Cardiac markers for assessing the acute coronary syndromes

A focus on cardiac troponins

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ABSTRACT

Markers of myocardial injury will continue to play an essential role in the assessment and management of patients presenting within the spectrum of acute coronary syndromes, a term representing the continuum of acute myocardial ischemia ranging from angina through Q-wave myocardial infarction. Coronary artery lesion instability can be detected by markers of plaque inflammation and disruption, platelets reactivity, and thrombosis. When myocardial injury occurs with severe impairment of coronary blood flow, several markers are released from the damaged myocyte. For many years, creatine kinase-MB isoenzyme has been the conventional marker for myocardial infarction. Despite its inadequate sensitivity and specificity for myocardial injury, creatine kinase-MB remains an essential component in assessing re-infarction or infarct extension, as well as in monitoring reperfusion after thrombolytic therapy when combined with myoglobin. Among the many cardiac markers for myocardial necrosis, cardiac troponins possess superior sensitivity and specificity for the detection of myocardial injury. In addition to their superior performance in detecting minor myocardial damage, cardiac troponins can be useful in detecting perioperative myocardial infarction, infarct size, improving risk stratification, and facilitating therapeutic decision making in patients with acute coronary syndromes.

Keywords: Cardiac markers, cardiac troponins, coronary syndromes.

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Determination of cardiac enzymes coupled with suggestive symptoms and electrocardiographic (ECG) changes has traditionally been used to distinguish between patients with and without acute myocardial infarction (MI) and extensive myocardial damage.[1] However, this distinction becomes blurred with other manifestations of acute coronary syndromes (ACSs) which include stable angina, unstable angina, and non-Q myocardial infarction.[2] History alone has proven to be a poor means of identifying patients with ACSs. Out of the 8 million people who visit the emergency room each year in the United States with a chief complaint of chest pain, only 30% have coronary artery disease as a cause of the pain.[3] Also symptoms of myocardial ischemia can be non-specific in up to one-third of patients, particularly in diabetics and elderly.[4]

Although ECG is an important tool for the early diagnosis of patients with chest pain, its diagnostic sensitivity may be as low as 50%.[2,5-7] Equivocal ECGs are usually seen with smaller degrees of myocardial necrosis, intraventricular conduction delays (such as left bundle branch block) and posterior MI.[8]

Serum aspartate transaminase (previously known as glutamic-oxaloacetic transaminase) was noted to

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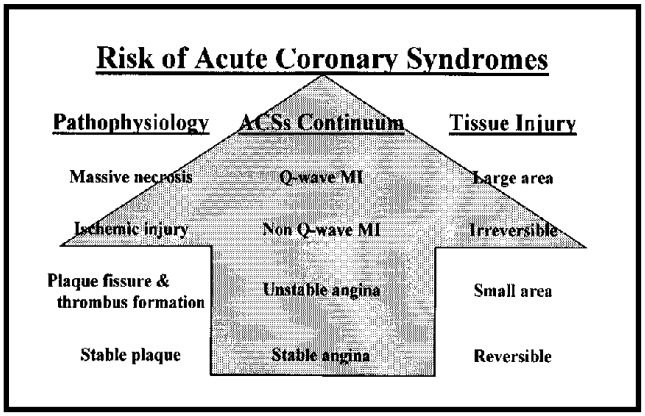

Figure 1 - Risk of Acute Coronary Syndromes (ACSs) in relation to pathologic activation and tissue injury.

