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Cardiac Troponin After Major Vascular Surgery

The Role of Perioperative Ischemia, Preoperative Thallium Scanning, and Coronary Revascularization

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OBJECTIVES We sought to determine the role of preoperative predictors, particularly ischemia, on preoperative thallium scanning (PTS) and coronary revascularization on low-level and conventional troponin elevations after major vascular surgery.

BACKGROUND Postoperative cardiac troponin (cTn) elevations have recently been shown to predict both short- and long-term mortality after vascular surgery.

METHODS The perioperative data, including PTS and subsequent coronary revascularization, continuous perioperative 12-lead ST-segment trend monitoring, cTn-I and/or cTn-T, and creatine kinase-MB fraction in the first three postoperative days, were prospectively collected in 501 consecutive elective major vascular procedures.

RESULTS Moderate to severe inducible ischemia on PTS was associated with a 49.0% incidence of low-level (cTn-I >0.6 and/or cTn-T >0.03 ng/ml) and 22.4% conventional (cTn-I >1.5 and/or cTn-T >0.1 ng/ml) troponin elevation. In contrast, patients with preoperative coronary revascularization had 23.4% and 6.4% low-level and conventional troponin elevations, respectively, similar to patients without ischemia on PTS. By multivariate logistic regression, ischemia on PTS was the most important predictor of both low-level and conventional troponin elevations (adjusted odds ratios [ORs] 2.5 and 2.7, $p = 0.02$ and 0.04, respectively), whereas preoperative coronary revascularization predicted less troponin elevations (adjusted ORs 0.35 and 0.16, $p = 0.045$ and 0.022, respectively). Postoperative ischemia (>10 min), the more so prolonged (>30 min) ischemia was the only independent predictor of troponin elevation if added with the preoperative predictors to the multivariate analysis (ORs 15.8 and 22.8, respectively; $p < 0.001$).

CONCLUSIONS Troponin elevations occur frequently after vascular surgery. They are strongly associated with postoperative ischemia, predicted by inducible ischemia on PTS, and reduced by preoperative coronary revascularization. (J Am Coll Cardiol 2004;44:569–75) © 2004 by the American College of Cardiology Foundation

Cardiac-specific troponins are powerful and independent predictors of prognosis in patients with acute coronary syndromes (1,2). Previous studies have shown that among patients with unstable angina and non–ST-segment elevation type infarction, even the smallest increases in cardiac troponin (cTn)-I or -T are associated with a worse outcome (3). This led to a shift in the current diagnostic definitions

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of myocardial infarction (MI), and a greater emphasis is now given to the rise and fall of biochemical markers, in particular, cardiac troponins (4), especially regarding non–ST-segment elevation MI. The diagnosis of postoperative MI is even more dependent on cardiac troponin elevations because of its silent nature, the associated subtle and transient ST-segment depression type ischemic changes (5), and the relatively low specificity of creatine kinase-MB fraction (CK-MB) (6).

We have recently reported that even minor elevations in postoperative serum troponin concentration, below the conventional cut-off level for the diagnosis of MI, are associated with significantly worse long-term survival after major vascular surgery (7). That study was accompanied by a call for a further in-depth analysis of the etiology and population at risk of low-level postoperative troponin elevation (8). Inducible ischemia on preoperative thallium scanning (PTS) predicts adverse postoperative and long-term cardiac events. It has also been recently shown that significant ischemia on PTS is an independent predictor of long-term mortality after major vascular surgery and that coronary revascularization in patients with significant ischemia on thallium scanning is associated with improved long-term survival (9). The effects of preoperative factors, in particular, PTS findings and coronary revascularization, on low-level versus conventional postoperative troponin elevation after

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CK-MB = creatine kinase-MB fraction
cTn = cardiac troponin
MI = myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention
PTS = preoperative thallium scanning

major vascular surgery have not been previously investigated.

METHODS

After approval by the institutional review board and informed consent, 501 consecutive elective major vascular surgical procedures performed in 447 patients at the Hadassah University Hospital from July 1997 to June 2001 were prospectively studied. This group has been described previously (5). Patients with an unstable coronary syndrome in the three months preceding surgery were excluded. All preoperative long-term cardiovascular medications, including beta-blockers and aspirin, were continued until the day of surgery and resumed as soon as possible postoperatively. After completion of surgery, patients were treated in the recovery room or intensive care unit until at least the morning after surgery and had intra-arterial blood pressure monitoring and continuous 12-lead ST-segment trend monitoring. The preoperative clinical findings and perioperative cardiac complications were recorded.

