

Clinical Study

Clinical Use of Ultrasensitive Cardiac Troponin I Assay in Intermediate- and High-Risk Surgery Patients

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Background. Cardiac troponin levels have been reported to add value in the detection of cardiovascular complications in noncardiac surgery. A sensitive cardiac troponin I (cTnI) assay could provide more accurate prognostic information. **Methods.** This study prospectively enrolled 142 patients with at least one Revised Cardiac Risk Index risk factor who underwent noncardiac surgery. cTnI levels were measured postoperatively. Short-term cardiac outcome predictors were evaluated. **Results.** cTnI elevation was observed in 47 patients, among whom 14 were diagnosed as having myocardial infarction (MI). After 30 days, 16 patients had major adverse cardiac events (MACE). Excluding patients with a final diagnosis of MI, predictors of cTnI elevation included dialysis, history of heart failure, transoperative major bleeding, and elevated levels of pre- and postoperative N-terminal pro-B-type natriuretic peptide (NT-proBNP). Maximal cTnI values showed the highest sensitivity (94%), specificity (75%), and overall accuracy (AUC 0.89; 95% CI 0.80–0.98) for postoperative MACE. Postoperative cTnI peak level (OR 9.4; 95% CI 2.3–39.2) and a preoperative NT-proBNP level ≥ 917 pg/mL (OR 3.47; 95% CI 1.05–11.6) were independent risk factors for MACE. **Conclusions.** cTnI was shown to be an independent prognostic factor for cardiac outcomes and should be considered as a component of perioperative risk assessment.

1. Introduction

In recent years, many high-risk patients have undergone major noncardiac surgeries and have suffered adverse cardiac events. Perioperative myocardial ischemia occurs in up to 40% of patients at risk of coronary artery disease, but it is usually clinically silent and therefore difficult to detect [1–3]. More importantly, it is a major factor related to long-term adverse events generally occurring in 5.6% of high-risk coronary artery disease patients [4, 5].

Several preoperative risk stratification scores have been developed and adjusted over recent years [4, 6–8].

Nonetheless, the prognostic accuracy of these scores is limited, given that only patient history and preoperative clinical status are considered to predict short-term morbidity and mortality or to identify patients in need of more detailed cardiac testing. Patient outcomes do not only depend on preoperative findings or the type of surgery performed but also on perioperative events.

Troponin elevation in the perioperative period has been reported to provide added diagnostic value to the detection of cardiovascular complications [9–18]. Several studies have demonstrated that monitoring cardiac enzymes after surgery

may help to identify a considerable proportion of silent perioperative myocardial infarctions, but most patients were restricted to vascular surgery or had coronary artery disease. Moreover, studies using different troponin assays with different accuracy and cut-off points have shown seemingly conflicting adverse results and large confidence intervals.

New-generation troponin assays are highly sensitive, more accurate at detecting earlier minor myocardial ischemia, and have prognostic impact in patients with acute coronary syndromes [19–21], stable coronary artery disease, [22] and heart failure [23]. Sensitive troponin assays have yet to be fully evaluated in the perioperative setting.

This study aimed to evaluate the prognostic value of a sensitive cardiac troponin I (cTnI) assay in the perioperative period of noncardiac surgery in intermediate- and high-risk patients and to identify predictors of troponin elevation.

2. Methods

2.1. Patient Selection. After approval by the Institutional Ethics Review Committee, all patients scheduled to undergo elective noncardiac surgery were screened for eligibility for this prospective observational study. Before participating, all patients provided written informed consent and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Patients eligible for inclusion in the study were ≥ 45 years of age, were hospitalized at least 1 day before surgery, had at least 1 Revised Cardiac Risk Index risk factor (history or presence of ischemic heart disease, heart failure, stroke or transient ischemic attack, insulin-dependent diabetes mellitus, or renal insufficiency (serum creatinine level ≥ 2 mg/dL or patients on renal replacement therapy)), and were undergoing intermediate- or high-risk surgery as defined by the American College of Cardiology/American Heart Association [24]. Between June 2010 and February 2011, 155 consecutive patients were included in the study. Ten patients (6.5%) had their surgeries canceled after enrollment, and 3 other patients were excluded because postoperative blood samples were missing. No statistically significant difference was found in the clinical characteristics of the 13 patients who did not undergo surgery and the 142 patients included in the study.

In accordance with previous studies [4, 5], the sample size of the cohort was calculated based on a 6% anticipated rate of combined major vascular events (vascular death, nonfatal myocardial infarction, and nonfatal cardiac arrest). Approximately 142 patients were expected to be included, assuming a hazard ratio of 4.0 for elevated postoperative troponin, with a statistical power of 80% and an alpha error of 5% [11].

