A Review on Role of Biomarkers in Myocardial Infarction.

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Submitted: 05-08-2022 Accepted: 14-08-2022

ABSTRACT

Myocardial infarction (MI), recognized as “heart attack,” is due to reduced or complete cessation of blood flow to a part of the myocardium. The etiology of acute myocardial infarction is decreased coronary blood flow. Biomarkers are measurable and quantifiable biological parameters which function indices for fitness and body structure assessments. The analysis of acute myocardial infarction (AMI) may be made with the detection of a rise/fall of cardiac troponin (as a minimum one fee above the 99th percentile of the top reference limit) and one in every of 1) symptoms of ischemia, 2) electrocardiogram (ECG) modifications of latest ischemia, 3) new pathological Q waves or 4) imaging proof of latest lack of possible myocardium. Two widely known biomarkers in use for prognosis of acute myocardial infarction are Creatine-Kinase-MB isoform and Cardiac Troponin. Generally used strategies consist of drug remedy, thrombolytic remedy, percutaneous coronary intervention [PCI], and coronary artery skip graft[CABG] surgery. The cardiac biomarkers cTnT, cTnI, BNP, and NT-proBNP offer essential data for clinicians with the aid of using supporting withinside the steering of diagnostic, prognostic, and remedy selections for sufferers providing urgently with symptoms and symptoms and signs and symptoms of MI. Rapid and correct diagnosis, chance stratification, and control selections will stay aided through biomarkers. They play a useful position in supplying powerful care whilst minimizing healthcare costs.

KEY WORDS: Myocardial infarction, classification, biomarkers, management.

I. INTRODUCTION

Myocardial infarction (MI), recognized as “heart attack,” is due to decreased or complete cessation of blood flow to a part of the myocardium. It is most usually due to a lower or stoppage of blood flow to a part of the heart, leading to cause necrosis of heart muscle. This is normally the end result of a blood clot withinside the epicardial artery that supplies that territory of heart muscle. It is now diagnosed that, primarily based totally on how AMI is defined, not all cases necessarily need a blood clot etiologically. In all living tissue includes heart muscle, the blood supply deliver should identical the oxygen demands of the muscle. This is termed as the supply–demand ratio.

It is now liked that an imbalance in this ratio (too little supply or an excessive amount of demand) as may arise with a very rapid heart rate (too much demand) or a drop in blood pressure (too little supply) may additionally lead to cause myocardial damage without the appearances of a blood clot. Myocardial infarction can also additionally “silent” and go undetected, or it may be a catastrophic event leading to hemodynamic deterioration and sudden death.

Most myocardial infarctions is associated with underlying coronary artery disease, the leading cause of death. With coronary artery occlusion, the myocardium is deprived of oxygen. Prolonged deprivation of oxygen supply to the myocardium can result to myocardial cell death and necrosis. Patients can present with chest discomfort or pressure that may radiate to the neck, jaw, shoulder, or arm. In addition to the history and physical examination, myocardial ischemia may be associated with ECG changes and elevated biochemical markers such as cardiac troponins. Acute myocardial infarction can be classified into two categories, non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI). Unstable angina is similar to NSTEMI. However, cardiac markers are not elevated.

An MI results in irreversible damage to the heart muscle due to a lack of oxygen. An MI may result to impairment in diastolic and systolic function and make the patient prone to arrhythmia. In addition, an MI can result to a number of serious complications. The key is to reperfuse the heart and restore blood flow. The earlier the treatment (less than 6 hours from symptom onset), the better the prognosis.
An MI is diagnosed when two of the following criteria are met:
1. Symptoms of ischemia
2. New ST-segment changes or a left bundle branch block (LBBB).
3. Presence of pathological Q waves on the ECG
4. Imaging study showing new regional wall motion abnormality
5. Presence of an intracoronary thrombus at autopsy or angiography.

