Myocardial Injury after Noncardiac Surgery and its Association with Short-Term Mortality

Running title: van Waes et al.; Myocardial injury after noncardiac surgery

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*contributed equally

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Abstract:

**Background**—To identify patients at risk for postoperative myocardial injury and death, it has been suggested to measure cardiac troponin routinely after noncardiac surgery. Such monitoring was implemented in our hospital. The aim of this study was to determine the predictive value of postoperative myocardial injury, as measured by troponin elevation, on 30 day mortality after noncardiac surgery.

**Methods and Results**—This observational single center cohort study included 2,232 consecutive intermediate to high risk noncardiac surgery patients aged 60 and above operated in 2011. Troponin was measured on the first three postoperative days. Log binomial regression analysis was used to estimate the association between postoperative myocardial injury (troponin I level >0.06 mcg/L) and all-cause 30-day mortality. Myocardial injury was found in 315 (19%) patients. All-cause death occurred in 56 (3%) patients. The relative risk of a minor increase in troponin (0.07-0.59 mcg/L) was 2.4 (95% CI 1.3-4.2, p<0.01), and the relative risk of a 10-100 fold increase in troponin (≥0.60mcg/L) was 4.2 (95% CI 2.1-8.6, p<0.01). A myocardial infarction according to the universal definition was diagnosed in 10 patients (0.6%), of which one (0.06%) had ST-elevation myocardial infarction.

**Conclusions**—Postoperative myocardial injury is an independent predictor of 30-day mortality after noncardiac surgery. Implementation of postoperative troponin monitoring as standard of care is feasible and might be helpful to improve the prognosis of patients undergoing noncardiac surgery.

**Key words:** ischemia, myocardial infarction, surgery, mortality, surveillance
Introduction

Perioperative adverse cardiovascular events are the leading cause of morbidity and mortality after noncardiac surgery.\textsuperscript{1} Despite efforts to prevent the occurrence of such events,\textsuperscript{2,3} the incidence of postoperative myocardial infarction (POMI) after noncardiac surgery is still high and varies depending on the definition used.\textsuperscript{4,5} Using the latest universal definition of myocardial infarction in a large cohort of patients undergoing noncardiac surgery, the incidence of POMI was as high as 5%.\textsuperscript{4,5,6} Because symptoms such as chest pain are easily masked by adequate postoperative pain management including opioids, the clinical course of POMI is mainly silent\textsuperscript{6}. As a result, POMI is recognized late or not recognized at all, but remains strongly associated with mortality.\textsuperscript{1,6-9} The mortality rate in patients with asymptomatic POMI is similar to that of patients who experience ischemic symptoms.\textsuperscript{6} Moreover, even patients with minor elevations of troponin after surgery, without any symptoms of ischemia or signs of myocardial infarction, seem to have a comparably high risk of cardiovascular complications and death.\textsuperscript{6,10-13}

Although the pathophysiology of such isolated postoperative troponin elevation is not yet fully understood,\textsuperscript{1,14} a meta-analysis of studies in predominantly high risk surgery patients showed that isolated troponin elevation was a strong independent predictor of mortality within the first year after surgery.\textsuperscript{10} Of note, troponin elevation was associated with a six fold increase in mortality.\textsuperscript{10} In addition, the recently published VISION study including over 15,000 surgical patients showed a strong association between peak troponin levels after surgery and 30 day mortality.\textsuperscript{11} Time to death after the peak troponin values was reported to vary between one and two weeks, potentially allowing for interventions to alter a patients risk of death.\textsuperscript{11} The accumulating evidence from VISION and other studies, suggests that implementation of postoperative troponin monitoring as care as usual in patients undergoing noncardiac surgery
might be useful for better risk stratification and management of patients.\textsuperscript{6,10-13}

Therefore, we implemented routine troponin measurement monitoring on the first three
days after surgery as part of our standard postoperative care in patients aged 60 or above
undergoing all types of intermediate to high risk noncardiac surgery. We hypothesized that the
results of this routine monitoring would improve risk stratification of patients at risk for early
postoperative death. The aim of the present study therefore was to determine the predictive value
of postoperative troponin elevation as a marker of myocardial injury on 30 day mortality after
noncardiac surgery.

Methods

Patients

This observational cohort study included consecutive patients undergoing noncardiac surgery
between January 3rd and December 15th 2011 at the University Medical Center Utrecht, The
Netherlands, a 1,000 bed tertiary referral hospital. Patients were eligible if they were aged 60
years or older, were undergoing intermediate to high risk noncardiac surgery under general or
spinal anesthesia and had an expected postoperative length of hospital stay of at least 24 hours.
For patients who underwent surgery more than once during the study period, the first surgery
was included in the analyses for all patients. A reoperation was included as a novel case if this
surgery took place during another hospital admission and at least 30 days after the first surgery.
Patients were excluded if they were lost to follow-up within 30 days after surgery.

The local medical ethics committee approved the study protocol. The need for informed
consent was waived, as only routinely collected patient data were used and data were
anonymized before analysis (UMC Utrecht Medical Research Ethics Committee 11-120/C).
Data collection

All preoperative and postoperative data were obtained from electronic medical and administrative records. Data collected in all patients included patient characteristics, preoperative physical status, comorbidities and death within 30 days. In those patients with postoperative TnI measurements, TnI levels were collected. Additionally, data on postoperative symptoms, ECG changes, the incidence of POMI and the treatment initiated by the consultant cardiologist were collected in those patients who had a cardiology consultation. The unique hospital patient identifier was used to merge databases. For data on 30-day mortality the municipal personal records database was consulted.