2.2. Data Collection. A standardized questionnaire was given to all patients. Data regarding demographic characteristics and detailed medical histories were collected. All patients were classified according to Goldman's Specific Activity Scale for the functional classification of cardiovascular disease [25], the Revised Cardiac Risk Index [4], and the American Society of Anesthesiologists class. The latter was obtained from the

structured evaluation conducted by the anesthesiologist that was included in the medical record.

2.3. Determination of Biochemical Markers. Blood samples were collected to obtain serum and were centrifuged within 10 minutes. After the determination of the cTnI level, the serum was frozen and stored in aliquots at -80°C . N-terminal pro-B-type natriuretic peptide (NT-proBNP) was measured and analyzed after completing the active inclusion period of the study. cTnI was evaluated on postoperative days 1 and 2 and whenever clinically indicated by signs and symptoms of myocardial ischemia or surgical complications. The Siemens cTnI-Ultra assay was performed with the use of the ADVIA Centaur immunoassay system (Siemens) and had a limit of detection of $0.006\ \mu\text{g/L}$, a 99th percentile cut-off point of $0.04\ \mu\text{g/L}$, and a coefficient of variation $<10\%$ at $0.03\ \mu\text{g/L}$, as specified by the manufacturer. NT-proBNP analyses were performed using the Roche Elecsys 2010 (Roche Diagnostics GmbH, Mannheim, Germany). NT-proBNP was measured in serum (electrochemiluminescence sandwich immunoassay, Elecsys ProBNP; Roche Diagnostics; sensitivity: $5\ \text{pg/mL}$, intra-assay and interassay coefficients of variance: $<3\%$) on the day before surgery and on postoperative day 2.

2.4. Perioperative Management. Serial 12-lead electrocardiogram recordings were performed postoperatively in cases with cTnI $\geq 0.04\ \mu\text{g/L}$ or whenever clinically indicated. Standard two-dimensional, M-mode Doppler echocardiography (Envisor C, iE33; Philips Medical Systems, Andover, EUA, Vivid 3 or Vivid 7; GE Healthcare, Milwaukee, EUA) was postoperatively performed by a cardiologist in cases with cTnI $\geq 0.04\ \mu\text{g/L}$ and a nondiagnostic electrocardiogram. However, echocardiography was not performed for 2 patients with early hospital discharge.

2.5. Follow-Up and Outcomes. During hospitalization, the study protocol and patient records were used for data collection and documentation. Patients were monitored for in-hospital outcomes until discharge. An independent investigator, blinded to the troponin results, monitored patients via telephone for the occurrence of cardiac events during the 30-day period after the index surgery. Events were validated by an independent senior investigator who was not involved in data collection.

The primary outcome was a combined endpoint of vascular death, nonfatal myocardial infarction, and nonfatal cardiac arrest within 30 postoperative days. In cases of hospital readmission or death after index surgery, hospital charts and death certificates were reviewed. In addition, information on noncardiac deaths was recorded. Vascular complications were documented by the study physicians and validated by two independent investigators.

Vascular death was defined as death due to myocardial infarction, stroke, arrhythmia, heart failure, or vascular events of the great vessels. Nonfatal cardiac arrest was defined as a cardiopulmonary event that led to the initiation of successful cardiopulmonary resuscitation. Nonfatal myocardial infarction was diagnosed by a typical increase and

