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Original Article

Role of high-sensitivity troponin T as a sensitive biomarker for postoperative myocardial infarction and outcome after isolated coronary artery bypass grafting surgery

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Abstract

Background

Uncertainty exists about the diagnosis of post-coronary artery bypass grafting (CABG) Perioperative myocardial infarction (PMI) owing to nonconsensus for elevated biomarkers diagnostic levels and associated criteria. Post-CABG studies concerning high-sensitivity troponin (hs-TnT) and its role in the diagnosis of postoperative MI are few.

Aim

We are aiming to figure out the diagnostic and prognostic role of hs-TnT in individuals undergoing isolated coronary artery bypass graft surgery and whether it has relations to other diagnostic criteria.

Patients and methods

A total of 50 patients with multivessel coronary artery disease who elected for isolated CABG were enrolled in the study. Our exclusion criteria included individuals with chronic renal impairment, sepsis, and pre-existing high level of hs-TnT (unless >50% increment significantly raises its postoperative difference). Moreover, patients who experienced marked intraoperative hypotension (mean arterial blood pressure <80 for >5 min) were excluded. Levels of 140 ng/l (10 times 99th percentile upper reference limit) and 500 ng/l (10 times coefficient of variation of 10% for fourth-generation troponin T applied to hs-TnT) were predetermined.

Results

We enrolled 50 patients who underwent elective CABG. Their mean age was 59.8 ± 6.5 years, and there were 30 (60%) males. hs-TnT level was significantly associated with a higher incidence of off-pump CABG, higher cardiopulmonary bypass time, and higher aortic cross-clamp time. The composite morbidity was significantly higher in patients with hs-TnT level more than 500 ($P < 0.001$). The mortality rate was significantly higher among patients with hs-TnT level more than 500 than those with hs-TnT level 141–500 ($P < 0.001$). No mortality was found in patients with hs-TnT level less than 140. Both hs-TnT more than 140 ng/l with ECG and/or echocardiographic criteria and ECG and/or echocardiographic criteria alone predicted 30-day mortality. The most predictive criteria for postoperative mortality was hs-TnT more than 140 ng/l + ECG and/or echocardiographic criteria (odds ratio: 4.9; 95% confidence interval: 1.6–16.1; $P = 0.00$).

Conclusion

The occurrence of post-CABG MI is associated with a higher level of hs-TnT as well as a higher incidence of morbidity and mortality. The use of hs-TnT to diagnose post-CABG MI with a cut point of 10 times 99th percentile upper reference limit especially if associated with ECG and/or echocardiographic criteria predicts 30-day mortality.

Keywords: High sensitivity, morbidity, mortality, myocardial infarction, postoperative, troponin

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Introduction

Nearly more than one million patients will have cardiac surgery worldwide every year, and 7–15% of them will experience a postoperative myocardial infarction (PMI) [1] in which the early conduit failure is incriminated [2]. More extended hospital stay and also diminished short-term and long-term results are some of the drawbacks of PMI [3].

Recognizing PMI in cardiac surgery patients is not a straightforward issue, as postoperative derangements mask most of the diagnostic criteria. Incisional pain and practice of analgesia may pretense important manifestations of PMI like chest pain and shortness of breath; moreover, direct myocardial insult and postoperative pericarditis produce ECG changes comparable to the PMI [4].

Specific cardiac-specific biomarkers, like creatine kinase M-band (CK-MB) and troponin (Tn), are commonly engaged in diagnosing myocardial damage. However, these cardiac biomarkers are not uncommon to be elevated above cutoff values used to diagnose PMI owing to, for example, occurrence of reperfusion injury following aorta de-clamping without an actual myocardial infarction (MI) [5].

Many surgeons have performed coronary artery bypass grafting (CABG) using cardiopulmonary bypass and cardioplegic arrest aiming to achieve a perfect graft in a nonbloody and nonbeating field [6]. However, considerable morbidity and mortality occur owing to the problem of perioperative MI [5].

Recently, PMI is considered as type 5 MI, and the cornerstone of its diagnosis is the presence of elevated cardiac biomarkers above 10 times the 99th percentile of the upper reference limit [7].

High-sensitivity troponin (Hs-TnT) is a consistent cardiac biomarker that has an excellent negative prediction and diagnostic precision for the detection of acute cardiac injury even with a very early presentation [8].

Patients and methods

This is a prospective research study on a cohort of successive 50 patients who had multivessel coronary artery disease. Being candidates for isolated surgical revascularization, these patients were elected. The data were collected and analyzed.

