in their 20s or 30s

Male gender
- CAD is known to be more frequent in men4 – although this gap closes with increasing age(9)
- It is thought that the ageing process of blood vessels progresses more quickly in men, and that oestrogen may have a cardioprotective role(10)

Family history of premature disease
- patients with a first-degree relative who has a history of premature heart disease (younger than 50) are at higher risk of developing cardiovascular disease themselves, particularly if that family member developed CAD at a young age(5)

Diabetes
- poorly-controlled diabetes and type 2 diabetes mellitus (T2DM) are particularly associated with increased CAD risk(4)
Prognosis

Risk of recurrence is greatest during the first two months after the acute event, and reduces thereafter. Subsequently, the clinical course of most patients with ACS is similar to that of patients with chronic stable coronary disease.

GRACE risk score factors (Global Registry of Acute Coronary Event, 29 which predicting 6-month mortality at discharge):

- based on age, heart rate, systolic blood pressure, history of congestive heart failure, history of MI, cardiac markers, cardiac arrest at admission, ST-segment depression, and in-hospital PCI29

TIMI risk score factors risk scores for STEMI30 and UA/NSTEMI31 designed to be used acutely to determine prognosis in hospital:

- STEMI: 0–14 score based on points assigned to age, diabetes mellitus, hypertension or angina, blood pressure, heart rate, Killip class, weight, anterior ST elevation or left bundle branch block (LBBB) on the ECG, and time to treatment (which in turn depends on time taken between the onset of symptoms and the patient’s first presenting)30
- unstable angina or NSTEMI: 0–7 score based on points assigned to age, number of CAD risk factors, prior coronary stenosis ≥50%, aspirin use, recent severe angina, cardiac markers, and ST segment deviation31
### Scoring systems for prognosis

<table>
<thead>
<tr>
<th>TIMI risk score factors (NSTE ACS)</th>
<th>TIMI risk score factors (STEMI)</th>
<th>GRACE risk score factors</th>
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</thead>
<tbody>
<tr>
<td>Age ≥65 years</td>
<td>Age</td>
<td>Age</td>
</tr>
<tr>
<td>At least 3 risk factors for CAD (family history, hypertension, hypercholesterolaemia, diabetes, smoking)</td>
<td>Diabetes, hypertension, or angina</td>
<td>Resting heart rate</td>
</tr>
<tr>
<td>Prior coronary stenosis ≥50%</td>
<td>Systolic blood pressure</td>
<td>Systolic blood pressure</td>
</tr>
<tr>
<td>'Aspirin' use in the past 7 days</td>
<td>Heart rate</td>
<td>History of congestive heart failure</td>
</tr>
<tr>
<td>At least 2 episodes of angina in 24 hours</td>
<td>Killip class</td>
<td>History of MI</td>
</tr>
<tr>
<td>ST segment changes ≥0.5 mm</td>
<td>Weight</td>
<td>ST-segment depression</td>
</tr>
<tr>
<td>Positive troponin T</td>
<td>Anterior STE or LBBB</td>
<td>In-hospital PCI</td>
</tr>
<tr>
<td></td>
<td>Time to treatment</td>
<td>Elevated cardiac enzymes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Serum creatinine</td>
</tr>
</tbody>
</table>
Killip classification

Killip class is a measure of haemodynamic compromise in a person presenting with myocardial infarction

- **Killip Class I**: Absence of rales over the lung fields and absence of S3 heart sounds (no evidence of heart failure)
- **Killip Class II**: Rales ≤50% of the lung fields or the presence of an S3 and systolic blood pressure (SBP) >90 mmHg (heart failure)
- **Killip Class III**: Rales over more than 50% of the lung fields and SBP >90 mmHg (severe heart failure; frank pulmonary oedema)
- **Killip Class IV**: Cardiogenic shock (systolic BP <90 mmHg for greater than 1 hour, not responsive to fluid resuscitation alone, and secondary to cardiac dysfunction, cool and clammy skin, oliguria, or altered sensorium)

An S3 heart sound is produced during passive filling of the left ventricle (LV) due to lower LV compliance.
The presence of an S3 heart sound is normally benign in children, pregnant females, and well trained athletes, however it may signal cardiac problems, such as a failing left ventricle.

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Coronary syndromes

Grech and Ramsdale, BMJ 2003
Management

• General management:
  – GTN
  – If pain no rerelieved: GTN, analgesis (morphin + metoclopramide) + ANP + bteblocker

• <12 h + STEMI or 12-24h STE
  – Fibrinolysis (<4h)
  – PTCA (>4h) or if fibrinolysis contraindicated or failed

• Non-STEMI
  – High risk (high troponins): heparin/LMWH + GPIIb/IIa antagonist
  – Low risk:
STEMI

Acute ST segment elevation myocardial infarction

Thrombolytic treatment
- Infarct artery not recanalised
  - Rescue angioplasty (1-2 hours after failed thrombolysis)
  - Elective angioplasty (if continued ischaemia)

Primary angioplasty
- Infarct artery recanalised, but significant residual stenosis
  - Adjunctive angioplasty
    - Deferred angioplasty (1-7 days after thrombolysis)

Grech and Ramsdale, BMJ 2003
Non-STEMI

Unstable angina or non-ST segment elevation myocardial infarction

TIMI risk assessment on presentation
(aspirin, clopidogrel, heparin, nitrates, β blockers)

Low risk
(TIMI risk score 0-2, negative troponin test)
Conservative management
Stress test
Negative
Discharge
Positive
Percutaneous coronary intervention plus glycoprotein IIb/IIIa inhibitor

Higher risk
(TIMI risk score ≥3, positive troponin test, dynamic ST changes, or haemodynamically unstable)
Invasive management
Possible glycoprotein IIb/IIIa inhibitor
Coronary angiography
Coronary artery bypass surgery
Medical treatment

Grech and Ramsdale, BMJ 2003
Percutaneous coronary intervention (PCI)
Percutaneous coronary intervention (PCI)

PTCA (Percutaneous transluminal angioplasty):
- Balloon angioplasty
- Coronary stenting
Coronary artery bypass grafting (CABG)
Later management

• Bed rest: 2 days
• Discharge: 10 days
• Follow up:
  – Lipids
  – ECG, X-ray, Echo
  – Exercise ECG
  – ANP
  – Betablockers
  – ACEI


