A REVIEW ON ROLE OF CARDIAC TROPONINS IN ACUTE CORONARY SYNDROME

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Abstract

Troponins are structural cardiac muscle proteins that are released during myocyte damage and necrosis. Cardiac troponins are absent in the plasma of a healthy subject, so that small elevations are indicative of myocardial damage. However modern assays are extremely sensitive and can detect low level of myocardial damage. Troponins are highly specific and sensitive marker. The concentration of troponins in the blood increases during an acute myocardial infarction, enabling clinician to quickly initiate appropriate therapy. So they are useful in diagnosing patients with acute coronary syndrome and for predicting the response during drug therapy. This review describes the role of cardiac troponins in acute coronary syndrome.

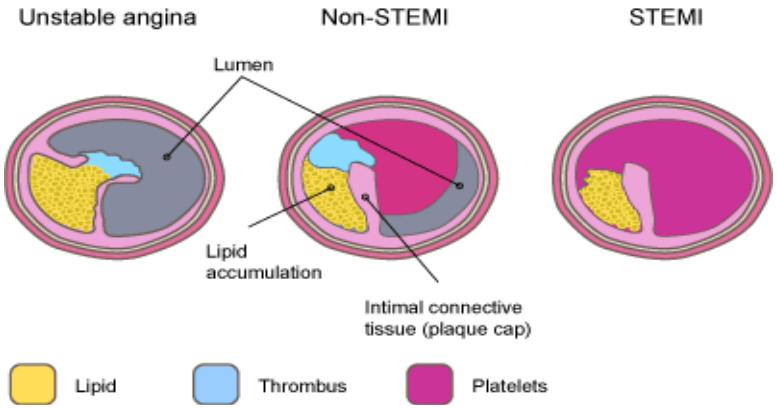
Key words: troponins, myocardial infarction (MI), acute coronary syndrome (ACS)

INTRODUCTION

Incidence and potential severity of an acute coronary syndrome (ACS) makes timely diagnosis and appropriate treatment essential for minimizing morbidity and mortality. Every year in United States approximately 2.5 million patients are admitted with an acute coronary syndrome, two third of whom are eventually diagnosed with unstable angina/ non ST segment elevated myocardial infarction[1]. Myocardial infarction (MI) occurs when blood flow to a section of heart muscle becomes blocked, usually by clot, otherwise known as heart attack. MI is the leading cause of death in industrialized nations[2]. When heart muscle is deprived of oxygen because of decreased blood supply, muscle cells die (necrosis). This is an infarct, lesser infarct undergo healing, in which muscle is replaced by scars made of connective tissue. Contractility of the heart is decreased around the scaring[2, 24]. Serum markers are useful to determine myocardial injury level[3]. Nowadays most widely used biomarkers to identify or predict ACS are high sensitivity C- reactive protein (CRP) and high sensitivity troponins that is troponin T and troponin I[4]. So early detection and timely management of patients with acute coronary syndrome is vital to preserve heart function[4].

ACUTE CORONARY SYNDROME (ACS)

Each year more than 5 million patients present to emergency rooms with chest discomfort and related symptoms, and approximately 1.5 million are hospitalized for acute coronary syndrome. Acute coronary syndrome is an emergency, which commonly results from rupture of an atherosclerotic plaque and partial or complete thrombosis of a coronary artery[5]. Most cases occur from disruption of an atherosclerotic lesion typified by a large lipid pool; numerous inflammatory cells; and thin, fibrous cap (soft plaque) (figure: 1).



This event is followed by platelet activation of coagulation cascade and vasoconstriction. This process culminates in intraluminar thrombosis and vascular occlusion. If thrombus occludes most of the blood vessels, and if the occlusion is untreated, necrosis of the cardiac muscle may ensue (Myocardial Infarction). 45% of people MI occur at an age above 65 year. 5%of people MI occur at an age of 40 year [6]. The acute coronary

syndrome may present either as ST-segment elevation myocardial infarction (STEMI), Non-ST-segment elevation myocardial infarction (NSTEMI), or as an unstable angina (figure 2). The symptoms and eventual diagnosis of a patient presenting with an ACS are dependent on the duration and degree of inadequate oxygenation, making the diagnosis challenging[7, 25]. Myocardial infarction (necrosis) is typified by increase in the serum level of biomarkers of myocardial necrosis[8, 26]. The biochemical markers of myocardial necrosis, predominately Creatinine Kinase (CK) and its MB isoenzyme (CK-MB) as well as cardiac troponin T and I are also essential in the diagnosis and prognosis of patients with an acute coronary syndrome [9, 14](ACS).

