Cardiac Markers Following Cardiac Surgery and Percutaneous Coronary Intervention

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KEYWORDS

• Laboratory medicine • Cardiac markers • Biomarkers • Troponin • CK-MB • Cardiac surgery • PCI • CABG

KEY POINTS

- Differentiation between perioperative myocardial injury and acute myocardial infarction (MI) is challenging.
- The current cardiac biomarker thresholds for MIs after cardiac procedures are largely arbitrary and, more importantly, lack therapeutic implications.
- Measurement of cardiac marker concentrations after percutaneous coronary intervention and cardiac surgery should currently be used as a marker of baseline risk, atherosclerosis burden, and procedural complexity rather than a conclusive marker to diagnose acute MI.
- Clinical scrutiny remains of the essence in the evaluation of patients with a clinical suspicion of a postprocedural MI.

INTRODUCTION

Myocardial injury leads to disruption of the normal cardiac myocyte membrane integrity and loss of intracellular content into the extracellular space. As a result, elevated levels of cytosolic and structural proteins, such as MB-creatine kinase (CK-MB) and cardiac troponin (cTn), can be detected in blood serum.[1] Both biomarkers are highly specific for myocardial injury and have, therefore, been granted a central role in the diagnosis of acute myocardial infarction (MI).[2]

However, varying concentrations of cTn and CK-MB can also be found in patients with skeletal muscle damage, heart failure, renal insufficiency, arrhythmias, pulmonary embolism, and in those undergoing cardiac surgery or a percutaneous coronary intervention (PCI).[1,3] The interpretation of cardiac biomarkers is especially complex after

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interventional cardiac procedures because both procedure-related myocardial necrosis and periprocedural MI may cause a (sizable) elevation of serum concentrations. High rates of electrocardiogram (ECG) abnormalities and the absence of clinical symptoms (resulting from use of strong analgesics) in the postinterventional period challenge adequate differentiation even more.[1,2]

In this article, the authors discuss both the diagnostic and prognostic value of cardiac biomarkers after cardiac procedures and analyze the scientific background of the current recommendations. In addition, an overview of the latest MI definitions will be provided.

TYPE 4 AND 5 MI

The interest in cardiac markers after cardiac procedures has strongly increased over the last 3 decades (Fig. 1), which led to multiple modifications of the definition of PCI- and cardiac surgery–related MI.[2]

The classic definition of MI was composed in 1979 by the World Health Organization and consisted of 2 or 3 of the following components: typical symptoms (ie, angina), an increase in cardiac enzymes, and a typical ECG pattern involving the development of Q waves. Definite MI was defined as the presence of unequivocal ECG changes and/or unequivocal enzyme changes, whereas angina was not an absolute necessity for a MI.[4] Notably, the interpretation of cardiac enzyme changes was troublesome at that time because of three factors. First, different assays were used to detect CK and CK-MB serum concentrations (ie, CK-MB was measured both by immune assay and mass). Second, serum CK-MB concentrations were influenced by surgery or trauma because of the expression of CK-MB in skeletal muscle.[5,6] Third, the introduction of cTn in the early 1980s led to conflicting thoughts on biomarker superiority.

2000 Universal Definition of MI

The pressing call of clinicians and researchers for a universal definition of MI compelled the formation of a consensus document in 2000 (Table 1). This document ushered in a new era of MI diagnostics by centralizing cardiac biomarkers.[7] Acute MI was redefined as a typical increase and/or decrease of cardiac biomarkers combined with at least one of the following: (1) ischemic symptoms, (2) development of pathologic Q waves on the ECG, (3) ECG changes indicating ischemia (ST segment elevation or depression), or (4) coronary artery intervention (eg, coronary angioplasty). Furthermore, in the appropriate

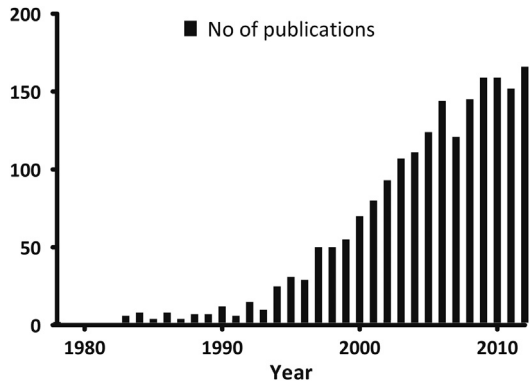

Fig. 1. Numbers of articles regarding cardiac biomarkers and cardiac surgery or PCI in MEDLINE database.