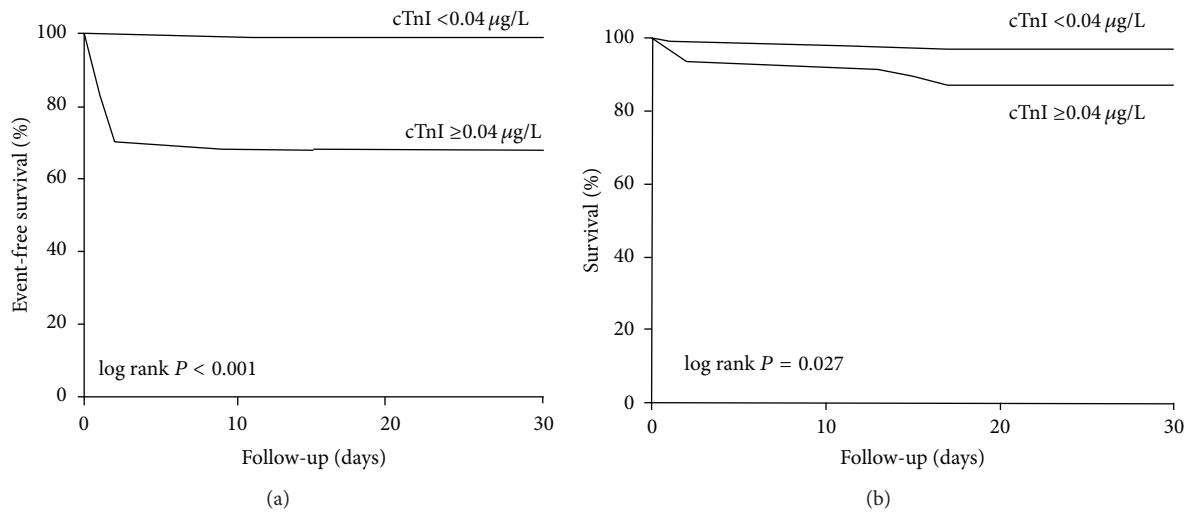


FIGURE 1: Primary event-free survival (a) and overall survival (b) stratified by postoperative cardiac troponin I (cTnI) peak levels less than or greater than 0.04 µg/L during the 30-day postoperative follow-up period.

decrease in cTnI ≥ 0.04 µg/L, with clinical signs, symptoms, or electrocardiographic findings (new Q waves or ST-T wave changes in at least 2 adjacent leads) suggestive of acute myocardial ischemia.

The secondary outcome was a combined endpoint of death, nonfatal stroke, congestive heart failure, atrial fibrillation, and acute coronary revascularization procedures. Stroke was defined as a new focal neurological deficit of vascular origin, with symptoms lasting for more than 24 hours. Diagnosis of congestive heart failure required ≥ 1 of the following conditions: development of symptoms or signs of pulmonary edema, evidence of left ventricular failure, or abnormal findings on chest radiography. Atrial fibrillation with hemodynamic compromise was considered significant. Acute coronary revascularization was defined as acute percutaneous coronary intervention or coronary artery bypass grafting due to persistent myocardial ischemia and hemodynamic compromise refractory to medical therapy. Major bleeding was defined as any bleeding requiring blood transfusion.

2.6. Statistical Analysis. The results are presented as the mean \pm SD, median and interquartile range (25th–75th percentile), or absolute and relative frequencies, as appropriate. Receiver operating characteristic (ROC) curves were constructed to assess the diagnostic accuracy of the primary outcome and overall mortality for cTnI. Optimal cut-off values of pre- and postoperative NT-proBNP were derived from ROC curves. Sensitivity, specificity, and predictive values were calculated. A Kaplan-Meier analysis was used to assess event-free survival. The event-time curve was separated into 2 curves according to the 99th percentile cut-off point of 0.04 µg/L, as specified by the manufacturer, and these curves were compared by the log-rank test. Univariate comparisons between patients with and without events were performed using the chi-square test, Fisher's exact test, the Mann-Whitney *U* test, or the Student *t*-test, as appropriate.

A multivariate logistic regression analysis was performed to determine independent factors associated with cardiac complications. Variables with *P* values < 0.20 in univariate analyses or with clinical relevance were included in the multivariate model. The level of significance was set at a two-tailed *P* value < 0.05 . Statistical analyses were performed with SPSS 18.0 for Windows (SPSS Inc., Chicago, IL).

3. Results

The baseline characteristics of all 142 patients are presented in Table 1, and the perioperative variables are shown in Table 2. During a median follow-up of 29 ± 8.7 days, 16 patients (11.3%) experienced major cardiac events. Forty-seven patients (33.1%) had a cTnI elevation (≥ 0.04 µg/L) in at least one of the postoperative samples collected. Fourteen of the 47 patients had a full-field diagnosis of acute myocardial infarction, and 7 were completely asymptomatic. The median cTnI levels were higher in patients who experienced postoperative primary cardiovascular events compared with event-free patients: 0.049 versus 0.017 µg/L for postoperative cTnI day 1 (*P* = 0.001) and 0.192 versus 0.018 µg/L for postoperative cTnI day 2 (*P* < 0.001). Figure 1 shows the Kaplan-Meier curve indicating primary event-free survival and overall survival in patients with cTnI peaks less than and greater than 0.04 µg/L.

