

Biochemical Markers of Myocardial Infarction

Biochemistry Team 437



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Cardiovascular block

EDITING FILE

Objectives:

- Describe the general sequence of events of myocardial infarction (MI)
- List the criteria for diagnosis of MI
- Discuss the features of an ideal MI marker
- Understand the significance of changes in plasma marker levels over time
- Identify the properties and diagnostic value of cardiac troponins, creatine kinase, h-FABP and BNP
- Know about markers with potential clinical use

Overview:

- Myocardial infarction (MI)
 - Criteria for diagnosis of MI
 - Case example for MI
 - Features of an ideal MI marker
 - Time-course of plasma enzyme changes
 - Cardiac troponins I and T
 - Creatine kinase (CK-MB)
 - Heart fatty acid binding protein (h-FABP)
 - B-type natriuretic peptide (BNP)
- How the lab can help in diagnosing MI “Rule it in or rule it out” ?

Myocardial Infarction

Occlusion of coronary arteries



when we have atherosclerosis or occlusion it will lead to ischemia

Restricted blood supply (oxygen) to heart tissue (**ischemia**)



it's the first stage and if it is prolonged it will lead to infarction

Damage to heart tissue (**infarction**)



Release of enzymes and other proteins into the blood (**markers**)

There are some enzymes that are not found normally in our blood. like troponin, so if we do blood test and we found even a small amount it's an indicator for MI and the patient should be hospitalized.

Criteria for Diagnosis of MI



- Recommended by the European Society of Cardiology and American College of Cardiology
- Requires presence of **at least two** of the following characteristics:
 1. Typical heart attack symptoms (Chest pain, shortness of breath, etc)
 2. Characteristic rise and fall pattern of a cardiac marker in plasma
 - a. Rise and gradual fall of cardiac troponins
 - b. More rapid rise and fall of CK-MB
 3. Typical ECG pattern (Sometimes are not found)

Reference: Alpert JS, Thygesen K, Antman E, Bassand JP. *J Am Coll Cardiol.* 2000, 36(3):959.



CASE 12.1

A 66-year-old man had experienced central chest pain on exertion for some months, but in the afternoon of the day prior to admission he had had a particularly severe episode of the pain, which came on without any exertion and lasted for about an hour. On admission there were no abnormalities on examination and the ECG was normal. The troponin was clearly detectable.

Comment on these results. Has he suffered a myocardial infarction?

Comments: He has an elevated troponin plus a typical history. This is sufficient to diagnose a myocardial infarction by the most recent definition, even in the absence of ECG changes.

1. Typical heart attack symptoms

2. Characteristic pattern of a cardiac biomarker

Troponin is found in the myocyte (Intracellular) so it's not supposed to be found in the blood like Na^+ and K^+ so if troponin is found this means we have myocardial infarction

Features of an Ideal Cardiac Marker

High concentration
in the myocardium

High specificity
(specifically detecting
damage of cardiac
tissue, and is absent in
non-myocardial tissue
injury)

Good prognostic
value (strong
correlation
between plasma
level and extent
of myocardial
injury)*

*It means when the injury is severe the troponin level will be very high, and when it's less severe the level will be lower.

High sensitivity
(detected even
in low
concentration
at early stages
of the disease)

Rapid release
into plasma
following
myocardial
injury

Easily measured
(detectable by
rapid, simple
and automated
assay methods)

Plasma Cardiac Markers

CURRENT MI MARKERS:

- Cardiac troponin T (cTnT)
- Cardiac troponin I (cTnI)
- Creatine kinase-MB (CK-MB)

MARKERS **NO** LONGER USED:

- Aspartate Transaminase (AST)
- Lactate dehydrogenase (LDH)
- Ischemia modified albumin (IMA)
- Myoglobin

MARKERS WITH POTENTIAL CLINICAL USE:

- Heart fatty acid binding protein (h-FABP)
(for detecting heart tissue ischemia)

Plasma Cardiac Markers

Markers of diagnostic value:

in MI:

- Cardiac troponins T and I
- Creatine kinase (CK-MB)

in tissue ischemia:

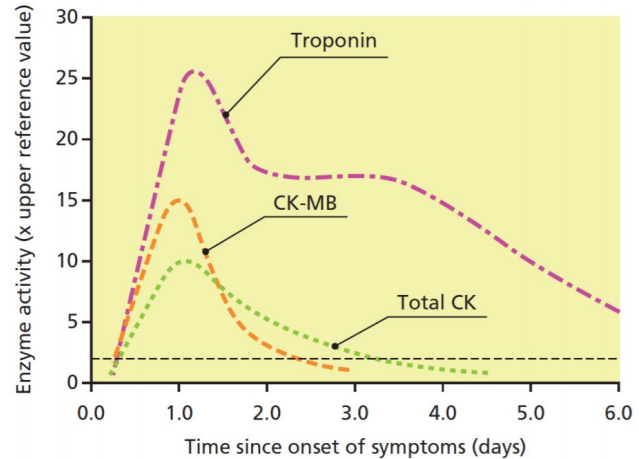
- Heart fatty acid binding protein (h-FABP)

in heart failure:

- B-type natriuretic peptide (BNP)
- Not used for MI

Time-course of Plasma Enzyme Changes

- Plasma enzymes follow a pattern of activities after MI.
- The initial lag phase* lasts for about 3 hours .
- Enzymes rise rapidly to peak levels in 18-36 hours .
- The levels return to normal based on enzyme half-life.
- Rapid rise and fall** indicates diagnostic value***.



**CK-MB: Rapid rise and fall.

Troponin: Rapid rise and gradual fall.

***Diagnostic value: since troponin stays in plasma for long, we can use it to detect MI after a while of the onset of MI

-Since CK disappears from plasma after few days, if it was found after a while it indicates a re-infarction, while troponin might still be high due to the first infarction.

*Lag phase : a phase where plasma enzymes conc. are not changed yet. "No elevation in markers appears"

Blood Samples Collected After MI

The types of blood samples taken depends on the time :

- Baseline (upon admission)
- Between 12 and 24 hours after the onset of symptoms.

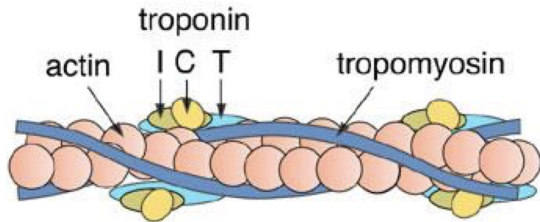
Time-course of Plasma Marker Changes After MI

Enzyme	Abnormal activity detectable (Hours)	Peak value of abnormality (Hours)	Duration of abnormality (Days)
Troponin T , I	4 - 6	12 - 24	3 - 10
CK-MB	3 - 10	12 - 24	1.5 - 3
Total CK	5 - 12	18 - 30	2 - 5

You have to know the numbers

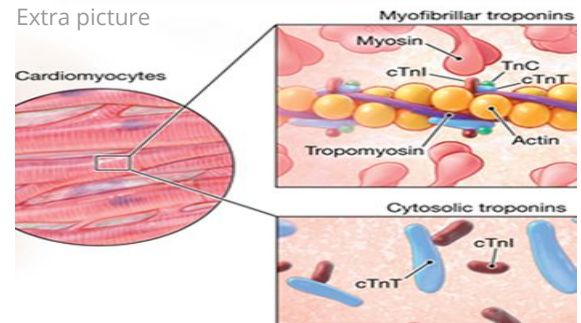
Troponins

- Troponins are structural proteins in cardiac myocytes and in skeletal muscles
- Cardiac troponins (cTn) are structurally different from muscle troponins “specific”
- Involved in the interaction between actin and myosin for muscle contraction



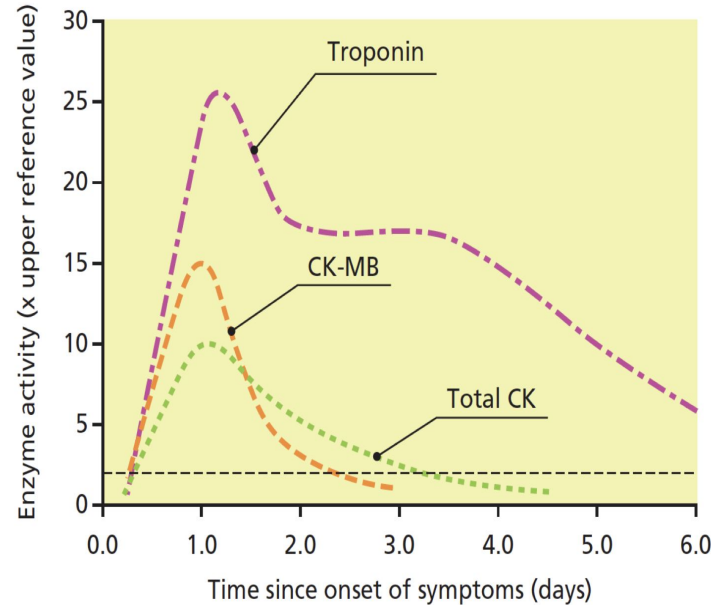
- cTn are mainly bound to proteins, with small amount soluble in the cytosol
- Highly specific markers for detecting MI (muscle injury)
- Two main cardiac troponins (cTn):
 - cTnI: inhibitory protein
 - cTnT: binds to tropomyosin

تسهيل الحفظ
cTnI = Inhibition
cTnT = ترتبط



Troponins

- Detectable in plasma in 4-6 h after MI.
- Level peaks in 12-24 h.
- Remain elevated for up to 10 days.
- After MI, cytosolic troponins are released rapidly into the blood (first few hours).
- Structurally bound troponins are released later for several days.