Table 1
Overview of guideline definitions of MI related to PCI and cardiac surgery

Year	Type	Description
1979[4]		Definite acute MI is diagnosed in the presence of unequivocal ECG changes and/or unequivocal enzyme changes; the history may be typical or atypical.
2000[7]	PCI-related MI	"Because PCI-related necrosis occurs as a result of myocardial ischemia, it should be labeled as an MI according to the new criteria. Large infarcts in this setting may be caused by a complicated procedure and can usually be recognized clinically. In contrast, small or tiny infarcts are more frequent and are probably the result of micro-emboli from the atherosclerotic lesion that has been disrupted during angioplasty or from the particulate thrombus at the site of the culprit lesion."
	Cardiac surgery-related MI	"No biomarker is capable of distinguishing damage due to an acute infarction from the usually small quantity of myocardial cell damage associated with the procedure itself. Nevertheless, the higher the value for the cardiac biomarker after the procedure, the greater the amount of damage to the myocardium, irrespective of the mechanism of injury."
2007[8]	4	MI associated with PCI; By convention, increases of biomarkers >3 times the ULN have been designated as defining PCI-related MI. If cardiac troponin is elevated before the procedure and not stable for at least 2 samples 6 h apart, there are insufficient data to recommend biomarker criteria for the diagnosis of periprocedural MI. If the values are stable or falling, criteria for reinfarction by further measurement of biomarkers together with the features of the ECG or imaging can be applied.
	4b	MI associated with stent thrombosis as documented by angiography or at autopsy
	5	Increases of biomarkers >5 times the ULN plus new pathologic Q waves or new LBBB, angiographically documented new graft or native coronary artery occlusion, or imaging evidence of loss of viable myocardium
2012[2]	4	MI associated with PCI is arbitrarily defined by elevation of cTn values >5 times the ULN in patients with normal baseline values (>ULN) or an increase of cTn values >20% if the baseline values are elevated and are stable or decreasing. In addition, (1) symptoms suggestive of myocardial ischemia, (2) new ischemic ECG changes or new LBBB, (3) angiographic loss of patency of a major coronary artery or a side branch or persistent slow- or no-flow or embolization, or (4) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.
	4b	MI associated with stent thrombosis is detected by coronary angiography or autopsy in the setting of myocardial ischemia and with an increase and/or decrease of cardiac biomarker values with at least one value more than the ULN.
	5	MI associated with CABG is arbitrarily defined by elevation of cardiac biomarker values >10 times the ULN in patients with normal baseline cTn values. In addition, (1) new pathologic Q waves or new LBBB, (2) angiographic documented new graft or new native coronary artery occlusion, or (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality are required.
	—	1. After aortic valve replacement, it seems reasonable to apply the same criteria for procedure-related MI as CABG. 2. An elevation of cTn values after ablation should not be labeled as MI.

Abbreviations: CABG, coronary artery bypass grafting; LBBB, left bundle branch block; ULN, Upper Limit of Normal.

setting, the committee designated any detectable cardiac necrosis as MI, which implied that revascularization-related necrosis should also be considered as such. Also, they argued that large periprocedural MI would be very likely to cause clinical signs and symptoms and that diagnostic difficulties would primarily occur in patients with (very) limited MI.

2007 Universal Definition of MI

In an updated form, the 2007 universal definition of MI acknowledged the clinical difficulties regarding procedure-related myocardial injury and designated PCI- and coronary artery bypass graft (CABG)–related MI as different entities (see **Table 1**).[8] PCI-related MI (type 4) was defined as a cTn concentration of more than 3 times the Upper Limit of Normal (ULN). A subtype of MI related to stent thrombosis was also recognized, and designated as type 4b.

CABG-related (type 5) MI was defined as an increase in biomarker concentration of more than 5 times the ULN during the first 72 hours following CABG. In addition, new pathologic Q waves, new left bundle branch block (LBBB), angiographically documented new graft or native coronary artery occlusion, or imaging evidence of loss of viable myocardium were required. Biomarkers, therefore, could not stand alone in the diagnosis of a type 5 MI.

