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An Update On Cardiac Biomarkers In Detection Of Myocardial Infarction

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ABSTRACT

Myocardial infarction (MI) is defined as significant heart attack occurs when the coronary blood supply is decreased or sudden complete cessation, harming the myocardium due to a lack of oxygen, which leads to ischemic injury to the heart and leads to dead. Globally incidence of MI is increasing day by day, which leads to major cause of cardiac dead compared to other pathological conditions. Early detection and accurate diagnosis of MI can reduce the incidence of mortality and increases the survival rate. To review updates on cardiac biomarkers and methods that can be used for the diagnosis of myocardial infarction. Globally incidence of MI is increasing day by day, and some studies are being conducted on the association between COVID-19 and myocardial infarction. Early detection is a key to properly treating the MI;thus, this study aims to do this by offering both tools and techniques as well as the most recent diagnostic techniques. Myocardial infarction is an ischemic disease that is difficult to diagnose based on single factor of diagnostic method. Therefore, it is necessary to use a combination of various methods to diagnose MI quickly and accurately. This review concludes use biomarker-based ELISA, SPR, gold nanoparticle, and aptamer technologies can be used to diagnose Myocardial infarction along with electrocardiogram and echocardiogram, which is required to diagnose myocardial infarction accurately.

Key words: Myocardial nfarction (MI), Heart attack, cardiac biomarkers, ELISA,aptamer,Surface Plasmon Resonance (SPR).

INTRODUCTION

Myocardial infarction (MI) is defined as significant heart attack occurs when the coronary blood supply is decreased or suddencomplete cessation, harming the myocardium due to a lack of oxygen, which leads to ischemic injury to the heart and leads to dead. Coronary artery disease is the most common etiology of MI[1]. Acute myocardial infarction (MI) can be caused due to acute coronary occlusion of one or multiple large epicardial coronary arteries for more than 20 to 40 minutes[2]. The coronary artery occlusion is commonly due to thrombotic embolization and also due to the rupture of a plaque formed in the coronary arteries, which leads to a lack of oxygen in the myocardium, results in sarcolemmal disruption and myofibril relaxation[3].

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The process of MI initiates with these ultrastructural changes, which are followed by mitochondrial alterations. The prolonged ischemia results in liquefactive necrosis of myocardial tissue, which spreads from sub-endocardium to sub-epicardium[4]. Increased collateral circulation in subepicardium delays its death and decreases the mortality rate. Depending on the territory effect by the infarction, the cardiac function is compromised. The infarcted area heals by scar formation due to the negligible regeneration capacity of the myocardium and the remodeling of heart characterized by dilation, segmental hypertrophy of remaining viable tissue, and cardiac dysfunction, which may also lead to cardiac arrest[5][6].

Diagnosis of Myocardial infarction:

Symptoms of Myocardial infarction are usually asymptomatic, in most the MI cases medical examinations are often ineffective in detecting them. As a result, electrocardiogram (ECG) is required to measure abnormally intense chest pain and changes in blood heart-related indicators, and to identify the abnormal rhythms of heart[7][8].

Electrocardiogram (ECG)

Electrocardiogram (ECG) is one of the most basic and quick procedures for assessing the electrical physiology of heart. ECG plays a vital role in the early diagnosis and evaluation of individuals with symptoms of MI especially the chest discomfort. Due to low cost, excellent safety, and quick reporting the ECG is performed as a standard procedure for diagnosing MI. Although ECG is the most common method of diagnosing acute MI, only 50–57% of patients with acute MI can be diagnosed accurately[9][10].

In addition, only using ECG is difficult to diagnose patient on MI because typical ECG pattern of MI are not recorded in Non-ST Elevated-Acute Coronary Syndrome (NSTE-ACS) patients. A comprehensive evaluation of changes in molecular markers such as Troponin-T along with ECG and ECHO is required to diagnose the non-ST elevation acute coronary syndrome (NSTE-ACS)[11].

Echocardiography

Echocardiography is a diagnostic test that uses ultrasound waves to create a real-time image of the heart. Echocardiography is used monitor the structure of heart, blood flow, and valves, which is also used to diagnose cardiovascular diseases such as MI[12].

It is an ideal method for assessing patients with MI because it is a quick, noninvasive, portable, and inexpensive imaging modality. The echocardiographic examination includes functional result of coronary artery disease (CAD), evaluation of global and segmental wall motion, and MI consequences[13].