Patients with morbidities known to be accompanied by elevated T Tn levels like long-standing renal impairment and sepsis have been ruled out. Moreover, we excluded patients with high preoperative levels of hs-TnT without apparent cause unless there was an increase in postoperative levels by 50% or more of the preoperative level.

Our measurements of the hs-TnT levels were consistent with that stated by the third worldwide designation of postoperative MI of 140 ng/l, which is the 10 times 99th percentile the higher reference value, and 500 ng/l, which is the 10 times coefficient of variation of 10% for fourth-generation Tn T applied to hs-TnT [9].

Age, sex, and existing risk factors for coronary artery disease such as the cohort's demographic and clinical variables were collected and recorded. Resting ECG with 12 leads was done consistently before and instantly after the surgery and then every 12 h. Patients with raised cardiac biomarkers and those requiring circulatory support with inotropes, vasopressing, drugs or intra-aortic balloon pump support had transthoracic echocardiography done to detect and follow the de novo developed wall motion abnormalities.

The same surgical and anesthesia teams did all the surgeries and implemented the same anesthetic technique. We approached all patients surgically through a median sternotomy. Myocardial protection was carried out through combined antegrade warm blood hyperkalemic arrest and mild systemic hypothermia (32°C) for on-pump surgeries.

Surgical technique, cardiopulmonary bypass time, aortic cross-clamp time, use of inotropes and vasopressors, length of mechanical ventilation more than 24 h, how long was the ICU and hospital stay, and routine renal and liver functions were recorded.

Blood samples for cardiac biomarkers (hs-TnT and CK-MB) were collected and processed as shown before [10].

Postoperative elevation of CK-MB serum level by five times the normal values associated with ECG and echocardiographic manifestations of a de novo myocardial wall motion abnormalities ensued PMI and was considered as the principal outcome. Meanwhile, the secondary outcomes were the duration of mechanical ventilatory support, ICU length of stays, and extent of hospital stay.

The mean ± SD was used to express the customarily distributed continuous variables. Parametric variables were expressed as number and percentage. The groups and variables were compared through parametric and nonparametric tests (Student's *t*-test and χ^2-test). A significant association is defined by a *P* value of up to 0.05.

Results

We designated 50 patients, all of them had multivessel ischemic heart disease. These patients were candidates for sole surgical coronary artery revascularization. The mean age of that cohort was 59.8 ± 6.5 years, and 60% were males. The remaining of the cohort variables are shown in Table 1.

In the Table 2, the baseline characteristics are assorted by postoperative hs-TnT levels of up to 140, 141–500, and more than 500 ng/l. There was no significant difference among the three groups of hs-TnT level and all the included preoperative baseline characteristics.

The use of the off-pump technique is accompanied by a significantly higher level of hs-TnT; this was an obvious

observation in our cohort. Moreover, patients stayed longer on bypass pump, and those with prolonged ischemia time (aortic-clamp time) have a significantly higher Tn level than the others. Meanwhile, on comparing the three assigned hs-TnT levels with the postoperative ECG changes with or without echocardiographic criteria or the following criteria alone, we found no significant correlations. The occurrence of hs-TnT levels more than 500 ng/dl was accompanied with increased composite morbidity such as renal impairment, surgical site infection (sternotomy), and cerebrovascular accidents (stroke) ($P < 0.001$).

The prevalence of prolonged ventilation more than 24 h was considerably higher in patients with hs-TnT level more than 500 ng/dl (2/10 patients, 20%) compared with the other designated level (141–500) (3/32, 9.4%) ($P < 0.001$).

Table 1: Baseline demographic and clinical characteristics

Patients	*N*=50
Age (years) (mean±SD)	59.8±6.5
Male [*n* (%)]	30 (60)
Past history of MI [*n* (%)]	22 (44)
Past history of PCI [*n* (%)]	18 (36)
Arrhythmia (AF only) [*n* (%)]	2 (4%)
Prevalence of diabetes mellitus [*n* (%)]	17 (34)
Unusual lipid profile (hyperlipidemia) [*n* (%)]	28 (56)
Hypertension [*n* (%)]	25 (50)
Current smokers [*n* (%)]	29 (58)
LMD >50% [*n* (%)]	20 (40)
TVD [*n* (%)]	35 (70)
EF (%) [*n* (%)]	
Normal (>50)	19 (38)
Mild impairment (40-50)	21 (42)
Moderate impairment (30-40)	10 (20)

EF, ejection fraction; LMD, left main disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; TVD, triple vessel disease.

Moreover, these patients had prolonged hospitalization than the others ($P < 0.001$) and a higher initial 30-days mortality (Table 3).