2012 Universal Definition of MI

The most recent universal definition of MI was published in 2012 (see **Table 1**).[2] It defined type 4 MI as a cTn concentration of more than 5 times the ULN in patients with normal baseline values or an increase of more than 20% if the baseline values are elevated and are stable or decreasing. In addition, the requirement of a second sign suggestive of acute ischemia was implemented (eg, angina, typical ECG signs, proven coronary occlusion, or new regional wall movement abnormalities).

The position of the consensus document regarding the diagnostic value of cardiac markers for CABG-related MI did not significantly change because the idea that biomarkers alone do not provide conclusive evidence was retained. A cTn threshold was implemented anyway: type 5 MI was arbitrarily defined as a cTn concentration of more than 10 times the ULN during the first 48 hours following CABG, occurring from a normal baseline value. A second finding suggestive of MI was also required: (1) new pathologic Q waves or new LBBB, (2) angiographically documented new graft or new native coronary artery occlusion, or (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. In regard to type 5 MI more than 48 hours after surgery, it was stated that the existing principles from the universal definition of MI should be applied.

The 2012 consensus document also underlined the potential predictive value of CK-MB and cTn for adverse outcomes after nonrevascularization cardiac procedures (eg, conventional cardiac surgery, transcatheter aortic valve implantation, mitral clips, and ablation procedures). However, because of a general lack of conclusive evidence, no recommendation was made. It was, therefore, pragmatically stated that after aortic valve replacement, "it appears reasonable to apply the same criteria for procedure-related MI as CABG."[2] Also, after ablation therapy, "an elevation of cTn values in this context should not be labeled as MI."[2]

MYOCARDIAL INJURY AFTER PCI

Myocardial injury after PCI is either a result of transient ischemia caused by balloon inflation or of permanent necrosis caused by coronary dissection, occlusion of a major

coronary artery or a side branch, disruption of collateral flow, slow flow or no reflow, distal embolization, and/or microvascular plugging.[2] The incidence and magnitude of myocardial injury is highly variable (ranging from 3.6%–48.8%) and depends on clinical history, angiography results, procedural characteristics, adequate administration of medication, and cardiac marker assays.[9]

Several studies performed in the early 2000s reported a correlation of CK-MB with the development of new pathologic Q waves, in-hospital death, and reduced long-term survival.[10–17] As a result, a threshold of 3 times ULN was chosen in 2007 as a cut-off value for PCI-related MI. However, this threshold appeared to be associated with a large number of false positives.[18] For instance, a large study (n = 8.409) reported no deaths in patients with CK-MB concentrations of 1 to 5 times the ULN. Moreover, that study reported associated risks of 4-month mortality of 8.9%, 1.9%, and 1.2% for patients with CK-MB less than 5 times, 1 to 5 times, and 1 or less times the ULN ($P<.001$), respectively. After 4 months, the survival curve seemed to nearly parallel for 12 months. By 4 years, an additional 2.0% and 4.5% excess mortality rate was observed for the CK-MB 1 to 5 times the ULN and more than 5 times the ULN groups ($P = .024$ and $P<.001$, respectively).[11]

Increasing concerns regarding the ideal cutoff for type 4 MI led to an elevation to 5 times the ULN in the 2012 consensus document. Also, superiority of cTn over CK-MB was hinted, which was striking because a clear association between cTn and impaired outcomes had not been irrefutably established.[19] This, in turn, was highly unexpected because cTn (a component of the cardiac contractile apparatus) conveys a higher sensitivity and specificity for myocardial necrosis than CK-MB (a cytosolic protein).[20] Two hypotheses were opted to explain this phenomenon.