Cardiac Biomarkers

The primary diagnosis of MI is made when severe pain radiates from chest to the arm, neck, or Jaw continues for more than 30 min. The diagnosis is made by checking changes in various factors, including basic examination, electrocardiogram measurement, and biomarkers. For an accurate diagnosis of myocardial infarction, it is necessary to diagnose using an objective numerical value in a way of confirming changes in biomarkers[13].

Cardiac troponins

Cardiac myocytes contain cytoplasmic proteins called cardiac troponin T and I which regulates the muscle contraction by binding to the actin tropomyosin complex. Troponin C is not much more sensitive biomarker to detect myocardial injury (Figure-1). As a response to myocardial damage, these proteins are released in the bloodstream, but hypertroponinemia can be present in a variety of non-cardiac diseases[14].

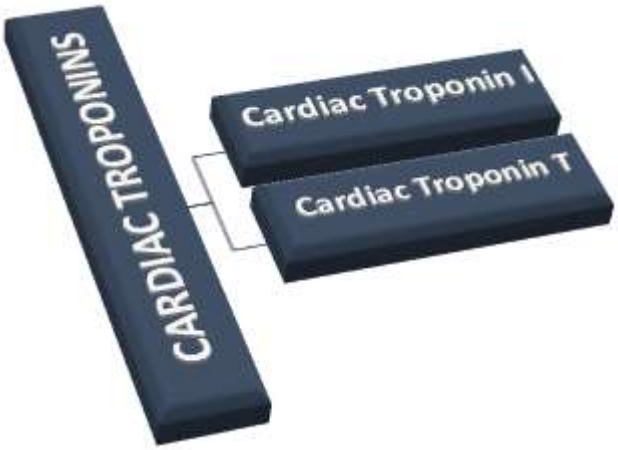

Figure. 1. Isoforms of Troponins

In clinical practice, they are used to identify potential myocardial injury and most importantly myocardial infraction and can provide prognostic information in cardiomyopathies and stroke. Apart from acute coronary syndromes, increased troponin levels can be found in patients with tachyarrhythmias, heart failure, pulmonary hypertension, ARDS and systemic diseases such as sepsis. The lack of standardization in the immunoassays used to determine cardiac troponin values, can lead to difficulties in the comparison of results from different studies, when only absolute troponin values are reported [15].

During the first period of the pandemic, increased troponin values described in patients in Wuhan were attributed to virus-related cardiac injury and were associated with poor prognosis. Patients with elevated levels of TnI and TnT leads to increased mortality. Elevated troponins levels were significantly higher in patients with severe disease or admitted in the ICU compared to the patients with mild and moderate disease[16].

Abnormal hs-TnI levels were found most commonly in older compared to youngsters, especially higher rates of comorbidities associate with male patients. According to a meta-analysis, patients with elevated TnI had increased risk of poor outcomes and were more likely to be admitted to the ICU. C-Reactive Protein, d-dimers, ferritin and other multiple inflammatory indexes have been positively correlates with elevated levels of troponin; thus, it concludes that myocardial damage is of inflammatory origin (Figure-2). Many research studies suggests that troponins and Brain natriuretic peptide (BNP) can be considered as first line biomarkers of myocardial injury and cardiac stress [17].

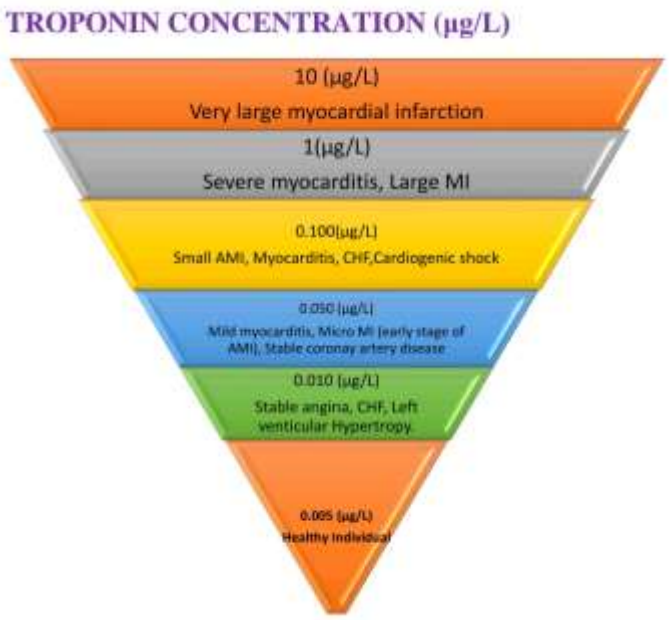

Figure. 2. Expression concentration of Troponin in healthy individuals to MI affected Patients