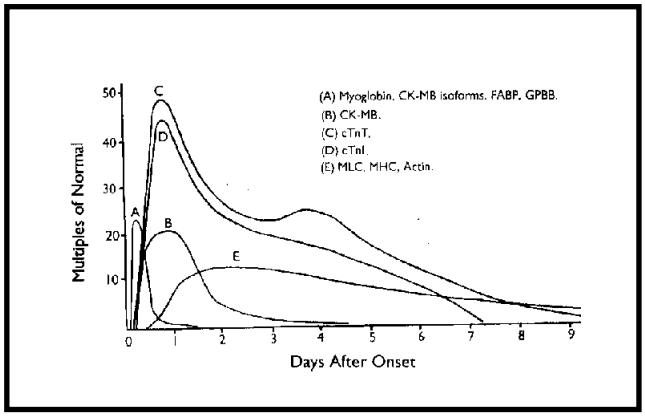

Figure 2 - Release kinetics of cardiac markers inpatients with acute myocardial infarction. CK-MB-creatine kinase MB, FABP-fatty acid binding protein, GPBB-glucogen phosphorylase isoenzyme BB, MLC-myosin light chain, MHC-myosin heavy chain, cTnT-cardiac troponin T, cTnI-cardiac troponin I.

be elevated in patients with acute MI approximately 40 years ago to be elevated.[9] About 10 years later, creatine kinase (CK) and its MB isoenzyme (CK-MB) provided superior cardiac sensitivity and specificity and the measurement of their levels has been used to diagnose myocardial injury since that time.[10] However, this measurement does not adequately allow for identification of patients with ACSs and minimal myocardial damage or microinfarction.[11,12] Further, CK-MB measurement is less reliable for the early and late retrospective diagnosis of cardiac necrosis. It is also associated with poor cardiac specificity in patients with concurrent skeletal muscle injury, thyroid disease, diabetes mellitus, pulmonary embolism, renal failure or intramuscular injections.[10,13]

In addition to diagnosing acute MI, there is also a need to identify patients who have a high risk of future cardiac events in order to provide safe and efficient triage to patients with chest pain. It is crucial to determine promptly whether a patient requires hospitalization, consideration for urgent revascularization, a short observation period, or discharge.

The inadequate sensitivity and specificity of CK and CK-MB for diagnosing myocardial injury and the need for improved safety and efficiency in the triage of patients with acute chest pain, has presaged the introduction of several novel markers for myocardial injury. Cardiac troponin T and I (cTnT and cTnI), CK-MB isoforms, and myoglobin are some of the current markers being evaluated for the diagnosis of myocardial injury.

It has also been reported recently that biochemical indicators of activation of leukocytes and coagulation are raised in some patients with unstable angina and normal markers of myocardial injury.[14,15] The former markers of plaque stability may provide an index hence the new cardiac markers need to provide more information than simply the presence or absence of an acute myocardial infarction. Application of these markers could improve risk stratification of patients with ACSs and aid in selection of different treatment strategies.

The purpose of this review is to provide an overview of the characteristics of these novel markers and to indicate their role in the clinical assessment and treatment of patients with ACSs.

Spectrum of acute coronary syndromes. Throughout life, series of genetic and environmental factors increase our risk of developing clinically significant atherosclerotic changes leading to clinical disease.[16] Clinical studies and experimental animal models have provided an improved insight into molecular events that transform healthy coronary arteries into the clinically diseased vessels with multifocal lesions. The early fatty streak progresses sequentially to the bulging foam cell-filled fibro fatty plaque, the fixed stenotic lesions visible on coronary arteriography,[17,18] and thence to the complicated lesion.

Patients with stable lesions may develop stable angina with reversible tissue injury and are at low risk for adverse events. With progression, inflammatory characteristics appear to accelerate the process leading to the instability of the coronary artery plaques.[19]

Plaque rupture, a process triggering throbogenesis, may occur repeatedly without clinical recognition and without proceeding to occlusion.[17] The propagation of thrombus, with subsequent occlusion, may produce ischemic injury and myocyte necrosis.[20,21] This destabilization of fatty plaque may provoke complete and sudden occlusion with distal infarction and obvious clinical event or none that are recognizable except by biochemical markers of myocyte necrosis.

ACSs represent a continuum of myocardial

ischemia ranging from angina that indicates reversible tissue injury, through frank Q-wave MI with extensive tissue necrosis. This continuum also includes unstable angina and non Q-wave MI which are frequently associated with minor myocardial damage.[2] The differentiation between these two conditions depends on the area of ischemic injury which is usually more with non-Q wave MI. In addition to reflecting the pathophysiological process of acute myocardial ischemia, the continuum of ACSs is a continuum of risk (Figure 1).