Multivariate analyses

Both hs-TnT more than 140 ng/l with ECG and/or echocardiographic criteria and ECG and/or echocardiographic criteria alone predicted 30-day mortality. The most predictive criteria for postoperative mortality was hs-TnT more than 140 ng/l + ECG and/or echocardiographic criteria (odds ratio: 4.9; 95% confidence interval: 1.6–16.1; $P = 0.001$; Table 4).

Discussion

Despite the broad implementation of well-known myocardial protection strategies, PMI continues to be a postoperative problem following CABG. The incidence of PMI is reported with great inconsistency to range from 3 to 30% owing to using different diagnostic criteria and heterogenous patient populations [11]. Although changes in the blood concentrations of cardiac biomarkers, such as CK-MB, myoglobin, and cardiac Tns are used in the diagnosis of PMI, standard diagnostic parameters were missing [11].

Postoperative detection of MI is unanimously reliant on the detection of elevated values of CK-MB exceeding five times the 99th percentile upper reference level accompanied by echocardiographic imaging criteria pathognomonic to cardiac muscle ischemia not present preoperatively (wall motion abnormalities), with either de novo pathological Q-waves, de novo left bundle branch block (LBBB) in 12-lead ECG, or native coronary or new graft impediment angiographically [7].

Myocyte death releases cardiac Tn, which is a highly specific biomarker. With the recent evolution of hs-TnT assays, the early detection of myocytes necrosis became more expeditious and allowed more rapid diagnosis of MI [12].

Table 2: Preoperative baseline characteristics grouped by postoperative high-sensitivity troponin T levels

Postoperative high-sensitivity troponin T levels (ng/l)	≤140 (*n*=8)	141-500 (*n*=32)	>500 (*n*=10)	*P*
Demographics				
Age (years) (mean±SD)	56.5±6.5	59.4±7.3	61.5±5.6	NS
Male [*n* (%)]	5 (62.5)	18 (56.2)	7 (70)	NS
Previous MI [*n* (%)]	4 (50)	13 (41)	5 (50)	NS
Previous PCI [*n* (%)]	3 (37.5)	11 (34.4)	4 (40)	NS
Atrial fibrillation [*n* (%)]	0	1 (3.1)	1 (10)	NS
Diabetes [*n* (%)]	2 (25)	11 (34.4)	4 (40)	NS
Dyslipidemia [*n* (%)]	5 (62.5)	17 (53)	6 (60)	NS
Hypertension [*n* (%)]	4 (50)	15 (46.9)	6 (60)	NS
Current smoker [*n* (%)]	5 (62.5)	19 (59)	5 (50)	NS
Left main stem stenosis >50% [*n* (%)]	3 (38)	14 (44)	3 (30)	NS
Three-vessel disease [*n* (%)]	6 (75)	21 (66)	8 (80)	NS
Ejection fraction (%) [*n* (%)]				
Normal (>50)	3 (38)	13 (41)	3 (30)	NS
Mild impairment (40-50)	3 (38)	15 (46.9)	3 (30)	NS
Moderate impairment (30-40)	2 (25)	4 (12.5)	4 (40)	NS

MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 3: Operative and postoperative variables grouped by postoperative high-sensitivity troponin T levels

Postoperative high-sensitivity troponin T levels (ng/l)	≤140 (*n*=8)	141-500 (*n*=32)	>500 (*n*=10)	*P*
Off-pump [*n* (%)]	3 (38)	7 (21.9)	1 (10)	0.001
Cardiopulmonary bypass time (mean±SD) (min)	81.5±22	95±29	120±40.5	0.001
Aortic cross-clamp time (min)	48±25	62±23	72±27	0.001
Postoperative outcomes				
ECG (new Q wave or left bundle branch block) [*n* (%)]	2 (25)	8 (28)	3 (30)	>0.05
Echocardiogram [new regional wall motion abnormalities (%)]	1 (12.5)	6 (19)	2 (20)	>0.05
ECG and/or echocardiographic criteria [*n* (%)]	3 (38)	14 (44)	5 (50)	>0.05
Composite morbidity [*n* (%)]	1 (12.5)	8 (28)	5 (50)	0.001
Prolonged ventilation >24 h [n (%)]	0	3 (9.4)	4 (40)	0.001
The operation to discharge (days)	6.5±2.5	8.5±4.5	10.5±5	0.01
30-day mortality [*n* (%)]	0	2 (6.25)	2 (20)	0.01

Table 4: Multivariate predictors of mortality

Predictors of 30-day mortality	HR	95% CI	*P*
Postoperative hs-TnT (/100 ng/l) (reference parameter)	1.07	0.93-1.23	0.36
Hs-TnT>140 ng/l	3.95	1.3-6.7	0.02
Hs-TnT>500 ng/l	4.7	1.6-13.4	0.009
ECG and/or echocardiographic criteria	4.4	1.5-12.7	0.01
Hs-TnT>140 ng/l+ECG and/or echocardiographic criteria	4.9	1.6-16.1	0.001
Hs-TnT>500 ng/l+ECG and/or echocardiographic criteria	5.9	1.8-17.9	0.001

CI, confidence interval; HR, hazards ratio; hs-TnT, high-sensitivity troponin T.