Surface plasmon resonance (SPR) is the biosensors, which are label-free and have more advantages in the early detection of Cardio Vascular Diseases (CVD). Due to its bulky size, the commercialized prism-coupled SPR biosensor is not suitable for the POCT device. The fiber-based SPR biosensor employs an optical fiber to transmit the surface plasmon excitation and reflection light, largely decreases the sensor's size and manufactory cost. Furthermore, the utilization of the integrated LED light source and the micro spectrograph enables the elimination of bulky testing equipment in the fiber-based SPR biosensors, which can promote the application of portable SPR biosensors for an onsite clinical CVD diagnosis[18].

Human troponin is made up of three subunits: TnC, TnT and TnI, which is used as a gold standard marker because of its exceptional specificity and sensitivity for the detection of Acute Myocardial Infarction (AMI), as well as the fact that it is found in heart muscles when there is a myocardial cell injury and has a higher blood concentration. The level of cTnI drastically increases in the bloodstream from the threshold level of 0.04 ng mL−1 to 1.4 ng mL−1 within 3–12 h. Using gold nanoparticles an enzyme-free nano-immunosensor for cTnI detection was formed and graphene quantum dots as enzyme mimics and signal amplification agents, where the disposable electrochemical sensor could achieve the determination of the biomarker in a wide concentration range (10–1000 pg mL−1) with an LOD of 0.5 pg mL−1 in 50% diluted human serum[19].

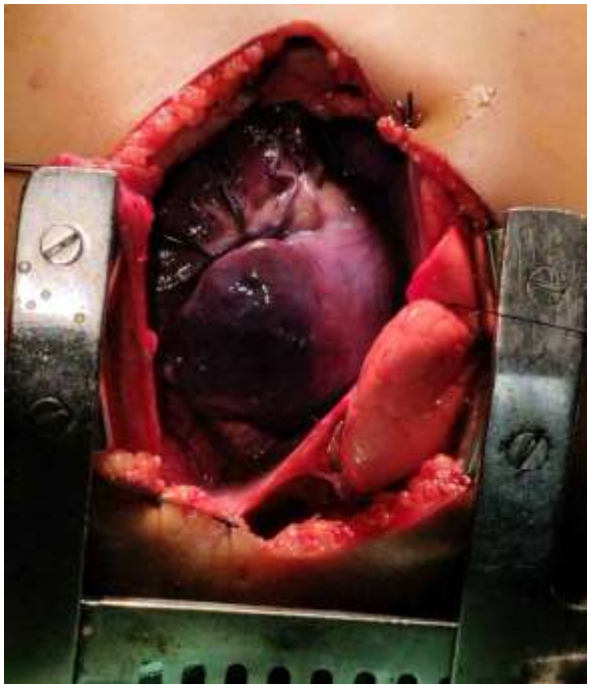

Figure-3. Ischemic damage of heart, which turned into blue due to poor organ perfusion (Increased oxygen demand)

The clustered regularly interspaced short palindromic repeat (CRISPR) are combined with nanostructure aptamers which is a powerful tool for genome engineering further improved the sensitivity of cTnI detection. Working electrode is made up of gold metal and decorated with the methylene blue-modified DNA[20].

The clustered regularly interspaced short palindromic repeat (CRISPR) are combined with nanostructure aptamers which is a powerful tool for genome engineering further improved the sensitivity of cTnI detection. Working electrode is made up of gold metal and decorated with the methylene blue-modified DNA. Then cTnI aptamer with modified magnetic nanoparticles was binding to its complement DNA in part. When the aptamer captured the cTnI, probe2 was released and hybridized with the CRISPR-derived RNA in the solution which triggered the trans-cleavage activity of CRISPR/Cas12a, resulting in the cleavage of probe1, leading to the decrease of the electrochemical signal[20].