In summary, identifying the location of an individual patient's disease in the continuum of ACSs has biological implications regarding the reversibility of injury and quantity of ischemic cell injury, as well as the patient's relative risk for an adverse outcome.

Markers of instability of coronary artery lesions. Plaque inflammation and local thrombus formation are major determinants of coronary artery plaque stability. Unstable coronary artery plaques are characterized by accumulation of macrophages and activation of proinflammation genes in smooth muscles and endothelial cells.[19] Plaque disruption causes release of cytokines from activated monocytes and macrophages at the disrupted site.[22] Among other effects, cytokines (including interleukin-6) promote hepatic synthesis of the acute phase proteins C-reactive protein (CRP) and serum amyloid A.[23,24] This results in higher levels of interleukin-6, CRP and serum amyloid A in blood of patients. Increased concentrations of these markers may have a role in identifying patients having unstable coronary plaques. Circulating levels of these markers were found to be higher in patients with unstable angina, compared with healthy persons and their measurement may have a role in identifying patients having unstable coronary plaques.[25-27] The levels of CRP and serum amyloid A were found to carry prognostic significance in patients with unstable angina.[23,28] CRP levels were also investigated for their ability to predict unfavorable outcomes and impairment of left ventricular function in patients with acute coronary necrosis or previous myocardial infarction.[29]

Since platelet activation is important in the mechanism of thrombus formation, indicators of platelet activation such as platelet function assays or P-selection may help assess a patient's tendency for intracoronary thrombosis. P-selection is an adhesion molecule expressed on the surface of platelets when activated by either exposed collagen, thrombus and or all other agonists reduced by plaque disruption.[30] Expression of this protein is increased on the surface of platelets in patients with symptomatic coronary artery disease.[30]

Markers of thrombosis, including soluble fibrin and fibrin degradation products, may also indicate a recent thrombotic process or risk of an impending event. Elevated levels of these markers are pathognomonic of procoagulant fibrinolytic activity and may predict patients at higher risk for MI-related complications.[31] Other indicators of activation of the coagulation system or inhibition of fibrinolytic activity were also elevated in patients with unstable angina.[32,33]

However, the use of the biochemical markers of inflammation and activation of coagulation is limited because of their low specificity for the presence of unstable coronary artery disease. Furthermore, testing for activation of coagulation suffers from lack of standardization of the analytical procedures and preanalytical difficulties.[25] Thus the use of these markers in the diagnostic work-up of patients with suspected acute coronary syndrome is uncertain.

Markers of myocardial injury. Myocardial injury starts with the loss of myocardial cell integrity induced by myocardial ischemia and ends with cell death and myocardial necrosis. With the development of new immunological techniques it became feasible to detect any cardiac constituent released following loss of myocardial cell integrity. Currently used markers for myocardial injury can be subdivided according to their intracellular compartmentation in the myocytes into three groups: cytosolic, structural, or both cytosolic and structural (Table 1).

The cytosolic group consists of unbound cytosolic proteins like myoglobin, CK and CK-MB isoenzyme, fatty acid binding protein (FABP) and glycogen phosphorylase BB (GPBB). The structurally bound protein group include myosin heavy chains (MHC), myosin light chains (MLC) and actin. The third group consists of cTnT and cTnI which are present in both minor cytosolic and major structurally bound protein pools.[12,34]

The release kinetics of a marker depends on its intracellular compartmentation. Unbound cytosolic markers appear early in circulation (Figure 2) and their serum concentration is significantly affected by perfusion of the infarct zone. The kinetics of myoglobin, FABP and GPBB are the same and characterized by earlier appearance, shorter time to peak value, and shorter duration of elevation compared with CK (Figure 2). The appearance in serum of the structurally bound myofibrillar proteins depend on the activation of proteolytic enzymes, leading to disintegration of the contractile apparatus. This process is time consuming and results in continuous release of these markers from necrotizing myocytes. As a consequence, the kinetics of all these markers are characterized by late appearance, long time to peak value, long duration of elevation, and not significantly affected by reperfusion of the infarct zone.[35]

Since cardiac troponins exist both in a free cytosolic and structurally bound protein pool, they have an early release kinetics resembling cytosolic and a late release resembling structurally bound

Table 1 - Cardiac markers and pathologic activation.