The association of perioperative cTnI with primary cardiovascular events was assessed using a ROC curve (Figure 2). The area under the curve (AUC) for primary events was 0.75 (95% CI 0.64–0.87; *P* = 0.001) for postoperative cTnI day 1, yielding a sensitivity of 56.3%, a specificity of 80%, a positive predictive value of 26.5%, and a negative predictive value of 93.5%. For postoperative cTnI day 2, the AUC was 0.87 (95% CI 0.76–0.98; *P* < 0.001), yielding a sensitivity of 86.7%, a specificity of 78%, a positive predictive value of 32.5%, and a negative predictive value of 98%. The combination of cTnI peak values had the best combined

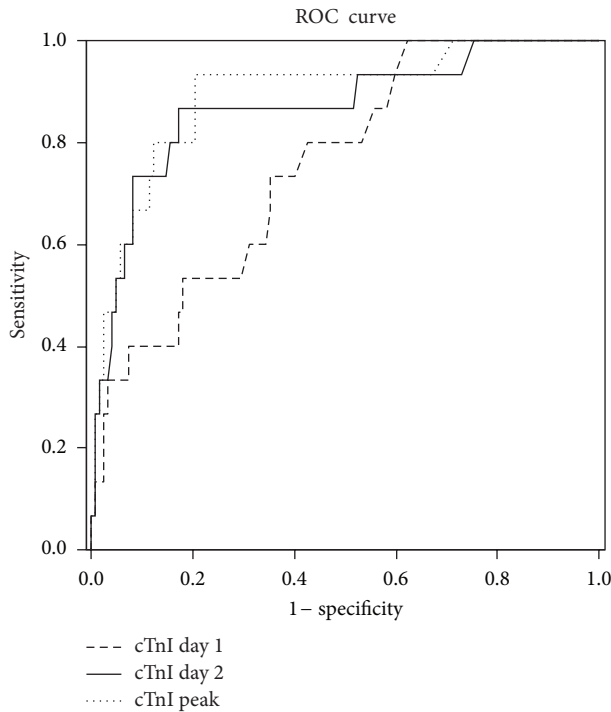


FIGURE 2: Receiver operating characteristic (ROC) curves for postoperative cardiac troponin I (cTnI) levels day 1, cTnI levels day 2, and cTnI peak levels for the prediction of the combined endpoint of vascular death, nonfatal myocardial infarction, or nonfatal cardiac arrest after index surgery.

sensitivity (94%), specificity (75%), positive predictive value (32%), and negative predictive value (99%) (AUC 0.89; 95% CI 0.80–0.98; $P < 0.001$). The ROC-derived optimal cut-off values for pre- and postoperative NT-proBNP were 917 and 2962 pg/mL, respectively. Changes in cTnI levels between the first and the second measurement were related to adverse cardiac events ($P = 0.001$). All patients with primary outcomes had a greater than 30% relative change in cTnI levels.

Predictors of postoperative cTnI elevation, excluding patients who had myocardial infarction, are presented in Table 3. Patients on dialysis (OR 3.38; 95% CI 1.01–10.5) or with heart failure (OR 3.0; 95% CI 1.15–7.84), transoperative major bleeding (OR 3.38; 95% CI 1.01–10.5), preoperative NT-proBNP levels ≥ 917 pg/mL (OR 3.65; 95% CI 1.56–8.55), or postoperative NT-proBNP levels ≥ 2962 pg/mL (OR 3.63; 95% CI 1.51–8.72) were more likely to have elevated cTnI values after surgery.

Twenty-eight patients experienced secondary outcomes (19.7%). The detailed data are shown in Table 4. Previous coronary revascularization, peripheral artery disease, transoperative major bleeding, functional capacity, pre- and postoperative NT-proBNP, vascular surgery, and postoperative cTnI levels were significantly associated with primary cardiac events in the univariate analyses (Tables 1 and 2). In a model adjusted for the Revised Cardiac Risk Index, previous coronary revascularization, preoperative beta-blocker use, vascular surgery, and pre- and postoperative NT-proBNP,

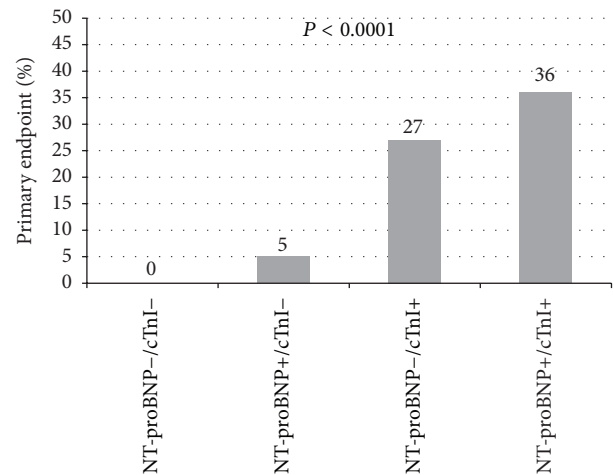


FIGURE 3: Primary endpoint (%) according to the combination of preoperative N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels less than (–) or greater than (+) 917 pg/mL and postoperative cardiac troponin I (cTnI) peak levels less than (–) or greater than (+) $0.04 \mu\text{g/L}$ during the 30-day postoperative follow-up period.