Preoperative thallium scanning was routinely performed in patients scheduled for aortic surgery or lower extremity bypass. Patients scheduled for carotid endarterectomy underwent thallium scanning according to the American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines (10). Patients did not undergo PTS if they had had coronary angiography within the year before surgery with no subsequent change in symptoms, a negative exercise stress test with no history of coronary artery disease (CAD), and no clinical evidence or history of CAD and a delay of the vascular surgery was perceived to be detrimental in terms of their leg ischemia.

Our protocol for PTS has been published previously (8). In brief, thallium defects were defined as either fixed or reversible. The defect size was determined based on a nine-sector model of the heart. A defect larger than two sectors was defined as large, one or two sectors as moderate, and less than one as small. Defect severity was evaluated based on the ratio of defect intensity to presumed normal myocardial area: mild defect = a reduction of 15% to 40% in counts; moderate = reduction of 40% to 50%; and severe = ≥50% reduction in counts (11). Patients with moderate or severe reversible defects, including partially reversible, or large areas (>2 sectors) of even mild but reversible defects on thallium imaging were defined as "moderate to severe reversible ischemia" and were referred to coronary angiography and possible revascularization by either percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) before vascular surgery. Preoperative PCI was performed for technically accessible, >70% coronary stenosis. The CABG was preferred in patients with significant (>50%) left main coronary stenosis, diabetic patients with multivessel disease, or patients with two- or three-vessel disease unsuitable for PCI.

Continuous 12-lead electrocardiographic (ECG) monitoring has been described previously (4). In brief, before induction of anesthesia, patients were connected to a continuous 12-lead ECG monitor (Solar 7000, Marquette Electronics, Milwaukee, Wisconsin) and a Cardiac Review Station (ST-Guard, Marquette Electronics). Monitoring was continued for at least 48 h and up to 72 h. Episodes of ST-segment deviation, defined as ST-segment depression or elevation of ≥0.2 mV in one lead or ≥0.1 mV in two contiguous leads that lasted more than 10 min, were automatically detected and marked by the ST-Guard. The ST-segment deviations lasting <10 min were ignored. Each patient's longest and cumulative ischemia duration, as well as the number of ischemic events, was recorded.

Biochemical markers of MI. Cardiac troponin I and/or T and CK-MB were measured in all patients immediately after surgery and every morning for the first three postoperative days. If either one of these markers was elevated, its measurement was continued for the next days until its return to normal values. Until January 1999, only cTn-I was available in our institution. From January 1999, cTn-T served as the primary indicator for MI, whereas cTn-I was used only for confirmation in patients with impaired renal function exhibiting high levels of cTn-T. Troponin I was measured using a Stratus II analyzer (Dade-Behring Inc., Marburg, Germany). Troponin T was measured by the Elecsys 2010 system (Boehringer Mannheim Corp., GmBH, Germany). Two different cut-off levels for cardiac troponins were examined: 1) cTn-I >1.5 and/or cTn-T >0.1 ng/ml. These were the receiver operating characteristic curve medical decision cut-offs for MI defined by the manufacturers of these assays. 2) A cTn-I >0.6 and/or cTn-T >0.03 ng/ml, corresponding to the lowest troponin levels with <10% imprecision or coefficient variation for these assays (12).

The CK level was measured by a Vitros dry chemistry analyzer (Ortho Clinical Diagnostics, Johnson & Johnson, Raritan, New Jersey). The upper limit of normal for CK was 170 IU. Two cut-off levels for CK-MB/total CK were examined: 5% and 10%.

Clinical MI was diagnosed by the treating physicians, independent of this study, if cTn-I >1.5 and/or cTn-T >0.1 ng/ml was associated with at least one of the following: typical ischemic symptoms, ECG changes indicative of ischemia, or new pathologic Q waves.