Pathophysiology		Cardiac Markers
Unstable coronary lesion	Plaque rupture	CRP, Serum amyloid A
	Intracoronary thrombosis	Platelet activation, P-selectin, soluble fibrin
Myocardial injury	Tissue ischemia	GPBB
	Tissue necrosis	Cytosolic: myoglobin, FABP, CK-MB Structural: MLC, MHC, Actin Cytosolic & Structural: cTnT, cTnI

CK-MB - creatine kinase MB, FABP - fatty acid binding protein, GPBB - glycogen phosphorylase isoenzyme BB, MLC - myosin light chains, MHC - myosin heavy chains, cTnT - cardiac troponin T, cTnI - cardiac troponin I

molecules (Figure 2). Reperfusion of the infarcted zone significantly affect the release kinetics of the cytosolic but not the structurally bound pool.[74]

Characteristics of markers of myocardial injury. Most cytosolic cardiac proteins lack cardiac specificity since they are also expressed in skeletal muscles and other tissues and are increased in renal failure patients probably as a consequence of skeletal myopathy.[36]

Over the years, CK-MB has proven useful in most situations in the accurate diagnosis of cardiac injury. Serial measurements and the characteristic rise and fall of the enzyme is nearly pathognomonic for diagnosing MI.[37] CK-MB is also an useful component in assessing re-infarction or infarct extension. CK-MB mass assay have been shown to be superior to activity based assays, such as immunoinhibition or electrophoresis.[38,39] Despite this excellent performance, CK-MB is not the ideal marker. Skeletal muscle has both higher total CK activity per gram of tissue and may have up to 3% CK-MB.[40] This results in nonspecificity, particularly in patients with concomitant myocardial and skeletal muscle injury. The calculation of the percent relative index [(CK-MB/total CK)x100] may assist in the differentiation between myocardial and skeletal muscle causes of increased CK.[41,42] Whilst other investigators have concluded that the relative index unacceptably degrades the sensitivity of CK-MB and should be abandoned.[43,44] In addition to the issue of tissue specificity[10,13] and its inadequacy in identifying patients with minimal myocardial damage,[11,12] CK-MB requires 8-12 hours to rise and falls 2-3 days after the onset of symptoms which makes it less reliable for the early and late retrospective diagnosis of cardiac necrosis.

Myoglobin has a low molecular weight which facilitates direct access into blood stream, thereby bypassing the lymphatics leading to the rapid release of the protein during acute MI.[45] As a result, serum myoglobin levels rise fast, reaching twice normal values within 2 hours and peaking within 4 hours of acute MI.[46] Due to this result, myoglobin is currently the marker of choice for timing the onset of necrosis[47,48] and monitoring of reperfusion.[49] (Table 2). A recent study showed that a diagnostic strategy which include myoglobin, CK-MB, and clinical indicators including time to treatment and the chest pain grade, show high efficiency and may provide an important new tool to assess reperfusion after thrombolytic therapy.[50] In addition, myoglobin enhances early sensitivity of biochemical testing for myocardial infarction.[51] But, since myoglobin is the same molecule in cardiac and skeletal muscle, it lacks cardiac specificity. Myoglobin is a very sensitive marker for skeletal muscle injury and is also increased in renal failure patients.[52,53]

Although the results of small recent studies suggest that FABP and GPBB might have slightly higher specificity than myoglobin,[54,55] it is uncertain whether these markers can replace myoglobin which has been evaluated in many trials during recent years.