Creatine Kinase

- Three main CK isoenzymes with two polypeptide chains B or M:

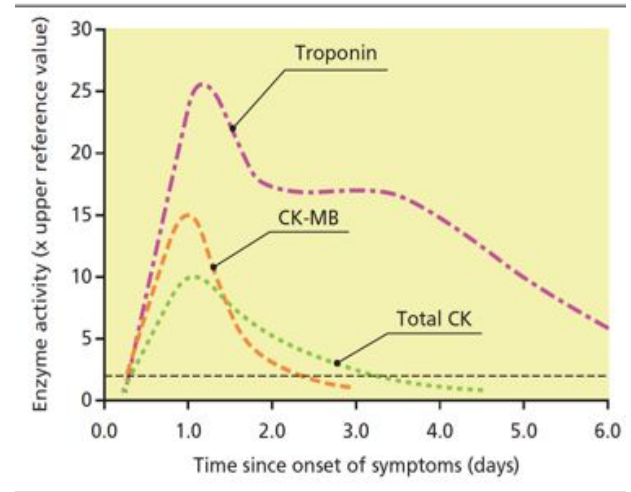
Type	Composition	Comment
Skeletal Muscle	98% CK-MM 2% CK-MB	Elevated in muscle disease
Cardiac muscle	70-80% CK-MM 20-30% CK-MB	Cardiac muscle has highest amount of CK-MB
Brain	CK-BB	
Plasma	Mainly CK-MM	

CK-MB is specific but not as specific as troponin, because it is found in high concentrations in heart, and in very small concentrations in skeletal muscles

CK-MB

- CK-MB is more **sensitive** and **specific** for MI than total CK.
- It rises and falls transiently after MI
- Detectable in plasma in **3-10 h.** after MI
- Peaks in blood in **12-24 h.**
- Returns to normal in **1.5-3 days**
- Relative index :
 - $(\text{CK-MB mass} / \text{Total CK}) \times 100$
 - **More than 5 %** is indicative for MI

“We use the ratio between CK-MB and CK”



CK-MB

Advantages:

- Useful for early diagnosis of MI. (detection within 3 hours)
- Useful for **diagnosis of re-infarction***

Disadvantages:

- Not significant if measured after 2 days of MI (delayed admission). (We have to measure troponin to know if he had an infarction)
- Not highly specific (elevated in skeletal muscle damage) (in trauma → high ck-mb)

*because it disappears after 1.5 - 3 days.
if the patient comes after 4 days with elevated ck-mb → re-infarction.
Patient comes with elevated troponin after 4 days → we don't know if its a reinfarction or not because troponin lasts in blood for 10 days.



CASE 12.2

A well-trained marathon runner collapsed as he was approaching the finishing line. An ECG was normal, but CK was elevated at 9500 U/L (reference range 30–200 U/L), and the CK-MB was 14% of the total CK (normally <6%). Troponin was undetectable. Comment on these results.

Comments: The total CK is substantially elevated, and CK-MB >6% can usually be taken to mean that it is of myocardial origin. However, the normal ECG and troponin are both reassuring. In trained endurance athletes, the proportion of CK-MB in muscle increases from the normal low levels and may be as high as 10–15%. An elevated CK-MB in such individuals can no longer be taken to imply a cardiac origin for the raised CK. Extreme exercise, especially in unfit individuals, causes an elevated CK, potentially to very high levels.

Heart Fatty Acid Binding Protein (h-FABP) (Heart issue ischemia marker)