- The first one states that cTn is simply too sensitive to be used as a prognostic marker for relevant major adverse cardiac events because it is affected by both very small (ie, non-prognostically relevant) areas of myocardial injury, and multiple periprocedural factors (eg, iatrogenic myocardial injury, cardiac dysrhythmias, transient cardiac strain, and post-PCI inflammation).[1] The fact that CK-MB is a more evident predictor of short-term adverse outcomes is, therefore, most likely attributable to the larger amount of myocardial necrosis that is required to elevate serum concentrations. However, CK-MB's relative insensitivity also has an obvious downside, because small, yet possibly long-term prognostically important, areas of myocardial necrosis may remain undetected.[21–23]
- A second hypothesis explaining the nonexistent correlation of cTn with adverse outcomes states that multiple influential studies have overlooked the importance of cTn dynamics at baseline.[3] As a consequence, it remains largely unclear whether the postoperative biomarker elevation was a result of the initial ischemic event or of procedure-related necrosis.[3]

The differences in sensitivity between CK-MB and cTn also underline the unlikelihood that an identical threshold (ie, 5 times the ULN) is applicable to both markers. Notably, this gap is even likely to increase due to the continuously improving sensitivity of current cTn assays.[24] For instance, a recent study reported that cTn concentrations of more than 60 times and more than 100 times the ULN conveyed similar risks of death as CK-MB more than 3 times and more than 5 times the ULN, respectively.[19]

Another important drawback of biomarker assessment after PCI procedures is the lack of therapeutic options in case of an elevated marker concentration. For example, if a percutaneous procedure has a complicated course (eg, in case of coronary dissection, distal embolization, a slow- or no-reflow phenomenon), the patient is

bound to fulfill the requirements for a perioperative MI. That same patient, however, is unlikely to benefit from reintervention. Of note, the only patients that are probable to benefit from a reintervention are those with (very) early stent-thrombosis (after an initially uncomplicated PCI), as elevated cardiac markers could be the first sign of acute ischemia.

In conclusion, the implementation of a dichotomous biomarker threshold, regardless of its height, may restrict the option to properly recognize an acute periprocedural MI and could provide a false feeling of safety. One might, therefore, argue that cardiac enzymes should be used as a marker of baseline risk, atherosclerosis burden, and procedural complexity rather than a marker with independent diagnostic significance. Clinical scrutiny remains essential in the evaluation of a perioperative myocardial injury and MI. Future studies should further address the value of minimally invasive imaging in high-risk patients (eg, those with elevated cTn concentrations). Also, the additional value of increased monitoring and/or drug administration in high-risk groups should be assessed.

Stent Thrombosis (Type 4b MI)

Stent thrombosis is a potentially lethal complication of a PCI procedure. Most of these events occur in the first postprocedural days and primarily relate to procedure characteristics and complexity.[25] In the subacute phase, other pathophysiologic mechanisms become a factor of importance. To adequately identify these mechanisms, a temporal component was implemented in the universal definition of MI of 2007 and 2012. Three periods were defined: early (0–30 days), late (31 days to 1 year), and very late (>1 year). These periods correlate to the pathophysiologic processes of thrombosis, neointimal hyperplasia, and neoatherosclerosis, respectively.[25]

Diagnostic difficulties are primarily experienced in patients presenting with a (very) early stent thrombosis, which is a result of a prolonged elevation of cardiac biomarkers after the initial ischemic event and the frequency of postprocedural ECG abnormalities. Predisposing factors of early stent thrombosis are described by Virchow's triad and include hypercoagulability, hemodynamic changes, and endothelial damage or dysfunction (**Fig. 2**).[26]

- *A hypercoagulable state* is inherently associated with PCI procedures and results from a strong increase in platelet reactivity caused by the implantation of an intracoronary foreign body. The degree of hypercoagulability is highly dependent on procedure characteristics and the extent of the coronary lesion.
- *Hemodynamic changes* are frequently observed during and after PCI procedures. Cardiac dysrhythmias, hypertension, and hypotension are common causes.
- *Endothelial damage* is caused by predilatation of the coronary lesion and expansion of the stent.[27,28]

Neointimal Hyperplasia

Neointimal hyperplasia is defined as the accumulation of smooth muscle cells and extracellular matrix in the intimal compartment.[29] It is the major disease process of patency failure between 1 month and 1 year after PCI and can lead to a 25% reduction of intimal space within 4 to 6 weeks (**Fig. 3**). Intimal hyperplasia in itself rarely causes significant stenosis or occlusion. However, it does create atherosclerotic-prone regions (ie, areas at high risk of developing both atheroma and atherosclerosis).[30,31]