the independent predictors of primary cardiac events were postoperative peak cTnI level (OR 9.4; 95% CI 2.26–39.18; $P = 0.002$) and a preoperative NT-proBNP level ≥ 917 pg/mL (OR 3.47; 95% CI 1.05–11.55; $P = 0.041$).

Patients with the combination of a preoperative NT-proBNP level ≥ 917 pg/mL and postoperative cTnI peak values $\geq 0.04 \mu\text{g/L}$ had 36% of the primary cardiovascular outcomes in comparison to an absence of events in patients without elevation of either cardiac biomarker ($P < 0.001$) (Figure 3).

4. Discussion

A perioperative increase in cTnI was found to be highly predictive of short-term major cardiovascular events and provided incremental prognostic information to previous risk scores that only considered preoperative information. Furthermore, postoperative cTnI was a predictor of total mortality (OR 4.48; 95% CI 1.07–18.82).

The results of this study are consistent with those of others that evaluated conventional commercial assays of troponin T or troponin I and demonstrated that these markers were independent prognostic factors for major cardiovascular outcomes [10–17]. Most former studies have found a strong association between troponin elevation and cardiovascular outcomes in selected populations of high-risk cardiovascular patients who underwent vascular surgeries.

Asymptomatic postoperative troponin elevation is a frequent event, and a substantial proportion of the patients participating in this study and diagnosed with myocardial infarction showed silent ischemia, which was only detected by active monitoring of cardiac markers. A strong association of perioperative ischemia with mortality is well

TABLE 1: Baseline characteristics of all patients, stratified by the occurrence of 30-day cardiovascular events.

	All patients (142)	Cardiovascular events		P
		Yes (n = 16)	No (n = 126)	
Men	69 (48.6)	7 (43.8)	62 (49.2)	0.79
Age, years	65.5 ± 9.6	65 ± 1	65.6 ± 9.7	0.80
ASA scoring system				0.47
Class II	52 (36.6)	4 (25)	48 (38.1)	
Class III	85 (59.9)	12 (75)	73 (57.9)	
Class IV	5 (3.5)	0	5 (4)	
Specific Activity Scale*				0.002
Class I	48 (33.8)	4 (25)	44 (34.9)	
Class II	40 (28.2)	2 (12.5)	38 (30.2)	
Class III	32 (22.5)	2 (12.5)	30 (23.8)	
Class IV	13 (9.2)	6 (37.5)	7 (5.5)	
Revised Cardiac Risk Index				0.29
Class II	13 (9.2)	1 (6.3)	12 (9.5)	
Class III	84 (59.2)	8 (50)	76 (60.3)	
Class IV	45 (31.7)	7 (43.8)	38 (30.2)	
Smoking	33 (23.2)	4 (25)	29 (23)	0.89
Hypertension	122 (85.9)	14 (87.5)	108 (85.7)	1.00
Diabetes mellitus	58 (40.8)	7 (43.8)	51 (40.5)	0.79
Atrial fibrillation	13 (9.2)	2 (12.5)	11 (8.7)	0.64
History of congestive heart failure	25 (17.6)	5 (31.3)	20 (15.9)	0.16
Left ventricular ejection fraction (%)**	61.3 ± 10.1	56.19 ± 12.3	62.17 ± 9.5	0.20
History of myocardial infarction	48 (33.8)	6 (37.5)	42 (33.3)	0.78
Previous percutaneous coronary intervention	23 (16.2)	6 (37.5)	17 (13.5)	0.025
Previous coronary artery bypass graft	16 (11.3)	3 (18.8)	13 (10.3)	0.39
History of cerebrovascular disease	47 (33.1)	6 (37.5)	41 (32.5)	0.78
Renal impairment***	35 (24.6)	5 (31.3)	30 (23.8)	0.54
Peripheral artery disease	30 (21.1)	9 (56.3)	21 (16.7)	0.001
Preoperative laboratory tests				
Hemoglobin, mg/dL	11.86 ± 2.3	11.4 ± 2.7	11.9 ± 2.3	0.43
Serum creatinine, mg/dL	1.12 [0.87–1.74]	1.48 [1.07–2.9]	1.09 [0.86–1.70]	0.23
Creatinine clearance, mL/min	58.40 ± 31.21	59.02 ± 29.94	53.28 ± 41.15	0.53
NT-proBNP, pg/mL	329.3 [117.4–1730]	1336 [181–10175]	288 [107–1303]	0.038
Preoperative medication				
Aspirin	65 (45.8)	8 (50)	57 (45.2)	0.79
Clopidogrel	11 (7.7)	1 (6.3)	10 (7.9)	0.39
Insulin	31 (21.8)	6 (37.5)	25 (19.8)	0.12
Statins	75 (52.8)	8 (50)	67 (53.2)	1.00
β-Blockers	72 (50.7)	11 (68.8)	61 (48.4)	0.18
ACE inhibitors	85 (59.9)	10 (62.5)	75 (59.5)	1.00