**ETIOLOGY**

The etiology of acute myocardial infarction is decreased coronary blood flow. The available oxygen supply cannot meet oxygen demand, resulting in cardiac ischemia. Decreased coronary blood flow is multifactorial. Atherosclerotic plaques classically rupture and lead to thrombosis, contributing to acutely decreased blood flow in the coronary. Other etiologies of decreased oxygenation/myocardial ischemia include coronary artery embolism, which accounts for 2.9% of patients, cocaine-induced ischemia, coronary dissection, and coronary vasospasm.12

**Non-modifiable Risk Factors**
- Sex
- Age
- Family history
- Male pattern baldness

**Modifiable Risk Factors**
- Smoking
- Dyslipidemia
- Diabetes mellitus
- Hypertension
- Obesity
- Sedentary lifestyle
- Poor oral hygiene
- Presence of peripheral vascular disease
- Elevated levels of homocysteine

**Other Causes of MI**
- Trauma
- Vasculitis
- Drug use (cocaine)
- Coronary artery anomalies
- Coronary artery emboli
- Aortic dissection
- Excess demand on the heart (hyperthyroidism, anemia)

1. Abdominal obesity (waist/hip ratio) (greater than 0.90 for males and greater than 0.85 for females)
2. Psychosocial factors such as depression, loss of the locus of control, global stress, financial stress, and life events including marital separation, job loss, and family conflicts
3. Lack of daily consumption of fruits or vegetables
4. Lack of physical activity
5. Alcohol consumption (weaker association, protective)13

The INTERHEART study showed that all the above risk factors were significantly associated with acute myocardial infarction except for alcohol consumption, which showed a weaker association. Smoking and abnormal apolipoprotein ratio showed the strongest association with acute myocardial infarction. The increased risk associated with diabetes and hypertension were found to be higher in women, and the protective effect of exercise and alcohol was also found to be higher in women.

Other risk factors include a moderately high level of plasma homocysteine, which is an independent risk factor of MI. Elevated plasma homocysteine is potentially modifiable and can be treated with folic acid, vitamin B6, and vitamin B12.24

**CLASSIFICATION OF MYOCARDIAL INFARCTION**

Type 1 Myocardial infarction is a medical proof of ischemia because of atherosclerotic plaque disruption ensuring in coronary thrombosis and detection of upward thrust and/or fall of cTn values with as a minimum one cost above the 99th percentile upper-reference limit [URL] 15,16. In addition, sufferers should additionally showcase one of the following signs and symptoms of myocardial ischemia conditions: new ischemic electrocardiogram changes, improvement of pathological Q waves, proof of latest lack of feasible myocardium or new nearby wall movement abnormality in a sample regular with ischemic etiology through imaging and identify of a coronary thrombus via way of means of angiography or autopsy.15

Type 2 Myocardial infarction additionally consist of the aforementioned symptoms, however is because of a supply-call for mismatch of myocardial oxygen with inside the absence of coronary thrombosis.15,16 Prior to 2017, differentiating sufferers with kind 1 and sort 2 MI-primarily based totally through scientific coding turned into no longer viable due to the fact an ICD code for every unique MI subtype did now no longer exist.17

Type 1 MI may be similarly divided into classifications: ST-elevation myocardial infarction [STEMI] and non-ST-elevation infarction[NSTEMI]. STEMI is described as an
acute coronary thrombosis or chronic ST-Phase elevation ≥1 mm in ≥2 contiguous electrocardiographic leads\textsuperscript{15,17} NSTEMI is described as ischemic signs at relaxation from an acute coronary plaque rupture or erosion, lasting ≥10 mins, happening inside 24 hours earlier than health center admission, and showing both extended cardiac biomarkers [both creatine kinase or cTn] inside 24 hours after preliminary presentation\textsuperscript{17}.

**BIOMARKERS**

Biomarkers are measurable and quantifiable biological parameters which function indices for fitness and body structure assessments\textsuperscript{18}. This consists of sickness hazard and analysis. The analysis of acute myocardial infarction (AMI)\textsuperscript{15} may be made with the detection of a rise/fall of cardiac troponin (as a minimum one fee above the 99th percentile of the top reference limit) and one in every of 1) symptoms of ischemia, 2) electrocardiogram (ECG) modifications of latest ischemia, 3) new pathological Q waves or 4) imaging proof of latest lack of possible myocardium.