The CK-MB isoforms (also termed subforms) have also been shown to be early markers for acute MI with a release kinetics similar to that of myoglobin.[56] Currently, CK-MB isoforms are most effectively measured by high-voltage electrophoresis, and are currently used only in a few routine hospital laboratories.[57,58] However, with simplification in analytical methodologies, the routine use of these markers might increase.

Structurally bound myofibrillar protein such as

Table 2 - Characteristics of cardiac makers.

Characteristics	Cardiac markers
Early release	Myoglobin, CK-MB isoforms, FABP, GPBB
Prediction of reperfusion	Myoglobin, CK,MB, CK-MB isoforms
High specificity	cTnT, cTnI, CK-MB isoforms, CK-MB
Wide diagnostic window	cTnT, cTnI, MLC/MHC
Prediction of outcomes	cTnT, cTnI, CK-MB

CK-MB - creatine kinase MB, FABP - fatty acid binding protein, GPBB - glycogen phosphorylase isoenzyme BB, MLC - myosin light chains, MHC - myosin heavy chains, cTnT - cardiac troponin T, cTnI - cardiac troponin I

MLC, MHC and actin lack cardiac specificity since they are expressed in skeletal muscles. Thus, despite of their potentially higher sensitivity and wider temporal diagnostic window,[35] these proteins are not routinely used.

Due to their unique biochemical makeup and location, cTnT and cTnI have emerged as sensitive and more cardio-specific indicators of myocardial cell necrosis which improved the risk stratification process (Table 2) and may facilitate therapeutic decision making in patients with acute coronary syndromes.

Cardiac troponins. Troponins T, I and C form a trimeric complex that regulates the calcium-modulated interaction of actin and myocin in both skeletal and myocardial striated muscles.[59,60] Troponin T functions to bind the troponin complex to the tropomysin strand; troponin I functions to inhibit the activity of actomyosin-adenosine triphosphate; and troponin C serves to bind 4 calcium ions, thus regulating contraction.[61,62] These subunits of the troponin complex are the product of different genes and are not related to each other in protein structure.[63] Troponin T and troponin I both have cardiac isoforms that are the product of unique gene sequences with corresponding unique protein structures.[63-68] This has allowed the development of monoclonal antibodies used in assays that differentiate the cardiac isoforms from those produced in skeletal muscle.[69,70] The aminoacid composition of troponin C is identical in cardiac and skeletal muscle tissue, precluding use of this protein as a specific cardiac marker.[59,71]

The ventricular myocardium contains 10.8 $mg.g^{-1}$ net weight of cTnT and half that amount of cTnI.[72] The molecular weights of cTnT are 37,000 and cTnI are 24,000 Da.[61,62] Whilst both proteins are predominantly found bound to the contractile apparatus of muscle, there is 6-8% free cytosolic pool for cTnT, compared with 3-4% for cTnI.[12,34] Cardiac troponin T appears in blood of patients with acute MI as a mixture of complexed cTnT-I-C and free cTnT. Cardiac troponin I is more hydrophobic and appears in blood predominantly in the binary complex cTI-C found with smaller amounts of the complexed cTnT - I-C.[73]

Following myocardial injury, a biphasic release pattern is usually noticed with an early peak corresponding to release from the free cytosolic pool and a sustained release of intact complexes from the myofibrils.[74] This is more clear with cTnT than cTnI, possibly because of the absence of free cTnI in the serum. This may also explain the shorter duration of elevation of cTnI (5-7 days) compared to cTnT (7-10 days) since the degradation of the complexed cTnI leads to faster clearance of the protein.[75]

Cardiac troponin I is not expressed in skeletal muscle throughout ontogeny. After the ninth postnatal month, it is expressed only in myocardium.[13] On the other hand, cTnT is expressed in fetal skeletal muscle and re-expressed in adult skeletal muscle after injury.[10,76] Early studies have questioned the clinical specificity of cTnT assays in patients with chronic renal failure.[77,78] With the development of a second-generation assay for cTnT, the frequency of positive results in these patients is lower than the frequency in the first-generation assay, although still higher than for cTnI.[79,80] Subsequent studies have shown that the antibodies in the second-generation assays are specific for cTnT isoforms, do not detect the cTnT isoforms expressed in diseased skeletal muscle, and therefore do not produce false-positive cTnT results in skeletal muscle disease and renal patients.[81,82] Preliminary reports showed that increased levels of cTnT in patients with chronic renal failure is associated with higher incidence of cardiac death.[83] The importance of these findings is not completely known and the prognostic significance of the low cardiac troponin level in chronic renal failure remains unclear, pending completion of ongoing outcome studies.[84]