Data are expressed as number (percentage), mean ± SD, or median [interquartile range] as appropriate. P value indicates differences between patients with and without primary cardiovascular events. ASA: American Society of Anesthesiologists; NT-proBNP: N-terminal pro-B-type natriuretic peptide; ACE: angiotensin-converting enzyme.

*n = 133, **n = 114; *** serum creatinine ≥ 2 mg/dL or renal replacement therapy.

established [1, 11, 26]. A recent meta-analysis has demonstrated that an isolated postoperative troponin leak (elevation of troponin below the diagnostic threshold for a perioperative myocardial infarction, without symptoms or ischemic electrocardiography changes or echocardiography signs) is strongly predictive of all-cause mortality at 30 days after vascular surgery (OR 5.03; 95% CI 2.88–8.79)

[27]. Levy et al. also demonstrated that although substantial heterogeneity was present in the observed correlations [28], increased troponin after noncardiac surgery was an independent predictor of long-term mortality (OR 3.4; 95% CI 2.2–5.2).

Recently, the VISION Study Investigators, in a prospective, international cohort study of 15,133 patients undergoing

TABLE 2: Perioperative characteristics of all patients, stratified by the occurrence of 30-day cardiovascular events.

	All patients (142)	Cardiovascular events		P
		Yes (n = 16)	No (n = 126)	
Postoperative laboratory tests				
NT-proBNP, pg/mL	1175 [586.97–2987]	3699 [926–12989]	1091 [588–2759]	0.013
cTnI postoperative day 1, $\mu\text{g/L}$	0.018 [0.009–0.036]	0.049 [0.020–0.425]	0.017 [0.008–0.032]	0.001
cTnI postoperative day 2, $\mu\text{g/L}$	0.019 [0.009–0.053]	0.192 [0.059–0.686]	0.018 [0.009–0.034]	<0.001
Delta cTnI > 30%*	86 (60.5)	15 (93.7)	71 (56)	0.001
Intraoperative events				
Hypotension (systolic < 100 mmHg)	91 (64.1)	9 (56.3)	82 (65.1)	0.58
Bradycardia (heart rate < 50 bpm)	33 (23.2)	4 (25)	29 (23)	1.00
Blood transfusion	18 (12.7)	5 (31.3)	13 (10.3)	0.033
Types of surgery				
Abdominal	71 (50)	4 (25)	67 (53.2)	0.046
Thoracic	10 (7)	0	10 (7.9)	
Vascular	45 (31.7)	9 (56.3)	36 (28.6)	
Prostate	4 (2.8)	0	4 (3.2)	
Hip	12 (8.5)	3 (18.8)	9 (7.1)	

Data are expressed as number (percentage), mean \pm SD, or median [interquartile range] as appropriate. P value indicates differences between patients with and without primary cardiovascular events. NT-proBNP: N-terminal pro-B-type natriuretic peptide. cTnI: cardiac troponin I.

*n = 137.

noncardiac surgery, demonstrated that the peak postoperative troponin T measurement during the first 3 days after surgery was significantly associated with 30-day mortality and showed a dose-response relationship [29].

Technological improvements have allowed manufacturers to provide fully automated cardiac troponin assays that meet the recommendations set out by the International Federation of Clinical Chemistry and Laboratory Medicine [30], a higher sensitivity compared to previous assays and improved precision at the lower limit of detection. These assays have a lower limit of detection (below the 99th percentile) in a normal reference population. Reichlin et al. have shown that sensitive cTnI levels measured in patients within 3 hours after the onset of chest pain had a greater accuracy to detect myocardial infarction [20]. Additionally, Omland et al. have found better diagnostic performance with sensitive assays compared to those traditionally used for patients with a suspicion of myocardial infarction. Troponin levels also appear to be independent predictors of cardiovascular mortality in patients with stable coronary artery disease [22].