Both the ECG and cardiac troponin are biomarkers, but the point of interest of this overview may be on serum proteins/markers that have turn out to be more and more critical to enhance our analysis of myocardial infarction, in some instances figuring out humans liable to having an infarct and in others to are expecting long time diagnosis following an actual event.

**What makes an excellent biomarker?**

A desirable biomarker is something this is without problems measured and may be used as a surrogate marker for sickness and its severity\textsuperscript{19}. For instance, blood sugar maybe used to diagnose diabetes\textsuperscript{18} while glycosylated hemoglobin (HbA1c) video display units blood sugar control. Because cardiovascular sickness is still a large burden in most countries, it's miles critical to pick out excessive hazard sufferers in order to save you morbidity or mortality in later life. Medications and remedies additionally come at a fee and therefore easy and reasonably-priced exams have turn out to be more and more important to determine a way to goal treatment. A desirable biomarker will diagnose or are expecting hazard accurately (this is, excessive specificity and sensitivity), directly offer inexpensive but significant results, and ought to offer this incrementally over current markers or medical characteristics.

**Biomarkers in acute myocardial infarction**

Some of those more recent biomarkers and their dating to diverse pathophysiological procedure are depicted in Figure 1\textsuperscript{20}.

![Figure 1. Pathophysiological procedure of biomarkers in MI](image)

**Diagnostic biomarkers**

Two widely known biomarkers in use for prognosis of acute myocardial infarction are Creatine-Kinase-MB isof orm and Cardiac Troponin. In 2000, Cardiac Troponin changed CK-MB because the biomarker of preference for diagnosing a myocardial infarction\textsuperscript{21}. Troponin is a protein launched from myocytes whilst irreversible myocardial harm occurs. It is tremendously precise to cardiac tissue and as it should be diagnoses myocardial infarction with a history of ischemic ache or ECG modifications reflecting ischemia.

Cardiac troponin stage is depending on infarct size\textsuperscript{22}, as a consequence giving clinicians an concept of the analysis following an infarct. However, following reperfusion therapy, the real troponin stage may be deceptive because of the washout phenomenon. Troponin tiers top at 12 hours, and live extended for 10 days or extra. Whilst using Troponin for diagnosing AMI and threat stratification to aid choice making has revolutionized the control of sufferers imparting with chest ache, the 12-hour wait for the tiers to top stays the Achilles heel of this biomarker.
Newer, extra touchy troponin assays\textsuperscript{23} have been brought to rectify this weakness. A nice Troponin is related to accelerated threat of an unfavorable final results at 30 days (HR 1.96, $P = 0.003$). In addition, the following biomarkers might also additionally assist facilitate early prognosis of AMI, despite the fact that neither has been in comparison with the more modern excessive sensitivity troponin assays.

**C-terminal-provasopressin (Copeptin)**

Copeptin is the extra solid surrogate of arginine vasopressin (AVP), with famous outcomes on osmoregulation and cardiovascular homeostasis\textsuperscript{32}. Post AMI, vasopressin is idea to\textsuperscript{25} boom peripheral vasoconstrictor pastime for that reason growing afterload and ventricular stress\textsuperscript{26}; (1) boom protein synthesis in myocytes main to hypertrophy\textsuperscript{27} and (2) vasoconstriction of coronary arteries.

These outcomes are mediated thru the V1 receptor, while outcomes at the V2 receptor mediate water retention with inside the renal tubules. These receptors are now objectives for pharmacological therapy\textsuperscript{28,29}. Copeptin is launched in stoichiometric share to vasopressin and is strong and without difficulty assayed. Copeptin can rule out MI in advance similarly to a terrible Troponin T test\textsuperscript{30}. At the time of presentation a copeptin degree of $< 14$ pg/ml and a Trop T degree of $< 0.01$ ought to rule out a myocardial infarction with a place under the curve (AUC) of receiver working characteristic curve (ROC) of 0.97 (terrible predictive cost of 99.7%), for this reason obviating the want for tracking and serial blood checks in a majority of patients.

