

Cardiac Biomarkers: Clinical Utility

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Case Presentation

Case 1

A 55-year-old patient with a history of DM, HT, CKD

On Examination

Fever, Chest pain - 2 h

Vitals

ECG - Normal

CPK MB positive, Troponin T positive (quantitative)

Question

Acute Coronary Syndrome

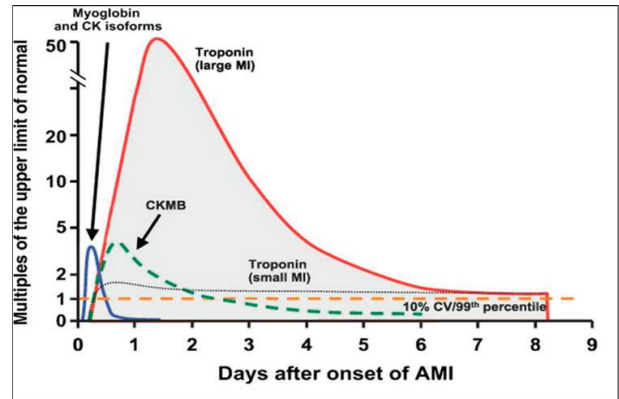
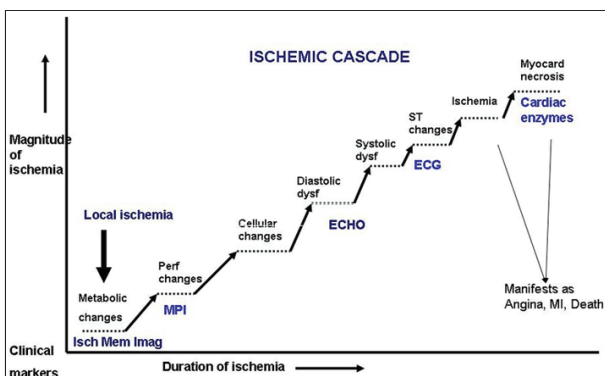
1) Yes

2) No

Investigation

The criteria for type 1 MI include detection of a rise and/or fall of cTn with at least one value above the 99th percentile and with at least one of the following Symptoms of acute myocardial ischemia,

- New ischemic electrocardiographic (ECG) changes,
- Development of pathological Q waves,
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology,
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.



Answer

Acute Coronary Syndrome

1) Yes

2) No

Definition of Biomarker

- A biomarker is a substance used as an indicator of a biological state that is objectively measured.
- Indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

Example

- CPK MB
- Troponins I and T
- Hs - TROP
- BNP/NT BNP

Table 1. Comparative Efficacy of Cardiac biomarkers⁸

Markers	Sensitivity	Specificity
Total CK	73.5%	84.6%
CK-MB	88.2%	93.2%
Troponin I	100%	96.3%

Cut-off Values

For both cTnT and cTnI, the definition of an abnormally increased level is a value exceeding that of 99% of a reference control group.

Cut off-of Trop T: 0.1 ng/ml and Trop I: 0.5 ng/ml.

Sensitivity and Specificity - Quantitative

With serial sampling up to 12 h after presentation, cTn offers a sensitivity > 95% and a specificity of 90%.
Single sample - sensitivity of 70–75%

Troponin I vs T

No convincing answer for superiority

Troponin I	Troponin T
Trop I more specific	Some Trop T in muscle
Trop I lack standardization	Trop T only by Roche
Trop I more appropriate in CKD	

Trop I assay

Commercially available 'new' generation cTnI assays

Assay	Manufacturer	LOD (ng/mL)	99th percentile (ng/mL)	WHO-ROC cut-off (ng/mL)	10% CV (ng/mL)
Architect TnI	Abbot	0.09	0.012	0.3	0.032
Advia Centaur TnI-Ultra	Siemens	0.006	0.04	0.9	0.03
Access AccuTnI	Beckman	0.01	0.04	0.5	0.06
Dimension RxL TnI (Dade)	Siemens	0.04	0.07	0.6–1.5	0.14
Stratus CS	Siemens	<0.03	0.07	0.6–1.5	0.06
Vitros TnI-ES	Orko Clinical Diagnostics (OCS)	0.012	0.034	0.12	0.034
Erenis TnI assay	Singulex	0.0002	0.01	-	0.0008