ISCHEMIA-MODIFIED ALBUMIN

Ischemia-modified albumin (IMA) is considered as a more sensitive and specific myocardial biomarker for myocardial ischemic damage because IMA is measurable in serum/plasma within minutes and peaks within 2 hours to 4 hours, but recent research studies suggests that for differentiating IMA from human serum albumin is difficult because of their similar antigenicity and epitopes, which results in not specific and accurate tool to detect myocardial ischemic damage (Figure-3). The mechanism of IMA generation remains idiopathic, but It is generally regarded that IMA is derived from oxidative stress and concurrently produced superoxide-free oxygen radicals that occur during ischemic events, which includes not only cardiac but also extracardiac events[21].

The major problem with IMA is due to lack of cardio-specificity to detect myocardial ischemic damage which is due to elevated serum IMA levels may also occur in acute stroke, pulmonary embolus, and end-stage renal disease. Serum IMA concentration represents the protein oxidative damage which considerably greater in morbidly obese patients than in healthy women. Moreover, circulating IMA showed variation according to circadian rhythm, with a negative correlation with melatonin levels in patients with STEMI and severe hypoalbuminemia may also affect the result of an Albumin Cobalt Binding (ACB) test, which will cause false-high result[22].

X-ray fluorescence (XRF) assay is a newly established assay which specifically detect the IMA levels accurately by subtracting unaltered albumin from the total albumin in a specimen, thus correcting IMA results for variations in total albumin concentration gives an accurate results to diagnose the MI. Especially the procedure can be completed within 30min, which is a conventional analytical approach in industry and environmental monitoring, has been utilized to realize rapid determination times[21][22].

ADRENOMEDULLIN (AM)

Adrenomedullin (AM) is a vascular-derived peptide hormone which have been recently emerged as a promising biomarker for assessment of MI and heart failure (HF). Adrenomedullin (AM) is expressed in cardiac tissue, and plasma AM levels increase in patients with acute myocardial infarction (MI), which tracks with mRAP and associates with measures of systemic congestion and with mortality in decompensated HF and MI independently from NT-proBNP[23].

Additionally, Adrenomedullin not only reacts as an biomarker but also administration of AM during the early period of MI improves the survival and ameliorated progression of LV remodeling and heart failure[24].

COPEPTIN

Copeptin is the carboxyl-terminus of the arginine vasopressin (AVP) precursor peptide, which has the main physiological functions of AVP are fluid and osmotic balance, cardiovascular homeostasis, and regulation of endocrine stress response. Copeptin is released in an equimolar mode with AVP from the neurohypophysis which had emerged as a stable and simple-to-measure surrogate marker of AVP and has displayed enormous potential importance in clinical practice[25].

Copeptin is a diagnostic and prognostic biomarker in cardio vascular diseases (CVD) which includes the rapid rule-out of acute myocardial infarction (AMI), mortality prediction in heart failure (HF), and stroke. Unlike cTn and other cardiac biomarkers, copeptin, which non-specifically reflects the endogenous stress level at the onset of AMI, has been advanced and widely validated for its clinical value in AMI[26].

As copeptin is considered as a biomarker of endogenous stress, it levels rise sharply after myocardial injury following a swift decline. Recent studies resultthat patient with AMI had higher copeptin levels than those without AMI. Comparatively, patients with non-ST-elevation myocardial infarction (NSTEMI) had a significantly lower level of copeptin than the patients with ST-elevation myocardial infarction (STEMI) but a higher level than the patients with unstable angina, which indicates that copeptin levels were strongly associated with the extent of myocardial necrosis[27,28].

CONCLUSION

Myocardial infarction is an ischemic disease that is difficult to diagnose based on single factor of diagnostic method. Globally incidence of MI is increasing day by day, which leads to major cause of cardiac dead compared to other pathological conditions.

Early detection and accurate diagnosis of MI can reduce the incidence of mortality and increases the survival rate. Therefore, it is necessary to use a combination of various methods to diagnose MI quickly and accurately. This review concludes use biomarker-based ELISA, SPR, Adrenomedullin (AM), Copeptinand aptamer technologies can be used to diagnose Myocardial infarction along with electrocardiogram and echocardiogram, which is required to diagnose myocardial infarction accurately.

Conflicts of Interest

Authors declare that there is no conflict of interests regarding the publication of this paper.

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