Copeptin is a superb marker of neurohormonal stress, making it additionally beneficial in risk stratification in sepsis\textsuperscript{31} and different illnesses and hence isn't particular to the cardiovascular system.

**Heart-Type Fatty Acid Binding Protein (H-FABP)**

H-FABP is a low molecular weight protein worried in myocardial fatty-acid metabolism\textsuperscript{32}. It is likewise discovered in small portions in brain, kidney and skeletal tissue and degrees can cross up in acute ischemic strokes and intense exercise. It is swiftly launched early in myocardial infarction and necrosis into the cytosol.

H-FABP has been proven in mouse research to be an early marker of ischemia\textsuperscript{33} (earlier than morphological proof of myocardial necrosis) and might consequently assist with analysis of MI earlier\textsuperscript{33-35}. However, research trying to use H-FABP on my own for early analysis of AMI has produced disappointing results. One overview of six research discovered that the pooled wonderful predictive cost to be 65.eight% and pooled bad predictive cost to be 82.0\textsuperscript{36}

Other more latest research verified that H-FABP degrees have been honestly related to the composite quit factor of demise, myocardial infarction and coronary heart failure at 10 months\textsuperscript{37,38}. When degrees of H-FABP have been measured postACS and divided into quartiles, the pinnacle quartile become related to all-reason mortality 6.59 instances better than the lowest quartile, after adjusting for hsCRP and Troponin. In fact, whilst introduced to Troponin for hazard stratification, a bad troponin and H-FABP level $< 5$ 5.8 mcg/L become associated with a 4.93-fold growth in hazard of demise and 7.93-fold growth in hazard if Troponin become wonderful and H-FABP $> 5.8$ eight mcg/L.

**Prognostic biomarkers**

Before broaching the situation of biomarkers it’s far essential to be aware that because of diverse randomized control trials and registry studies, diverse threat elements have been diagnosed and entered into scoring structures that permit a clinician to threat stratify disease\textsuperscript{39}. Popular gear include the TIMI rating\textsuperscript{40}, derived from the Thrombolysis in Myocardial Infarction study, and the PURSUIT rating\textsuperscript{41} (from Platelet glycoprotein IIb/IIIa in risky angina: Receptor suppression the usage of Integrally Therapy).

The GRACE rating is any other especially sturdy medical tool\textsuperscript{42}, which makes use of medical signs to calculate threat. (from the Global Registry of Acute Coronary Events study), using weighted facts approximately renal dysfunction, hemodynamic fame, age, Killip Class, cardiovascular records, and records of a cardiac arrest, in addition to elevated cardiac enzymes and form of ECG changes. On its own this rating has an brilliant c-statistic of 0.eighty four for predicting in-health facility death. Newly added biomarkers must supplement and have incremental prognostic price over and above these easy threat scores.

It is consequently no wonder that biomarkers presenting prognostic facts following an acute coronary syndrome mirror the diverse physiological pathways defined with inside the GRACE rating (for example, hemodynamic fame vs. biomechanical pressure and neurohumoral pathways). Currently, the handiest regular biomarker affecting an alternate in control of a
patient with an acute coronary syndrome is the cardiac troponin.

**Other biomarkers**

C-Reactive protein [CRP]. CRP is a beneficial prognostic indicator in sufferers with ACS, as expanded CRP ranges are impartial predictors of cardiac death, AMI and congestive coronary heart failure. It is a maximum extensively used inflammatory markers in habitual medical practice.

**Inflammation Biomarkers**

Interleukin-6 in addition to CRP, is a critical irritation biomarker that can be implicated withinside the diagnosis, hazard stratification, and diagnosis of sufferers with AMI. IL-6 expression is proven to be improved in induced myocardial infarction via way of means of Trans-coronary ablation of septal hypertrophy, suggesting its diagnostic role.