Kavsak et al. measured high-sensitivity troponin T preoperatively and postoperatively in 325 adults who underwent noncardiac surgery. Postoperatively, 45% of patients had a high-sensitivity troponin T level ≥ 14 ng/L [31]. In a recent study, Alcock et al. determined the incidence and predictors of myocardial necrosis in 352 patients at high cardiovascular risk who were undergoing elective major noncardiac surgery using high-sensitivity troponin T. Preoperative high-sensitivity troponin T was elevated in 31% of patients, and postoperative myocardial necrosis occurred in 22% of patients, although most events were clinically undetected. Predictors of elevated baseline high-sensitivity troponin T included age, male gender, diabetes requiring insulin therapy, and chronic kidney disease [32].

Prior to our study, the prognostic values of sensitive cTnI assays had yet to be fully evaluated for cardiovascular adverse outcomes in patients undergoing noncardiac surgery. This study demonstrated that troponin peak values ≥ 0.04 $\mu\text{g/L}$ on postoperative day 1 or 2 had the best combined sensitivity (94%) and specificity (75%) and a high negative predictive value (99%) for the prediction of 30-day adverse cardiovascular outcomes.

Perioperative myocardial infarction identification is a challenge because patients do not often have the classical symptoms or electrocardiographic changes associated with myocardial infarction. Nonetheless, the routine measurement of troponins in postoperative care is not a standard practice. There is reasonable concern regarding false-positive results when using sensitive assays, potentially resulting in unnecessary tests or treatment interventions. Some strategies could be used to increase the clinical value of using troponins in the postoperative setting. First, serial measurement seems to be more reliable than a single value. Similar to type-1 myocardial infarction patients [19], this study demonstrated that perioperative changes in sensitive cTnI levels >30% improved the diagnostic and prognostic information. Second, clinical conditions other than ischemic heart disease are known to be associated with increased troponin levels [33].

Our study demonstrated that heart failure, renal insufficiency on dialysis, intraoperative major bleeding, and pre- and postoperative NT-proBNP were predictors of postoperative cTnI elevation in patients in whom myocardial infarction was excluded. Patients with these clinical conditions were predisposed to suffer myocardial injury, which is a proposed mechanism for troponin elevation in the absence of clinical, electrocardiographic, and echocardiographic abnormalities. Therefore, particularly at low cTnI concentrations, the criterion of the increase and decrease of the troponin

TABLE 3: Predictors of postoperative troponin peak level in patients without myocardial infarction ($n = 128$).

	Troponin < 0.04 $\mu\text{g/L}$ ($n = 95$)	Troponin $\geq 0.04 \mu\text{g/L}$ ($n = 33$)	<i>P</i>
Men	49 (51.6)	14 (42.4)	0.42
Age, years	65.5 \pm 9.2	66.3 \pm 10.1	0.67
Revised Cardiac Risk Index			0.95
Class II	9 (9.5)	3 (9.1)	
Class III	57 (60)	19 (57.6)	
Class IV	29 (30.5)	11 (33.3)	
Specific Activity Scale*			0.86
Class I	32 (36)	12 (37.5)	
Class II	29 (32.6)	10 (31.3)	
Class III	23 (25.8)	7 (21.9)	
Class IV	5 (5.6)	3 (9.4)	
Vascular surgery	27 (28.4)	11 (33.3)	0.66
Smoking	22 (23.2)	7 (21.2)	0.38
Diabetes mellitus	38 (40)	14 (42.4)	0.84
Atrial fibrillation	6 (6.3)	5 (15.2)	0.15
Heart failure	12 (12.6)	10 (30.3)	0.031
Hypertension	84 (88.4)	26 (78.8)	0.24
Coronary artery disease	49 (51.6)	17 (51.5)	1.00
Myocardial revascularization	21 (22.1)	8 (24.2)	0.81
Cerebrovascular disease	34 (35.8)	8 (24.2)	0.28
Renal impairment	20 (21.1)	12 (36.4)	0.10
Dialysis	7 (7.4)	7 (21.2)	0.047
Peripheral artery disease	14 (14.7)	8 (24.2)	0.28
Preoperative hemoglobin,mg/dL	12 \pm 2.2	11.2 \pm 2.1	0.08
Preoperative NT-proBNP ≥ 917 pg/mL	20 (21.5)	16 (50)	0.003
Postoperative NT-proBNP ≥ 2962 pg/mL	16 (16.8)	14 (42.4)	0.004
Preoperative medication			
Aspirin	46 (48.4)	12 (36.4)	0.31
ACE inhibitors	53 (55.8)	22 (66.7)	0.31
Beta blocker	45 (47.4)	18 (54.5)	0.55
Statin	55 (57.9)	13 (39.4)	0.07
Transoperative events			
Hypotension (systolic < 100 mmHg)	58 (61.1)	24 (72.7)	0.29
Bradycardia (heart rate < 50 bpm)	23 (24.2)	7 (21.2)	0.81
Major bleeding	7 (7.4)	7 (21.2)	0.047