Statistical analyses. The *t* test was used for continuous variables, and the chi-square test was used to compare dichotomous variables between groups of patients. Univar-

Table 1. Preoperative Demographic and Clinical Data

	All Vascular Procedures (n = 501)
Age (yrs)	68 ± 10
Gender (male/female)	349/152 (69.7/30.3)
Surgery	
Carotid endarterectomy	231 (46.1)
Abdominal aortic surgery	77 (15.4)
Infra-inguinal bypass procedure	193 (38.5)
Diabetes mellitus	125 (24.9)
Hypertension	320 (63.9)
Hyperlipidemia	154 (30.7)
Smoking history	279 (55.7)
History of IHD	206 (41.1)
Status after MI	131 (26.1)
Angina pectoris	76 (17.0)
Congestive heart failure	38 (7.6)
Kidney disease, creatinine ≥2 mg/dl	13 (2.9)
Preoperative thallium scanning	295 (58.9)
Moderate-severe reversible defects	96 (19.2)
Moderate-severe fixed defects	56 (11.2)
Preoperative coronary angiography	73 (14.6)
Preoperative PTCA/CABG	58 (11.6)
Prior PTCA (any time in the past)	83 (16.6)
Prior CABG (any time in the past)	99 (19.8)
Medications	
Beta-blockers	197 (39.3)
Calcium channel blockers	239 (47.7)
ACE inhibitors	243 (48.5)
Diuretics	134 (26.7)
Hypolipidemic agents	151 (30.1)

Data are presented as the mean value ± SD or number (%) of subjects.
ACE = angiotensin-converting enzyme; CABG = coronary artery bypass graft surgery; IHD = ischemic heart disease; PTCA = percutaneous transluminal coronary angioplasty; MI = myocardial infarction.

iate and multivariate logistic regression analyses were used to find an association between preoperative and postoperative variables, and a stepwise backward conditional selection method was used to select the independent predictors of postoperative markers and calculate odds ratios (ORs) and 95% confidence intervals. A p value of ≤0.05 was considered statistically significant. All the analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, Illinois).

RESULTS

The demographic and preoperative clinical findings are summarized in Table 1. Preoperative thallium scanning was performed before 295 (58.9%) of the vascular procedures, and moderate to severe ischemia was observed in 96 (32.5%) of them. Fifty-eight (11.6%) vascular procedures were preceded by PCI (n = 43) or CABG (n = 15) in the year before vascular surgery, and in 47 (81.0%) of them, coronary revascularization was performed as a result of the preoperative thallium findings (PCI in 35 patients and CABG in 12 patients). The time from PCI to surgery was 84 ± 78 days (range 1 to 329 days) and between CABG and surgery 112 ± 105 days (range 7 to 302 days). In nine patients, PCI with an intracoronary stent was performed, and the shortest duration between coronary stenting and vascular surgery was 21 days.

During 25,622 patient-hours of continuous 12-lead ECG monitoring (51.4 ± 15.7 h/patient), 69 patients had 108 transient ischemic episodes (>10 min), and all episodes except for one were characterized by ST-segment depression. In 44 (8.7%) of the procedures, the longest ischemic episode lasted >30 min, and in 23 (4.6%), ischemia lasted >60 min.

Myocardial infarction. Depending on the biochemical marker and the threshold level used to define MI, between 14 (2.8%) and 116 (23.1%) of all 501 procedures were complicated by postoperative MI (Table 2). Using the lower cut-off level of troponin (cTn-I >0.6 and/or cTn-T >0.03 ng/ml), 23.1% had postoperative MI, as compared with only 9% if the conventional cut-off levels (cTn-I >0.6 and/or cTn-T ng/ml >0.03) were used. Similarly, if CK-MB >5% was used, 7.4% of the procedures were complicated by postoperative MI, as compared with 2.8% if the threshold of CK-MB >10% was utilized. Symptoms attributable to infarction, such as prolonged chest pain, congestive heart failure, or new-onset arrhythmia, were recorded in only 18 (3.6%) of the patients. None of the patients had new Q waves. Patients who had moderate to severe ischemia on PTS had higher incidences of cTn-I >0.6 and/or cTn-T >0.03 ng/ml (37.5%), CK-MB