BIOCHEMICAL MARKERS OF MYOCARDIAL DAMAGE

Cardiac biomarkers are most commonly used in the diagnosis of cardiac disorders. The ideal biochemical markers should be at high concentration in myocardium, absent in non cardiac tissue. They are released rapidly during myocardial necrosis. Aspartate amino transferase, lactate dehydrogenase isoenzymes are the earliest biomarkers employed in the detection of ischemia. Next generation of cardiac biomarkers include creatine kinases (CK) that are most abundant in heart. More recently, two other enzymes specific for injured myocardial tissue, Troponin I and Troponin T levels are very specific and sensitive to myocardial damage[9, 8, and 7].

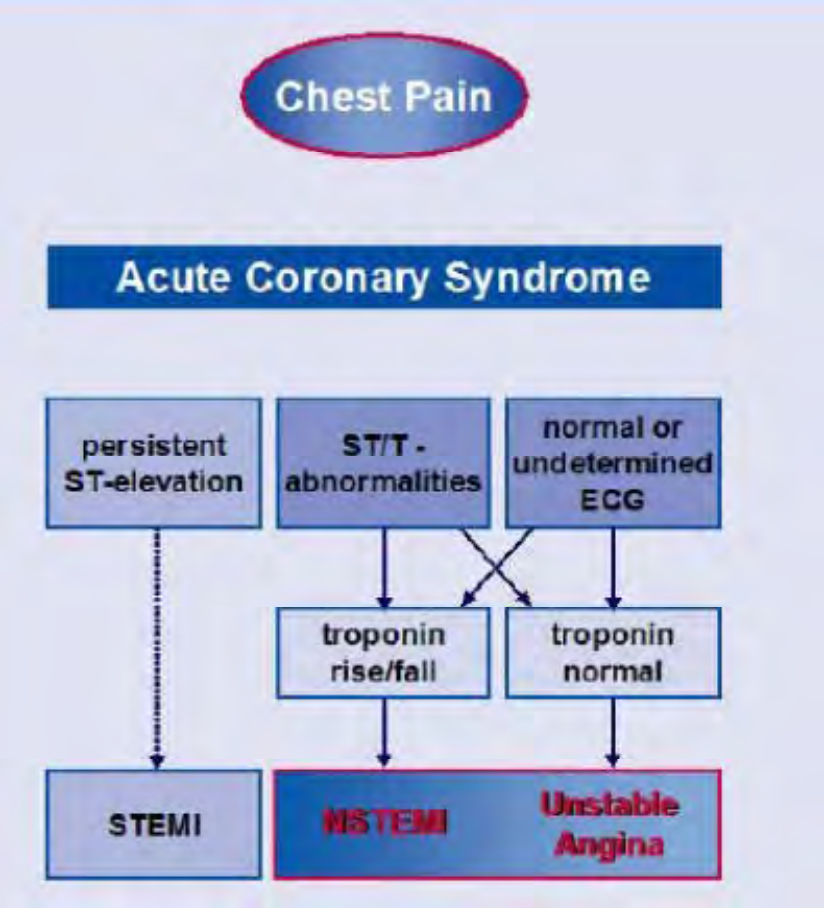


Figure: 2

CK and CK – MB isoenzyme (CK-MB) were the primary biochemical markers used to evaluate patients with chest pain. However several properties of CK and CK – MB limit their predictive value, including their presence at low levels in the blood under normal condition, and in non cardiac sources, especially skeletal muscles. Accordingly cardiac troponins have become the preferred markers of myocardial necrosis. Troponins are more specific and sensitive for myocardial necrosis than CK and CK-MB. Measurements of troponins allow myocardial necrosis to be detected approximately in one third of patients with unstable angina and normal CK – MB levels[10, 1].