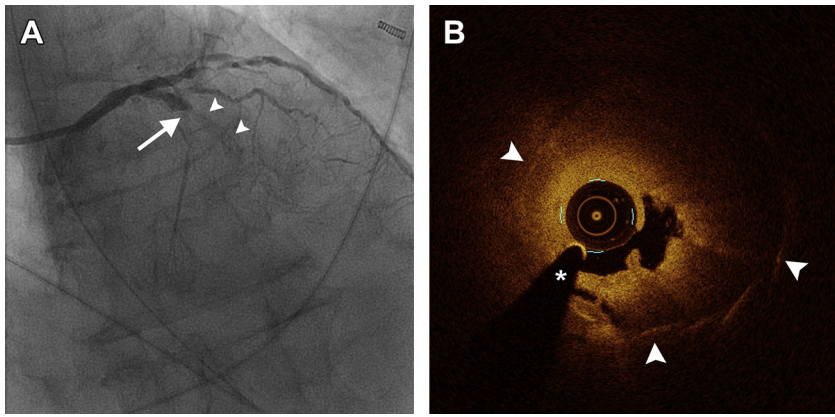

Fig. 2. Early (in-stent) thrombosis. (*A*) Angiographic image showing an occlusion of the proximal left anterior descending artery (*arrow*) located at the exact same position of the bare metal stent (*arrowheads*) that was implanted 5 days earlier during PCI for unstable angina. (*B*) The corresponding optical coherence tomography (OCT) image shows extensive thrombus obscuring the stent struts (*arrowheads*); guidewire artifact (*asterisk*). Additional OCT imaging after repeated thrombosuction revealed stent underexpansion with stent strut malposition. (*Courtesy of* F. Nijhoff, MD, P. Agostoni, MD, PhD, Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands.)

Neo-atherosclerosis

The dominant process of coronary stent failure beyond 12 months is neo-atherosclerosis (**Fig. 4**). This process is partly caused by progression of native coronary atherosclerosis, yet mainly a result of accelerated formation of new atherosclerotic plaques in the targeted vessels.[32]

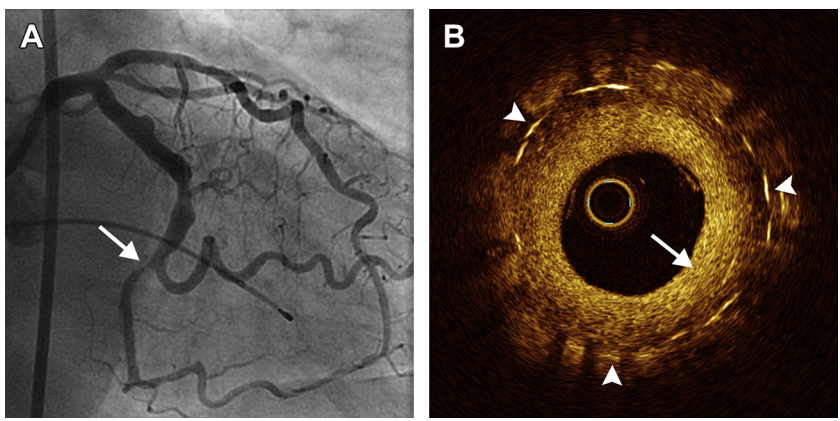

Fig. 3. Neointimal hyperplasia. (*A*) Angiographic image revealing a focal in-stent stenosis (*arrow*) in the circumflex artery, 6 months after implantation of a bare metal stent for acute ST-elevation MI. (*B*) The optical coherence tomography image captured in the same vessel segment demonstrates a circumferential homogeneous, high-backscattering neointima (*arrow*) within the stent (stent struts indicated by *arrowheads*). (*Courtesy of* F. Nijhoff, MD, P. Agostoni, MD, PhD, Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands.)