Table 2. Association of Preoperative Thalium and Coronary Revascularization With Postoperative Ischemia and Infarction

	cTn-I >0.6 and/or cTn-T >0.03 ng/ml	cTn-I >1.5 and/or cTn-T >0.1 ng/ml	CK-MB >5%	CK-MB >10%	Ischemia >10 min	Ischemia >30 min	Clinically Diagnosed MI
All patients (N = 501)	116 (23.1)	45 (9.0)	37 (7.4)	14 (2.8)	81 (1.2)	44 (8.8)	16 (3.2)
No moderate-severe reversible defects	52 (26.1)	19 (9.5)	13 (6.5)	3 (1.5)	31 (15.6)	15 (7.5)	5 (2.5)
With moderate-severe reversible defects	36 (37.5)	14 (14.6)	12 (12.5)	5 (5.2)	30 (31.2)	15 (15.6)	9 (9.4)
p value	**0.032**	0.14	0.069	0.07	**0.021**	**0.028**	**<0.001**
No moderate-severe fixed defects	66 (28.4)	25 (10.8)	16 (6.9)	5 (2.2)	39 (16.3)	19 (8.2)	10 (4.2)
With moderate-severe fixed defects	21 (37.5)	7 (12.5)	8 (14.3)	2 (3.6)	19 (33.9)	8 (14.3)	4 (7.1)
p value	0.12	0.43	0.069	0.41	**0.049**	0.13	0.06
With moderate-severe reversible defects but no coronary revascularization	24 (49.0)	11 (22.4)	8 (16.3)	3 (6.1)	16 (32.7)	14 (28.6)	9 (9.4)
With preoperative coronary revascularization (CABG/PTCA)	11 (23.4)	3 (6.4)	4 (8.5)	2 (4.3)	4 (8.5)	1 (2.1)	0
p value	**0.015**	**0.024**	0.19	0.52	**0.003**	**<0.001**	**0.001**

Data are presented as the number (%) of subjects. Boldface indicates statistically significant values (<0.05).
CK-MB = creatine kinase-MB fraction; cTn = cardiac troponin; other abbreviations as in Table 1.

Table 3. Peoperative Predictors of Postoperative Troponin (Logistic Regression Analysis)

	Univariate Analysis					
	cTn-I >0.6 and/or cTn-T >0.03 ng/ml		cTn-I >1.5 and/or cTn-T >0.1 ng/ml		ST-Segment Depression Type Ischemia >10 min	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.02 (1.00–1.04)	**0.039**	1.02 (0.99–1.05)	0.11	1.005 (0.97–1.03)	0.076
Gender (female vs. male)	0.87 (0.53–1.42)	0.53	0.92 (0.47–1.83)	0.87	0.38 (0.16–0.86)	**0.022**
Surgery						
AAS (vs. CEA)	1.26 (0.68–2.33)	0.44	1.77 (0.77–4.05)	0.17	2.19 (0.85–5.66)	0.105
Infra-inguinal (bypass vs. CEA)	1.48 (0.93–2.34)	0.09	1.73 (0.89–3.36)	0.10	2.92 (1.39–6.13)	**0.005**
Diabetes mellitus	1.73 (1.09–2.71)	**0.018**	1.75 (0.96–3.34)	0.07	2.08 (1.11–3.91)	**0.022**
Hypertension	1.48 (0.95–2.32)	0.082	1.94 (0.91–4.04)	0.083	1.10 (0.56–2.16)	0.77
Hyperlipidemia	1.06 (0.67–1.68)	0.79	0.94 (0.49–1.78)	0.85	1.23 (0.63–2.38)	0.53
Smoking history	1.14 (0.72–1.80)	0.56	1.25 (0.68–2.31)	0.46	1.16 (0.62–2.18)	0.63
History of IHD	1.82 (1.18–2.80)	**0.006**	1.74 (1.02–3.03)	**0.048**	1.97 (1.06–3.67)	**0.032**
S/A MI	1.46 (0.93–2.29)	0.098	1.05 (0.55–2.00)	0.87	1.23 (0.64–2.35)	0.52
Angina pectoris	1.55 (0.88–2.71)	0.28	1.42 (0.66–3.02)	0.36	1.69 (0.80–3.53)	0.16
Congestive heart failure	2.24 (1.13–4.46)	**0.021**	1.19 (0.37–3.24)	0.87	1.33 (0.31–2.77)	0.91
Kidney disease, creatinine ≥2 mg/dl	1.14 (0.37–3.53)	0.81	1.24 (0.23–4.63)	0.74	1.56 (0.24–14.21)	0.56
Preoperative thallium scanning						
Moderate-severe reversible defects	1.84 (1.08–3.11)	**0.024**	1.39 (0.67–2.84)	0.37	2.63 (1.25–5.55)	**0.011**
Moderate-severe fixed defects	1.41 (0.79–2.51)	0.25	1.10 (0.49–2.46)	0.80	1.58 (0.69–3.63)	0.27
Preoperative PTCA/CABG	1.19 (0.64–2.19)	0.57	0.38 (0.11–1.28)	0.12	0.13 (0.02–0.96)	**0.046**
Medications						
Beta-blockers	0.67 (0.37–1.21)	0.19	1.42 (0.66–3.02)	0.36	1.02 (0.46–2.24)	0.95
Calcium channel blockers	0.87 (0.50–1.49)	0.61	0.96 (0.46–1.99)	0.91	0.63 (0.28–1.39)	0.25
ACE inhibitors	1.27 (0.74–2.17)	0.38	0.93 (0.45–1.93)	0.85	0.99 (0.46–2.11)	0.98
Diuretics	1.15 (0.61–2.18)	0.66	1.13 (0.48–2.63)	0.77	0.89 (0.35–2.22)	0.81
Hypolipidemic agents	0.74 (0.41–1.33)	0.28	0.92 (0.55–1.89)	0.88	1.12 (0.40–1.98)	0.67