Continuing analytical issues have promoted manufacturers of troponin assays to produce new generation kits to improve assay sensitivity and specificity. A clear example was the problem of nonspecific binding of skeletal muscle troponin encountered by the first-generation assay of cTnT and was corrected with the subsequent generation of assays.[82] Ongoing issues include lack of standardization of cTnI assays. Results from different manufacturers produce cTnI values that differ by a factor of 20 or more.[73] This is not a problem with cTnT assays which are available from only one manufacturer and are standardized to a single material.[73] Other issues that involve all cardiac troponin assays include within-run and total imprecision variability between commercial runs and the potential for false-positive results because of the

presence of fibrin clots and heterophile antibodies.[85]

Role of cardiac troponins. Due to their exceptionally high specificity for myocardial injury, cardiac troponins have gained special interest in a variety of clinical situations (Table 3). Thus cardiac troponins may be useful to confirm a suspected myocardial infarction, aid in the diagnosis of difficult cases, and assist in the triaging of patients with chest pain, a procedure for which demand is increasing.[38] Because of their particular kinetics, cardiac troponins have a wide diagnostic window, permitting both very early and late detection of MI after the onset of symptoms.[12,86]

Measurement of cardiac troponins can reliably detect MI with a sensitivity and specificity superior to CK-MB. Recent studies, however, show that the sensitivity of troponins to detect MI is greater than CK-MB after 6-12 hours but before this time, levels of CK-MB or myoglobin have equal or superior sensitivity.[87,88] Also, there is evidence that cardiac troponin measurement can be used for the estimation of MI size. The extent of cardiac troponins release and scintigraphic evidence of infarct size has been correlated.[89,90] A single cardiac troponin level measured 3-5 days after MI may be useful for estimating infarct size in a wide variety of circumferences.[91]

The measurement of cardiac troponins provide an absolutely cardiac specific marker for patients with minor degrees of myocardial damage. Elevated levels of cardiac troponins can be detected in some patients with normal levels of CK-MB in the serum and no diagnostic ECG changes. The detection of this minor degree of ischemic damage is very important in defining the severity of disease within the spectrum of acute coronary syndromes. In addition, several studies have demonstrated an increased number of cardiac events in patients with elevated cardiac troponins, even in those without elevated CK-MB levels.[92-95] Recently, large prospective studies showed that patients with detectable levels of cardiac troponins have a significantly worse prognosis when compared with those without elevated levels.[96-98]

In the global use of strategies to open occluded coronary arteries IIa (GUSTO IIa) trial, 854 patients who presented within 12 hours of the onset of acute myocardial ischemia were studied in a large prospective analysis.[96] The investigators found that elevated troponin levels were associated with significantly higher mortality rates within 30 days, both in total study population (11.8% vs. 3.9%) and in all electocardiographic subgroups examined. another separate study, termed the fragmin during instability in coronary artery disease (FRISC) study, examined peak cTnT over the 24-hour period after initial presentation in 976 patients with unstable coronary artery disease.[97] This study concluded that the risk of an adverse cardiac outcome increased as the cTnT level increased, indicating that cTnT measured in the first 24-hour provides a valuable prognostic information over the following 5 months, which is independent of age, hypertension, number of antianginal drugs, and ECG changes.[97] Similarly, when cTnI was investigated in 1404 patients with unstable angina or non-Q wave MI in the thrombosis in myocardial infarction IIIb (TIMI IIIb) study,[98] increased levels of cTnI were associated with significantly higher mortality at 42 days (3.7% vs 1% in patients with undetectable levels of the marker).