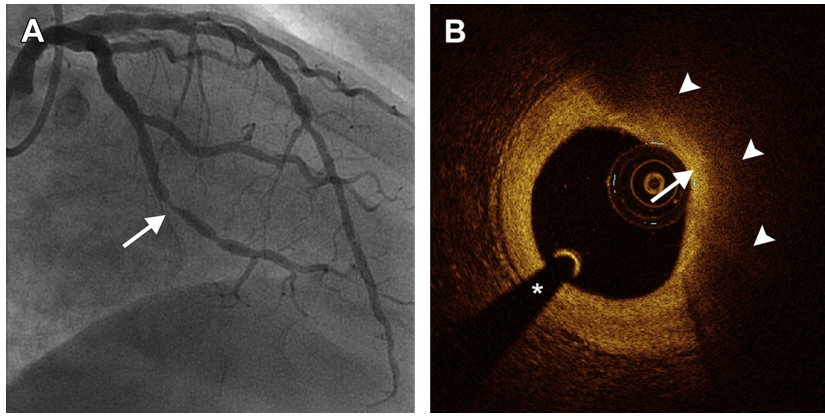

Fig. 4. Neo-atherosclerosis. (*A*) Angiographic image demonstrating a significant stenosis (*arrow*) in the distal circumflex coronary artery. (*B*) Optical coherence tomography (OCT) imaging shows a low signal (*arrowheads*) with poor delineated borders and a cap (*arrow*) indicating the presence of fibroatheroma; guidewire artifact (*asterisk*). (*Courtesy of* F. Nijhoff, MD, P. Agostoni, MD, PhD, Department of Cardiology, University Medical Center Utrecht, Utrecht, Netherlands.)

MYOCARDIAL INJURY AFTER CARDIAC SURGERY

Numerous factors can lead to myocardial necrosis during and after cardiac surgery.[33–35] The most important ones are

1. Suture placement or manipulation of the heart
2. Coronary dissection
3. Global or regional ischemia related to inadequate intraoperative cardiac protection
4. Microvascular events related to reperfusion
5. Myocardial injury induced by oxygen free radical generation
6. Failure to reperfuse areas of the myocardium that are not subtended by graftable vessels
7. Cardiac or coronary manipulation
8. Intraoperative defibrillation
9. Size mismatch between graft and target vessel

Cardiac Markers and CABG

The 2007 and 2012 universal definitions of MI state that biomarkers alone cannot provide conclusive evidence in the diagnosis of a type 5 MI. Strikingly, a threshold was implemented anyway to address the increasing demand for a perioperative MI cutoff.[2,8] The 2007 threshold of 5 times ULN was primarily based on studies that reported a significant correlation of CK-MB with adverse events, such as death, shock, and prolonged length of intensive care unit stay.[36,37] One of the leading studies in this regard was performed by Klatte and colleagues,[36] who reported that CK-MB was an independent predictor of 6-month mortality (odds ratio [OR] 1.90 [1.04–3.48], 1.97 [0.94–4.14], and 4.78 [2.37–9.64] for 5–10, 10–20, and >20 times the ULN, respectively). Consecutive area under the receiver operating characteristics curve analysis suggested that the optimal cutoff point ranged from 5 to 10 times the ULN. Higher cutoff values (>10 times the ULN) were associated with higher specificity and negative predictive values, yet suffered from lower sensitivity.

Multiple studies were performed after that period to determine the exact predictive value of both CK-MB and cTn. These studies initially reported varying prognostic values of cTn, yet have recently shown that cTn is an equal or even better predictor of adverse events than CK-MB.[38–43] For instance, Mohammed and colleagues[41] reported that a postoperative cTn-T concentration of 1.60 ng/mL or more was an independent predictor of 12-month mortality (OR 3.20 [1.5–6.9]). The sensitivity was 56% (95% confidence interval [CI] 21–86); the specificity was 73% (95% CI 69–76); and the negative predictive value was 99.3%. A similar cTn-T threshold (1.58 ng/mL) was opted by Januzzi and colleagues,[39] who reported a correlation with in-hospital mortality (OR 31.0 [95% CI 3.67–263.1]) and death/MI (OR 60.1 [95% CI 7.34–492.1]). Lower optimal cutoff values for type 5 MI were also suggested. For example, Nesher and colleagues[42] reported an optimal threshold of 0.80 ng/mL (OR 2.7 [95% CI 2.08–3.5]), which correlated with a specificity of 97.2%, and a sensitivity of 27.8%. As a result of conflicting ideas about optimal cTn thresholds, an arbitrary cutoff point of 10 times the ULN was implemented in the 2012 universal definition of MI.