Boldface indicates statistically significant values (<0.05).
AAS = abdominal aortic surgery; CEA = carotid endarterectomy; other abbreviations as in Tables 1 to 3.

>5% (12.1%), and postoperative ischemia >10 min (19.8%) than patients without such thallium results (Table 2). Among patients with moderate to severe ischemia on thallium scanning, those without preoperative coronary revascularization had the highest incidences of low-level troponin elevation (49%), CK-MB >5% (22.4%), and ischemia >10 min (32.7%), significantly higher than in patients with preoperative coronary revascularization (Table 2).

Myocardial infarction was clinically diagnosed by the treating physicians in 16 patients (3.2%), based on the combination of elevated cardiac troponin levels above the conventional cut-off levels (cTn-I >1.5 and/or cTn-T >0.1 ng/ml), with ECG findings and/or prolonged chest pain. In all but one of these patients, MI was diagnosed already in the first three postoperative days. The distribution of these patients according to their preoperative findings is summarized in Table 2. Two of these patients died shortly after postoperative infarction (8 and 32 days postoperatively).

Predictors of myocardial ischemia and MI. Table 3 shows the univariate logistic regression analysis of all preoperative predictors of low-level troponin elevation (cTn-I >0.6 and/or cTn-T >0.03 ng/ml), conventional troponin elevation (cTn-I >1.5 and/or cTn-T >0.1 ng/ml), and myocardial ischemia (>10 min). In this analysis, a history of ischemic heart disease, diabetes mellitus, and moderate to severe ischemia on PTS were associated with the markers of ischemia and infarction. A history of congestive heart failure was associated with elevated postoperative troponin levels, and preoperative coronary revascularization was associated with less postoperative ischemia on univariate analysis.

Table 4 summarizes only the independent preoperative predictors of postoperative troponin and ischemia after stepwise selection by the multivariate logistic regression model. Moderate to severe ischemia on thallium scanning independently predicted an increase in troponin (both threshold levels) and postoperative ischemia. Conversely, preoperative coronary revascularization independently predicted fewer troponin elevations (both threshold levels) and less postoperative ischemia. It is noteworthy that moderate to severe ischemia on thallium scanning was the only independent predictor of troponin elevation, even after exclusion from the analysis of patients with postoperative troponin above the conventional cut-off levels (cTn-I >1.5 and/or cTn-T >0.1 ng/ml; adjusted OR 2.53, 95% confidence interval 1.17 to 5.47; $p = 0.018$).