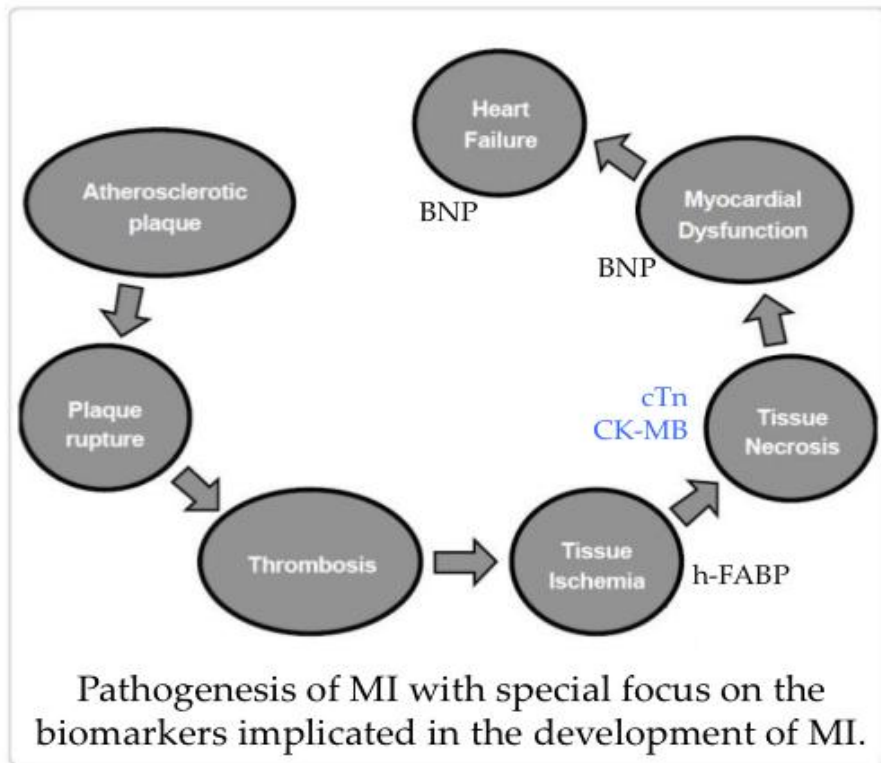
- A cytosolic protein involved in fatty acid transport and metabolism
- A promising marker to be used in combination with troponins
- Higher amounts in myocardium** than in brain, kidney and skeletal muscle
- **Appears in plasma as early as 30 min*** (only one that starts in 30 minutes and finishes it 30hrs). after acute **ischemia**
- Peaks in blood in 6-8 h.
- Returns to normal levels in 24-30 h.

*Early marker for diagnosis because it is important to diagnose ischemia before necrosis happens.

**Not specific in myocardium because it is a protein that carries fatty acid and fatty acid is everywhere but more in myocardium.

B-type natriuretic peptide (BNP) (Heart failure marker)

- A peptide produced by the ventricles of the heart in response to:
 - Myocardial stretching and ventricular dysfunction **after MI**.
- Causes vasodilation, sodium and water excretion and reduces blood pressure.
- A marker for detecting **congestive heart failure** .
- Its serum levels are high in some pulmonary diseases But in heart failure its levels are **markedly** high.
- An important marker for **differential diagnosis of pulmonary diseases and congestive heart failure** .



Take Home Messages

cTn:

- Currently the most definitive markers and are replacing CK-MB Highly
- specific to heart muscle damage
- They remain elevated in plasma longer than CK-MB
- They have higher sensitivity and specificity than CK-MB

CK-MB:

- Its main advantage is for detecting re-infarction

h-FABP:

- An early marker for detecting acute ischemia prior to necrosis

BNP:

- A cardiac marker that can be used for differential diagnosis of pulmonary diseases and heart failure



MCQs:

1- patient came to the ER with shortness of breath and other symptoms for congestive heart failure what can you find in his blood test?

A- little raise in BNP level. **B-** markedly high BNP level. **C-** elevated troponin. **D-** elevated CK-MB.

2- Which of the following isoenzyme of CK is raised in MI?

A- CK-MB. **B-**CK-MM. **C-**CK-BB. **D-** non of them.

3-what does BNP cause?

A- vasodilation. **B-** decrease blood pressure. **C-**sodium and water excretion. **D-**All of theme.

4-Troponin appears in the blood within?

A-3-10 days. **B-** 3-10 h. **C-**4-6 h. **D-**12-24 h.

Summary

Enzyme	Detectable within	Peak value	Back to normal in	Else
Markers of diagnostic value in <u>MI</u>				
Troponin	4-6 h	12-24 h	3-10 days	<ul style="list-style-type: none"> -sudden rise and gradually decrease. -Highly specific markers for detecting MI -2 main cTn: cTnT - cTnI -mainly bound to proteins "90%" with small amount in the cytosol "10%"
CK-MB	3-10 h	12-24 h	1.5-3 days	<ul style="list-style-type: none"> -rise and falls fast. -Useful for diagnosis of re-infarction -Not significant if measured after 2 days of MI -elevated in skeletal muscle damage so it's not highly specific.
Markers of diagnostic value in <u>tissue ischemia</u>				
h-FABP	30 min after acute ischemia	6-8 h	24-30 h	Present also in the kidney, brain, skeletal muscle but in lesser amount than heart
Markers of diagnostic value in <u>heart failure</u>				
BNP	-	-	-	<ul style="list-style-type: none"> -peptide produced by ventricles - cause vasodilation, Na and water excretion and reduce BP -serum levels are high in some pulmonary diseases but its markedly high in CHF.

Girls team

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- لى الصباغ
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- رزان الزهرانى
- لىان المناع
- مشاعل القحطانى
- رىما الدىحان

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- سعىء القحطانى
- نواف اللوىمى
- عبءالرحمن التركى
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