CARDIAC TROPONINS

Cardiac troponins are regulatory proteins. It can control calcium mediated interaction of actin and myosin, this result in contraction and relaxation of striated muscles[11]. The complex troponins are made up of three subunits, Troponin T, Troponin I and Troponin C. Troponin C binds with calcium. Troponin I will inhibit actin-myosin interactions. Troponin T helps to facilitate contraction by binding thin troponin complex to tropomycin. Troponin T and troponin I are mostly found in cardiac muscles.[11.28 (]figure: 3)

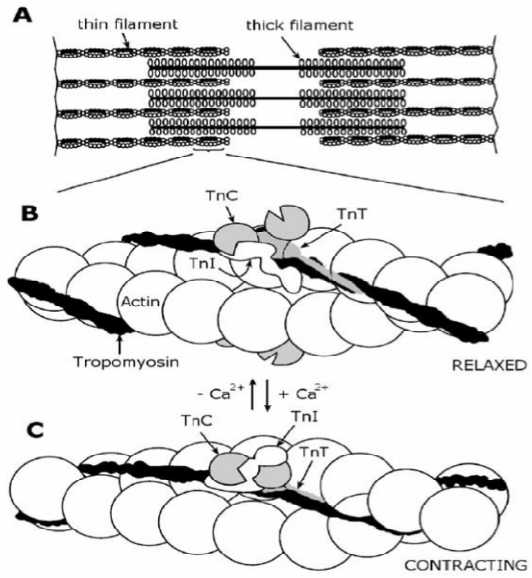


Figure 3: The cardiac troponin subunit and their role in muscle contraction.

These markers become detectable after myocyte necrosis causes the loss of cell membrane integrity, which eventually allows these molecule to diffuse in to the peripheral circulation [11, 10](figure:4). Troponin T and troponin I are structural cardiac muscle proteins that are released during myocyte damage or necrosis, and represent the corner stone of the diagnosis of acute myocardial infarction[12, 20]. However modern assays are extremely sensitive and can detect very low levels of myocardial damage, so that elevated plasma troponin concentrations are seen in other acute conditions, such as pulmonary embolism, septic shock and acute pulmonary oedima. [13, 4]