The capability of highly sensitive troponin T (hsTnT) for detection of PMI after CABG or noncardiac surgery. Wang *et al.* [13] reported that postoperative hs-cTnT as a sole parameter independently predicted medium-term mortality and morbidity after CABG, whereas Negele *et al.* [14] reported that preoperative hs-cTnT concentrations were significantly associated with postoperative MI and long-term mortality in high-risk patients undergoing major noncardiac surgery.

From this study, we had many significant results. First, after CABG, the prediction of 30-day mortality when the guidelines for the diagnosis of PMI were used (high-sensitivity assay or dual criteria of hs-TnT levels >140 ng/l in the presence of ECG and/or echocardiographic) was strongly apparent. Second, higher mortality occurred with cutoff point more than 500 ng/l associated with ECG and/or echocardiographic changes. Third, the observation of elevated hs-TnT and associated ECG and/or echocardiographic evidence of MI complied with the suggestion of Third Universal Definition of MI with hs-TnT. Fourth, higher morbidity was associated with higher hs-TnT levels.

Our results were in agreement with the study of Emel *et al*[10]. who studied the correlation between cardiac biomarkers and perioperative myocardial injury (PMI) and apoptosis after isolated CABG surgery and compared the role of cardiac markers in the detection of PMI. They studied 37 patients undergoing elective CABG and found that PMI and apoptosis occurred in all cases. The concentrations and net releases of the evaluated cardiac biomarkers significantly increased ($P < 0.001$ for CK-MB and CK-MB mass, $P < 0.01$ for cTnI, $P < 0.05$ for hs-cTnT) after removal of the aortic clamp. Moreover, a positive correlation between the time of aortic cross-clamp ($r = 0.448$, $P = 0.007$), cardiopulmonary bypass ($r = 0.342$, $P = 0.047$), and a net release of hs-cTnT was found, and they concluded that both cTnI (cardiac troponin I) and hs-cTnT may be used as specific and efficient biomarkers in the detection of myocardial apoptosis and injury after on-pump coronary artery bypass (ONCAB), and the effectiveness of hs-cTnT over cTnI in the detection of perioperative myocardial apoptosis and injury was noticeable also; high postoperative hs-TnT levels alone predicted 30-day mortality and composite morbidity [10]. Previous studies with various modern Tn T and Tn I assays have reported similar results [15–17].

In this study, the isolated hs-TnT more than 140 ng/l was accompanied by mortality and combined morbidity and the cutoff hs-TnT more than 500 ng/l was related to higher mortality and predicted composite morbidity. These findings of a requirement of a high cutoff point are similar to the results of other studies with various assays, including point of care, none of which was guideline obedient [18] used cut points 7.8–170 times upper reference limit [19]. Hs-TnT more than 500 ng/l was an independent predictor of composite morbidity, consistent with an elevation of hs-TnT being a marker of myocardial injury owing to various causes and not attributed to ischemia alone (e.g. heart failure, sepsis, and renal failure) [20].

The essential predictors of post-CABG mortality in this study were the appearance of new signs of MI on the ECG in the presence or absence of new wall motion abnormalities. ECG and/or echocardiographic criteria, however, did not foresee combined postoperative morbidity, viewing their specificity for MI. Our results showed the mortality could be better predicted when using double criteria. These criteria were a strong predictor of 30-day mortality in multivariate analyses

among the other criteria tested. It implements the powers of both hs-TnT's sensitivity for myocardial injury with the specificity of de novo Q-waves and LBBB on ECG for MI. An elevated level of hs-TnT more than 500 ng/l with ECG and/or echocardiographic solely predict mortality at 30 days.

Wang and colleagues found that the highest area under the curve for mortality with dual criteria were 0.64–0.70, whereas previous studies [15,21] have reported area under the curves of 0.73–0.82 using single criteria with modern I or T Tn assays.

Conclusion

The occurrence of post-CABG MI is associated with a higher level of hs-TnT as well as a higher incidence of morbidity and mortality. The use of hs-TnT to diagnose post-CABG MI using hs-TnT with a cut point of 10 times 99th percentile upper reference limit especially if associated with ECG and/or echocardiographic criteria predicts 30-day mortality.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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