Causes of acute elevation of troponin in absence of ACS

1. Heart diseases	2. Others
Myocarditis	Hypotension/shock
Pericarditis	Pulmonary embolism
Tachyarrhythmia	Stroke
Acute heart failure	Acute aortic dissection
Radiofrequency catheter ablation	Sepsis
Cardiac contusion	Subarachnoid hemorrhage
Left ventricular hypertrophy	Acute lung edema
Cardiac Amyloidosis	Pulmonary hypertension
Electrical cardioversion	Chronic kidney disease
Heart surgery	Strenuous exercise
Percutaneous coronary intervention	Sympathomimetic drugs
Heart transplantation	Chemotherapy
Coronary vasospasm	
Electrical impulse of implantable cardioverter defibrillator	
Takotsubo cardiomyopathy	
Dilated cardiomyopathy	
Hypertrophic cardiomyopathy	
Endocarditis	

Current AHA guidelines for cTn measurement recommend testing on presentation and again at 8–12 h post symptom onset and the National Academy of Clinical Biochemistry recommends an early marker at 0–6 h and a definitive marker at 6–9 h post-presentation.

Highly Sensitive Troponin

The definition of high-sensitivity cTn is not clearly established, but last-generation assays can detect cTn in approximately 95% of normal individuals.

New 5th generation hs-cTn T and I assays can detect troponin at concentrations 10–100 fold lower than conventional assays.

Increases the sensitivity of cTn in the first few hours after coronary occlusion.

The Negative Predictive Value (NPV) of hs-cTn assays is 95% for AMI exclusion when patients are tested on arrival at the ED.

These hs-cTn assays have allowed the diagnostic cut-off to be lowered to the level of the 99th percentile or lower while maintaining precision at a CV of <10%. For hs-cTn assays - single sample sensitivity 90%, specificity 90%, and the NPV 97–99%.

Moreover, among patients presenting within 3 h of chest pain, high-sensitivity assays - sensitivity 80–85%.

October Report

	KHC	KCN	TOTAL
Hs Trop T	0	0	0
Trop I	74 (70)	167 (100)	167 (100)
Trop T	276 (201)	8 (8)	8 (8)

B Type Natriuretic Peptide (BNP)

Hormones are released in response to volume expansion and increased intra cardiac pressure. BNP has diuretic, natriuretic and hypotensive effects. BNP is found in the myocardium and released by the ventricles.
NT -BNP: stable molecule and longer half-life.

October Report

	KHC	KCN	TOTAL
NT BNP	66 (10)	79 (18)	145
BNP	2	0	2

Cut-off levels

100–400 pg/ml (90 % predictive value)
Low in obesity, Flash pulmonary edema
Higher in elderly, females, renal failure (NT - BNP) or volume overload state.

Case Series 2

A 42 year old patient with a history of HTN

On Examination

Atypical angina for 12 h, Sweating.

Vitals

ECG - ST elevation in Lead 2, 3, avf
Echo - Normal

Question

1. ACS
2. Not ACS

Investigation

Troponins CPK MB - Negative
CRP - negative

D dimer - positive, Non-specific, Good Negative predictive value.



Answer

1. ACS
2. Not ACS

Case 3

A 75-year-old patient with a history of COPD, CKD, CAD - Class 3 Dyspnea

Vitals

ECG - sinus tachy, Q3 T3
Echo - RA, RV dilated, severe TR

Investigation

Troponin T positive
D dimer positive
NT -BNP elevated

Diagnosis

- Pulmonary Embolism
- Heart Failure
- COPD exacerbation
- Confusion

No Overdoing

Appropriate test for appropriate Scenario

Point of Care Cardiac Markers

There are many commercial POC kits for the measurement of biomarkers including cTn, CKMB, myoglobin and BNP/NT-proBNP.

Shown to reduce turn-around times compared with standard testing.

It has been recommended that if std lab testing exceeds a max 60-min turn-around time (avg - 65-128 min) or 25% of decision time, then a POC device should be implemented.

Turnaround time for our lab - 45 min.

Triple Test

Trop
NT - BNP
D - dimer

At 8 h - 90% sensitivity.

Qualitative troponins are sensitive and specificity - 85% if troponins cross more than 0.5 ng/ml.

Less than 6 h = HS trop is the only marker.

NT BNP is not for CKD.

Conclusion

Measurement of biomarkers may be useful in conjunction with risk assessment to improve diagnosis, treatment and prognosis.

Insufficient data at present to recommend novel biomarkers.

Be wary of confounding factors.