Effect of postoperative ischemia. Both low-level and conventional troponin elevations were strongly associated with postoperative >10 min ischemia (OR 3.95 and 9.77, $p < 0.001$) and with prolonged (>30 min) ischemia (ORs 7.2 and 24.9, $p < 0.001$). Postoperative (>10 min) ischemia was the only independent predictor of conventional troponin elevation when analyzed with multivariate logistic regression analysis, together with all preoperative predictors (OR 15.8, $p < 0.001$). Only postoperative (>10 min)

Table 4. Peoperative Predictors of Postoperative Troponin as Selected by the Multivariate Logistic Regression Analysis

	Multivariate Analysis							
	cTn-I >0.6 and/or cTn-T >0.03 ng/ml		cTn-I >1.5 and/or cTn-T >0.1 ng/ml		Ischemia >10 min		Ischemia >30 min	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.03 (0.99–1.07)	0.060	1.04 (0.99–1.07)	0.081				
Type of surgery								
AAS					2.85 (1.14–7.11)	**0.025**		
Infra-inguinal bypass					1.80 (0.81–4.00)	0.15		
Moderate-severe reversible defects	2.55 (1.16–5.62)	**0.020**	2.74 (1.03–7.28)	**0.041**	3.88 (2.03–8.74)	**<0.0001**	5.06 (2.06–12.44)	**<0.0001**
Preoperative PTCA/CABG	0.35 (0.13–0.97)	**0.045**	0.16 (0.03–0.76)	**0.022**	0.19 (0.06–0.62)	**0.006**	0.07 (0.009–0.60)	**0.015**

Boldface indicates statistically significant values (<0.05).
AAS = abdominal aortic surgery; CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

ischemia and moderate to severe reversible ischemia on thallium scanning independently predicted low-level troponin elevation (ORs 4.5 and 2.2, $p < 0.001$ and 0.023, respectively). Similarly, prolonged (>30 min) postoperative ischemia was the only independent predictor of conventional troponin elevation if added with the preoperative predictors to the multivariate analysis (OR 22.8, $p < 0.001$).

DISCUSSION

Recent studies reported a decreasing incidence of perioperative MI after major vascular surgery. This is also supported by the present study, where the incidence of clinically identified postoperative MI was only 3.2%. However, our data further show that this apparently low incidence of postoperative MI represents only a small fraction of all postoperative myocardial injuries or infarctions. After major vascular surgery, conventional postoperative troponin elevations (cTn-I >1.5 and/or cTn-T >0.1 ng/ml) occur in 9.0% and low-level troponin elevations (cTn-I >0.6 and/or cTn-T >0.03 ng/ml) are found in 23.4% of patients, both of which are associated with worse long-term survival (7). Moreover, the present study shows that patients with moderate to severe reversible ischemia on PTS have up to a 49.0% incidence of low-level troponin elevations and 22.4% conventional troponin elevations, except if they undergo preoperative coronary revascularization. In the latter case, the incidence of troponin elevation is similar to that of patients without significant reversible ischemia on PTS (23.4% and 6.4%, respectively) (Table 2). Two major factors predicted elevated postoperative troponin levels, as well as silent ischemia, in our study: the severity of CAD, as indicated by the presence of moderate to severe ischemia on PTS, and preoperative coronary revascularization. Moderate to severe ischemia on thallium scanning was associated with an up to 2.7-fold increase in the incidence of postoperative troponin elevation ($p < 0.02$) and an up to 5.0-fold increase in the incidence of postoperative ischemia ($p < 0.001$). In contrast, preoperative coronary revascularization by either PCI or CABG was associated with a significant reduction, although not complete elimination of both the incidence of troponin elevation and postoperative ischemia (adjusted ORs 0.35 and 0.19, $p = 0.045$ and 0.006, respectively) (Table 4).

Several studies have demonstrated that inducible ischemia on preoperative thallium scanning predicted cardiac events after major noncardiac surgery (13–15), although two studies disagreed with these results (16,17). A few studies also suggested that preoperative coronary revascularization improves the cardiac outcome early after major noncardiac surgery (18,19). We have recently shown that preoperative coronary revascularization in patients with moderate to severe reversible ischemia on thallium scanning is associated with improved long-term survival after major vascular surgery (9). However, none of the previous studies explored the association of PTS results or coronary revascularization with postoperative cardiac troponin and ischemia duration after major surgery. Furthermore, no previous study has investigated the high incidence of low-level postoperative troponin elevations associated with preoperative CAD. These missing links to prognosis are provided in the present study.