Data are expressed as number (percentage) or mean \pm SD as appropriate. *P* value indicates differences between patients without and with troponin elevation. NT-proBNP: N-terminal pro-B-type natriuretic peptide.

* $n = 121$.

concentration should be carefully followed before classifying a troponin elevation as a myocardial infarction [34].

The correlation between NT-proBNP and cTnI elevation is not a new finding, although its mechanism is not completely understood [35]. A recent meta-analysis suggests that an increased BNP level can identify inducible myocardial ischemia as detected by standard noninvasive stress tests, even in patients without ventricular dysfunction [36]. In a study involving 133 patients, Bolliger et al. have demonstrated a correlation between an increase in cardiac biomarkers and major cardiac events up to 1 year after major vascular surgery. When considered together as a single variable, the prognostic value of preoperative BNP concentrations and postoperative

cTnI measurements indicated a greater than 20-fold higher risk for subsequent major adverse cardiac events, including mortality, in comparison with patients with normal preoperative BNP values, regardless of the postoperative elevation of cTnI [37]. We hypothesize that BNP values and troponins reflect myocardial injury under stress conditions that cannot currently be identified by traditional methods.

Some methodological considerations should be noted for this study. The number of patients studied was relatively small. Although it was possible to identify clinical predictors of postoperative cTnI elevation in patients without myocardial infarction, this study could not determine whether the elevation of troponin in these patients could be considered

TABLE 4: Events stratified by postoperative troponin peak level during the follow-up period.

	All patients <i>n</i> = 142 (%)	Troponin \geq 0.04 $\mu\text{g/L}$ <i>n</i> = 47 (%)	Troponin $<$ 0.04 $\mu\text{g/L}$ <i>n</i> = 95 (%)	OR (95% CI)	<i>P</i>
Primary outcome	16 (11.3)	15 (31.9)	1 (1.1)	44.06 (5.60–346.9)	<0.001
Cardiac death	2 (1.4)	2 (4.3)	0	10.5 (0.5–218.97)*	0.19
Nonfatal cardiac arrest	2 (1.4)	1 (2.1)	1 (1.1)	2.04 (0.12–33.40)	1.00
Nonfatal MI	14 (9.9)	14 (29.8)	0	82.67 (4.87–1402.27)*	<0.001
Secondary outcome	28 (19.7)	17 (36.2)	11 (11.6)	4.32 (1.82–10.28)	0.001
Death	9 (6.3)	6 (12.8)	3 (3.2)	4.48 (1.07–18.82)	0.06
Nonfatal stroke	5 (3.5)	0	5 (5.3)	0.17 (0.01–3.11)*	0.17
Congestive heart failure	12 (8.5)	9 (19.1)	3 (3.2)	7.26 (1.86–28.30)	0.002
Atrial fibrillation	7 (4.9)	6 (12.8)	1 (1.1)	13.75 (1.60–117.92)	0.005
Coronary revascularization	1 (0.7)	1 (2.1)	0	6.16 (0.25–150.94)*	0.33

OR: odds ratio; CI: confidence interval; MI: myocardial infarction. *P* value indicates differences between patients with and without troponin elevation.

*Adjusted by adding 0.5 in each cell in case of zero frequency.

as a false-positive result. Furthermore, preoperative cTnI was not measured in the population studied. These results cannot be applied to patients with a lower risk profile or those undergoing minor surgeries because only patients at intermediate and high risk of coronary artery disease were evaluated.

5. Conclusion

A sensitive cTnI assay can be used to detect postoperative minor myocardial injury in intermediate- and high-risk patients undergoing noncardiac surgery. Postoperative cTnI elevation identifies patients at a high risk of cardiovascular events and predicts short-term total mortality. Heart failure, renal insufficiency on dialysis, intraoperative major bleeding, and pre- and postoperative NT-proBNP levels are related to cTnI elevation. Hence, cTnI measurement should be considered as a component of perioperative risk assessment in this population.

Conflict of Interests

All authors declare that there is no conflict of interests regarding the publication of this paper.

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