Table 3 - Role of cardiac troponins.

Confirmation of suspected MI
Early and late detection of MI (6 hours - 1 week)
Estimation MI size
Detection of minor degrees of myocardial damage
Assessment in triaging patients with chest pain
Risk stratification in patients with acute coronary syndromes
Guide therapeutic decisions with LMWH, Gp IIb/IIIa inhibitors and questionable PTCA
Differentiation of skeletal from cardiac muscle injury
Detection of perioperative MI and assessment of cardioprotective measures
Assessment in the diagnosis of myocarditis

MI-myocardial infarction, LMWH-low molecular weight heparin, Gp-Glycoprotien, PTCA-percutaneous transluminal coronary angioplasty

In addition, qualitative assays of both cTnT and cTnI were investigated in patients having a non-diagnostic ECG and were found useful for predicting risk in this patient population.[99] In his trial, Hamm et al showed that patients with elevated levels of cardiac troponins had a high incidence of short term cardiovascular events, whereas those with no detectable levels of cardiac troponins had a low event rate. Therefore, cardiac troponins can be used to triage patients for appropriate placement within the hospital. It should be noted, however, that in the TIMI IIIb study as well as in the study by Hamm et al, absence of cardiac troponins does not equal to the absence of cardiovascular risk. Those patients with chest pain and undetectable cardiac troponins can still suffer short term cardiovascular events, although at a much lower rate.[98,99] Thus, those patients still require subsequent but less urgent testing to determine if their chest pain is related to coronary ischemia.

Because of their ability to identify high-risk patients, cardiac troponins may also facilitate therapeutic decision making. Recent studies showed that increased cardiac troponins concentrations can clearly identify patients who would benefit from treatment with low molecular weight heparin or

glycoprotein IIb/IIIa inhibitors.[100-102] Given the relatively high cost of these medications when compared with other standard antithrombotic and antiplatelet therapies, it is hoped that the measurement of cardiac troponins will allow for the optimum utilization of these treatments. Furthermore, a recent study of 860 patients with ACSs without ST segment elevation showed that early catheter-based intervention was associated with low incidence of postintervention MIs and death even in those patients with increased levels of troponins.[103] This suggests that such patients may benefit from intervention-based strategy. However, more studies are required before the recommendation of such strategy.

Cardiac troponins can also distinguish true myocardial damage from concomitant skeletal muscle injury seen in acute skeletal muscle trauma or chronic muscle disease, including patients with Duchenne muscular dystrophy, polymyositis and chronic myopathy, as well as well-trained marathon runners.[13] Serum levels of cardiac troponins may be also used to identify and measure perioperative myocardial damage and may be useful in assessing the efficiency of cardioprotective measures.[104-108] Because of their cardiac specificity and wide diagnostic window, cardiac troponins may be useful in diagnosing myocarditis, particularly if patients present late after the onset of symptoms.[109]

In conclusion, markers of myocardial injury will continue to play an essential role in the assessment and management of patients presenting within the spectrum of acute coronary syndromes, a term representing the continuum of acute myocardial ischemia ranging from angina through Q-wave myocardial infarction. Coronary artery lesion instability can be detected by markers of plaque inflammation and disruption, platelets reactivity, and thrombosis. When myocardial injury occurs with severe impairment of coronary blood flow, several markers are released from the damaged myocyte. For many years, creatine kinase-MB isoenzyme (CK-MB) has been the conventional marker for myocardial infarction. Despite its inadequate sensitivity and specificity for myocardial injury, CK-MB remains an essential component in assessing re-infarction or infarct extension, as well as in monitoring reperfusion after thrombolytic therapy when combined with myoglobin. Among the many cardiac markers for myocardial necrosis, cardiac troponins possess superior sensitivity and specificity for the detection of myocardial injury. In addition to their superior performance in detecting minor myocardial damage, cardiac troponins can be useful in detecting perioperative myocardial infarction, infarct size, improving risk stratification, and facilitating therapeutic decision making in patients with acute coronary syndromes.

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