Cardiac myosin binding protein C [cMyC] is one of the three isoforms of myosin binding protein C expressed withinside the cardiac tissue while the alternative isoforms are expressed withinside the skeletal muscle. Following cardiac myocyte necrosis, cMyC seems withinside the circulation in advance as compared to hs-cTn. Notably, the cMyC has a better efficacy for ruling out and ruling in patients than hs-cTn, whilst the diagnostic accuracy is similar.

**TREATMENT**

The remedies of myocardial infarction in particular awareness at the recanalization of the occluded coronary artery to repair perfusion and save you myocardial necrosis. To do this, generally used strategies consist of drug remedy, thrombolytic remedy, percutaneous coronary intervention [PCI], and coronary artery skip graft [CABG] surgery.

Traditional drug treatment plans consist of angiotensin-changing enzyme inhibitors [ACEI], angiotensin receptor blockers [ARBs], aldosterone receptor antagonists, beta receptor blockers and so on. The principal reason of these remedies is the prevention of left ventricular remodeling.

Thrombolytic remedy is currently the principle technique for the remedy of myocardial infarction. Principles of thrombolytic remedy in treating acute myocardial infarction are recanalization of the occluded coronary artery and recovery of the perfusion as quickly as possible.

A huge wide variety of scientific research indicated that thrombolytic remedy that taken inside 6 hours after the onset of myocardial infarction completed the quality healing effect and the sooner remedy is started, the higher the healing effect.

**Percutaneous Coronary Intervention**

Take the restrictions of thrombolytic remedy into consideration, percutaneous coronary intervention [PCI] has progressively grow to be some other desire to repair perfusion. This process efficaciously restore the blood glide and recovers the characteristics of Coronary heart muscle through putting a unique catheter right into the blood vessel and inflated on the narrowed location of the coronary artery. Compared with thrombolytic remedy, PCI eliminated the thrombus and the reperfusion price after the intervention is 95%-99%. But PCI additionally has a few feasible risk, which include bleeding or contamination of the catheter insertion site, hypersensitive reaction to the assessment dye use, blood clot dealt with blood vessel , rupture with coronary artery and whole remaining of the coronary artery.

Coronary Artery Bypass Grafting [CABG] is an powerful surgical remedy of coronary heart sickness and myocardial ischemia, which could successfully relieve symptoms. It is likewise an powerful approach for the remedy of restenosis and acute head ache in sufferers after PCI. Once a intense headache arise after surgery, emergency CABG will limit myocardial harm and decrease help centre mortality and detrimental events. CABG is an essential opportunity or mixture remedy to PCI.

**II. CONCLUSION**

The cardiac biomarkers cTnT, cTnI, BNP, and NT-proBNP offer essential data for clinicians with the aid of using supporting withinside the steering of diagnostic, prognostic, and remedy selections for sufferers providing urgently with symptoms and symptoms and signs and symptoms of MI. cTnT and cTnI have developed through numerous assay revisions and presently the touchy and excessive sensitivity variations of those assays are the exceptional to be had exams for medical use in MI diagnosis. Currently, clinicians commonly degree both cTn or BNP/NT-proBNP while encountering sufferers with suspected acute coronary syndromes or coronary heart failure, primarily based totally at the suggestions posted via way of means of the
European Society of Cardiology or American Heart Association.

These laboratory exams becomes of growing significance throughout the world and especially in Southeast Asia with the converting demographics and healthcare landscape. The developing international epidemic of weight problems and diabetes mellitus will bring about extra sufferers offering to the emergency branch with the diagnostic quandary of MI as opposed to different reasons in their symptoms and symptoms and symptoms. Rapid and correct diagnosis, chance stratification, and control selections will stay aided through biomarkers. They play a useful position in supplying powerful care whilst minimizing healthcare costs.

We nonetheless want to perceive greater novel biomarkers to complement ECG or X-rays and offer greater correct and toughy strategies for cardiovascular disorder diagnosis, threat stratification, and management.

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