Several limitations have to be recognized. For instance, study reproducibility is low because of a limited number of long-term follow-up outcomes and the use of suboptimal composite end points, such as the need for ventilatory support.[41,43] In addition, no evident correlation was found between either cardiac markers and MI on autopsy or magnetic resonance imaging studies or the formation of new Q waves or new LBBB.[44–46] The influence of perioperative or patient-related characteristics, therefore, cannot be totally discarded.

Furthermore, no uniform cTn threshold can be established because of the heterogeneity in study populations and procedure characteristics. For instance, on-pump CABG and CABG combined with valve replacement is associated with higher median cTn levels than off-pump CABG. Median cTn concentrations consequently vary and frequently exceed 10 times the ULN.[41] This variability potentially leads to misinterpretation and an excessive percentage of patients diagnosed with an acute MI.

Another major drawback of cardiac marker assessment after CABG is the lack of therapeutic options after a marked serum elevation. Only a small portion of patients will truly benefit from a reoperation (eg, those with a complicated procedure or acute graft thrombosis). As a consequence, clinical scrutiny remains essential. Also, the value of biomarker dynamics should be assessed further.

In conclusion, the combination of a limited availability of routine imaging and the impotence of ECG monitoring may force clinicians to consider cardiac markers as a relevant diagnostic and prognostic factor for a type 5 MI. However, the influence of perioperative and patient characteristics combined with the absence of clear therapeutic options argues for distancing from the idea that cardiac markers are a definitive indicator of a type 5 MI, especially in the absence of conclusive evidence of acute graft loss or surgical complications. Perioperative measurement of cardiac markers should currently be restricted to research purposes and (modest) risk stratification. Future studies should address cTn's value as a stratification tool for minimally invasive imaging modalities (eg, computed tomography angiography). Also, large interventional studies are required.

Graft Thrombosis

Diagnostic difficulties are primarily experienced in case of a clinical suspicion of a (very) early graft thrombosis. Main causes of such difficulties include postoperative biomarker elevations, ECG abnormalities, and use of strong analgesics. Because the current universal definition does not recognize a type 5b MI, the risk factors of thrombosis associated with CABG are only briefly discussed.

- *A hypercoagulable state* is primarily attributable to increased platelet activation. This situation is caused by procedural characteristics such as an extracorporeal circulation (ie, in case of on-pump surgery) and the inability of the venous endothelial wall to produce sufficient amounts of nitric oxide and prostacyclin (ie, in case of saphenous vein grafting).[47,48] Of note, the degree of hypercoagulability is highly dependent on procedure characteristics (eg, on-pump or off-pump CABG, the combination of a valvular replacement, and/or duration of cardioplegia).
- *Hemodynamic changes* are also observed during and after CABG because factors such as postoperative atrial fibrillation, hypertension, and hypotension are common. Also, patients that undergo CABG surgery frequently require (multiple) packed cells to correct (severe) anemia.[49]
- *Endothelial damage* is inevitable because of manual distension and mechanical trauma.[50] Loss or significant distension of the endothelial monolayer results in the accumulation of fibrin to the luminal surface, the adherence of platelets and neutrophils, and a reduction in tissue plasminogen activator production.[51] Also, the extrinsic coagulation cascade is activated via the expression of tissue factor.

Cardiac Markers and Nonrevascularization Cardiac Surgery

Myocardial damage after cardiac surgery is primarily a result of direct manipulation of cardiac structures. The degree of damage and risk of coronary occlusion or embolization is highly dependent on the procedure and the clinical condition of the patients.[52] Therefore, combined with a general lack of conclusive evidence, no recommendation can be made regarding the value of cardiac markers after these procedures. Current use should be restricted to scientific purposes.[53]

SUMMARY AND RECOMMENDATION

Differentiation between cardiac procedure-related necrosis and postprocedural MI is challenging because of the inherent association of these procedures to varying levels of myocardial injury. To improve risk stratification of patients at risk of an acute MI, biomarker thresholds were implemented in the universal definition of MI. The cutoff points for these thresholds, however, are largely arbitrary and, more importantly, lack therapeutic implications. Measurement of cardiac marker concentrations after PCI and cardiac surgery should, therefore, be used as a marker of baseline risk, atherosclerosis burden, and procedural complexity rather than a conclusive marker to diagnose type 4 or 5 MI, respectively. Considerably more data (primarily derived from interventional studies) are required to justify routine assessment of cardiac markers.

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