The importance of the present data is evident in light of recent publications that cardiac troponin, per se, after major noncardiac surgery predicts both short- and long-term cardiac morbidity and survival. Two studies have shown that conventional postoperative troponin elevations are associated with an up to 5.9-fold increase in mortality and cardiac complications in the first six months after major noncardiac surgery (20,21). We have recently demonstrated, in the same cohort of patients, that not only conventional but also minor postoperative troponin elevations predicted a greater risk of long-term (up to five years) mortality after major vascular surgery.

Cardiac troponins are sensitive and specific markers of myocardial injury. Even minor elevations in troponin are associated with a higher risk of death and re-infarction among patients with non–ST-segment elevation acute coronary syndromes (22,23). In the setting of acute coronary syndromes, troponin elevations are also associated with a

higher incidence of multivessel disease, complex coronary lesions, visible thrombus, distal embolization of platelet micro-aggregates, and abnormal myocardial tissue level perfusion (24). However, troponin elevation may also occur after apparently minor insults, due to causes other than acute coronary syndromes (i.e., following prolonged tachycardia with or without hemodynamic compromise), even in patients without angiographic significant CAD (<50% stenosis) (25), in patients with sepsis (26,27), and after prolonged strenuous endurance exercise (28). Low-level serum troponin elevation has been documented in patients with chronic heart failure and shown to correlate with increased cardiac filling pressures, serum beta-type natriuretic peptide, and worse long-term survival (29). The pathophysiology behind serum troponin elevations in heart failure is believed to be distinct from that seen in acute coronary syndromes and most probably results from progressive myocyte loss through necrotic and apoptotic cell death (30,31). Other reports proposed a relationship between troponin and death in clinical scenarios in which ventricular wall stress is increased, such as massive pulmonary embolism (32), subarachnoid hemorrhage (33), and acute medical illness requiring intensive care (20). Increased myocardial wall stress leads to reduced subendocardial perfusion, even in the absence of CAD, resulting in a decline in systolic function (34,35).

Tachycardia, hemodynamic instability, prolonged adrenergic stimulation, increased cardiac filling pressures, ventricular wall stress, and heart failure are frequent phenomena during and after major surgery. These may potentially lead to acute coronary events, but also to non–acute-coronary-event type postoperative ischemia, troponin elevations, and mortality (1). As evident from this and previous studies (36), the overwhelming majority of postoperative cardiac events, myocardial injuries, and infarctions are preceded by ST-segment depression rather than ST-segment elevation type ischemia. Prolonged ST-segment depression type ischemia is the most common precursor of postoperative MI, whereas ST-segment elevation is relatively rare in this setting (5). In this study, postoperative ischemia was the only independent predictor of conventional troponin elevation, and together with preoperative moderate to severe ischemia on thallium scanning, ischemia independently predicted low-level postoperative troponin elevation. It is suggestive therefore that both low-level and conventional troponin elevations (myocardial injury and infarction) represent a continuum of events in which longer duration postoperative stress-induced ischemia is associated with a higher troponin elevation (5) and worse survival (7). Based on these findings, it is also understandable why therapeutic measures to reduce perioperative stress, such as prophylactic perioperative beta-adrenergic blockade, reduce perioperative and long-term adverse cardiac events (37,38).

Several important caveats deserve special emphasis in light of these data. Not all postoperative cardiac troponin elevations are necessarily related to CAD. Subsequently, not all postoperative cardiac troponin elevations can be totally eliminated by preoperative coronary interventions. Moreover, even in patients who undergo preoperative coronary interventions, revascularization is not always complete because of technical or anatomic considerations, thus explaining the low yet not negligible incidence of postoperative troponin elevations in patients with preoperative coronary revascularization.

Conclusions. Low-level postoperative troponin elevations frequently occur after major vascular surgery, especially in patients with inducible ischemia on preoperative testing, who did not undergo coronary revascularization. Preoperative coronary revascularization significantly reduces but does not eliminate postoperative troponin elevation. Prolonged ischemia is the most important precursor of postoperative troponin elevation. Further studies are required to define the best methods for preventing postoperative troponin elevations.

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