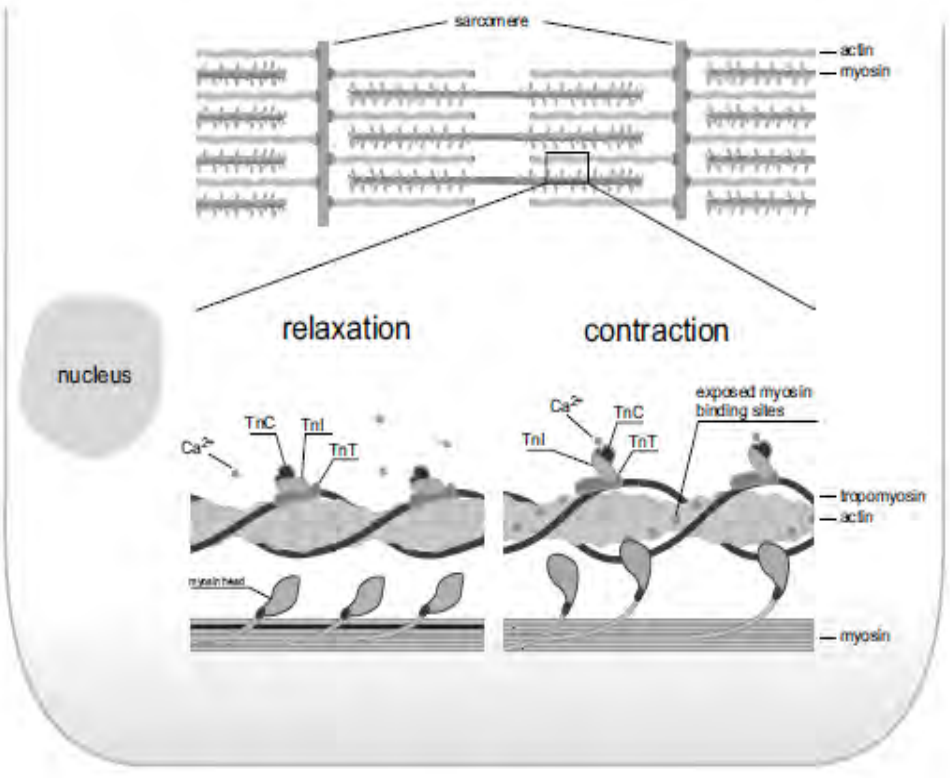


Figure 4: structural characteristics of human myocytes with a focus on their contractile apparatus (sarcomeres) and the regulatory functions of cTnI, cTnT, and cTnC upon calcium stimulation.

During cardiac injury, like ischemia or various other cases, troponins are released from cardiomyocyte into the blood stream in proportion to the degree of damage [14, 12].

Cardiac troponins offer extremely high tissue specificity and sensitivity but do not discriminate between ischemic and non ischemic mechanism of myocardial injury. The definition of myocardial infarction has been refined and now includes all patients with a history of cardiac chest pain or ECG changes and elevated serum troponins. These troponins are the cardiac muscle proteins which are released following myocardial damage and are highly specific and sensitive for myocardial infarction [15, 6, 5].

Troponin T appears slightly earlier than Troponin I after cardiac damage. Troponin T is better at showing slight cardiac damage and predicting 30 day mortality for cardiac patients. Troponin I can also be used to monitor critically ill patients in the critical care settings [16, 12]. Furthermore, the concentration of troponin I increase within 2-4 hrs of an acute MI, and level persist to 1-2 weeks which helps to enabling clinician to quickly initiate appropriate therapy. Serum levels can remain elevated for up to 4-7 days for troponin I and 10-14 days for troponin T. Troponins I level greater than 2ng/ml are suggestive of acute myocardial injury. Troponins also remain elevated for about 10 days compared to the 2-3 day elevation typically observed with CK-MB[17, 25, 27].

Therefore the blood samples should be withdrawn both at presentation and 6-9hrs later to optimize both clinical specificity for ruling out MI and the sensitivity for ruling out MI. The troponin value is usually measured in the blood to differentiate between unstable angina and myocardial infarction in patients with chest pain or acute coronary syndrome[18, 19]. Normal value of troponin T is less than 0.1ng/ml and the troponin I is less than 0.4ng/ml. If troponin value is between 0.5-2.3 ng/ml there is intermediate or suspicions for myocardial injury. If the value is greater than 2.3ng/ml it is positive for myocardial injury[20].

Other than acute coronary syndrome the troponin levels are elevated in patients with congestive heart failure, inflammatory conditions of the heart like pericarditis and myocarditis, cardiomyopathy, coronary artery spasm. It can be see that several procedures like cardiac surgery, heart transplantation, percutanious coronary intervesion were the level of troponins become high. Renal failure, renal insuffiency, pneumonia, septic shock, pulmonary hypertension, pulmonary oedima are the non cardiac situations where the serum troponin levels are raised [21, 22.]

Undetected heart damage may occur that delays the recovery. Studies are being done to see if troponin may be useful for ongoing monitoring of cardiac injury so that medications can be given[23, 16].

CONCLUSION

Acute coronary syndrome is a leading public health problem in world wide. Cardio vascular disease an enormous health problem in the western world, and is high in the list of causes of death. Acute coronary syndromes are unstable coronary condition prone to ischemic recurrences and other complications that may lead to the death or myocardial infarction in short and long term. Cardiac troponins are preferred biomarkers for diagnosing acute myocardial infarction, because elevated levels correlate with more accurate diagnosis; predict high risk of future cardiac events. Evidence from clinical trial suggests that prevention of acute coronary syndrome can significantly decrease cardio vascular death and mortality.

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