Troponin measurements

According to the hospital protocol, cardiac troponin I (TnI) measurements were ordered for the first three days after surgery by the attending anesthesiologist immediately after completing the case in the operating room. In case of a TnI elevation above the clinical cut-off level during the first three days after surgery, the ward physician was notified. As the optimal treatment of patients with postoperative troponin elevation is not yet known and obviously has to be interpreted in consistency with a patient’s clinical course, it was left at the discretion of the treating physician whether further diagnostic procedures including an ECG or a consultation of the cardiologist was indicated in individual patients. In this, troponin elevation was considered simply as a marker for myocardial injury, warranting for additional attention.

In this study, myocardial injury was defined as a TnI > 0.06mcg/L, which was the lowest value measurable with a 10% coefficient of variation above the 99th percentile of 0.04mcg/L of the assay used. TnI was analyzed using the third-generation enhanced AccuTnI assay (Beckman Coulter, Brea, California). For each patient, the highest value of all routine TnI
measurements was used in the analysis.

Outcomes

The primary outcome was defined as all-cause mortality within 30 days after surgery. Secondary outcomes included the incidence of POMI and length of hospital stay. Myocardial infarction was defined according to the universal definition.15

Statistical analysis

The analysis was performed by using SPSS (release 20.0 for Windows). In advance of data analysis we were aware that TnI results would not be available in all patients, as adherence to a new protocol in daily clinical practice takes time. Therefore, we compared baseline characteristics and the incidence of death in patients in whom TnI was measured to those in whom it was not, in order to determine whether the missing TnI measurements could be considered as missing at random. To check whether excluding the missing values from the analysis influenced the association between postoperative myocardial injury and death, we repeated the multivariable regression analysis after multiple imputations of the missing TnI values. Five datasets were imputed using the method of fully conditional specification. The baseline characteristics were used as predictors of the TnI values.

In the primary analysis, we first looked at the distribution of the first TnI elevation over the postoperative days. Second, the primary outcome and the incidence of POMI were compared for patients with and without myocardial injury using the Chi-square test, and relative risks with 95% confidence intervals were calculated. In this, TnI was included both as a continuous as well as a categorical variable. In the latter, TnI was categorized into four groups on a logarithmic scale: TnI ≤0.06, 0.07-0.59, 0.60-5.99, ≥6.00 mcg/L. The median time to death was calculated, and the median length of stay in the hospital of both groups was compared using the Mann-
Whitney test. Kaplan-Meier survival analysis was used to determine the survival of patients in each category of TnI elevation.

Subsequently, a log binomial multivariable regression model was developed to adjust the association between myocardial injury and death for preoperative variables known to predict postoperative cardiovascular events. We used log binomial regression analysis to facilitate presenting effect measures as relative risks. In this we used model-based covariance estimates. The model included TnI and age, sex, emergency surgery and renal failure (preoperative glomerular filtration rate <50ml/h). Emergency surgery was defined as surgery required within 72 hours. Because the number of patients with a TnI level >6.00mcg/L was considered too small to obtain relevant results, in this analysis the two upper TnI categories were merged into one (i.e. with TnI ≥0.60mcg/L). We compared the predictive value of a model with only preoperative variables to a model in which TnI was added to these variables using the area under the receiver operating characteristic curve (AUROC) and integrated discrimination improvement (IDI) analysis. We preferred the latter method over using the net reclassification improvement (NRI) because it does not require (arbitrary) classification of the mortality risk.

Results
In total 2,232 patients were eligible for inclusion. Sixteen patients (0.7%) were lost to follow-up and excluded from the analysis: three patients were transferred to another hospital on the day of surgery, six patients died on the day of surgery (i.e. TnI could not be measured in these patients) and in seven patients mortality data could not be obtained as they were not known by the municipal personal records database. Baseline characteristics of the 2,216 remaining patients are given in Table 1. TnI was measured in 1627 (73.4%) patients. It was measured consecutively on
all three postoperative days in 907 (55.7%) patients and elevated at least once in 315 (19.4%) patients. Within the group of patients with myocardial injury, the first elevated TnI was found on the first postoperative day in 162 (51.4%) patients (Figure 1). Stratification of the patients into decades of age showed that the incidence of postoperative myocardial injury increased with age (Figure 2).

Postoperative myocardial injury was associated with an increased risk of death. Twenty-seven of the 315 patients (8.6%, 95% CI: 6.0-12.2%) with myocardial injury died within 30 days, compared to 29 of the 1,312 patients (2.2%, 95% CI: 1.5-3.2%) with normal TnI levels (p<0.01). The median time to death after TnI elevation was 12 days (IQR 13). Patient characteristics of the three categories of troponin elevation are given in Table 2. The unadjusted relative risk of death was 3.0 in case of a minor increase in TnI (0.07-0.59 mcg/L), and 7.9 in case of a 10-fold increase or higher in TnI (≥0.60mcg/L) (Table 3). The survival in each of these categories is shown in Figure 3. The analysis including TnI on a continuous scale showed an increase in relative risk for each 0.1mcg/L increase in TnI level (RR 1.003, 95% CI 1.001-1.004).

After adjustment of the association between myocardial injury and death for variables known to predict postoperative cardiovascular events, only emergency surgery and TnI remained significantly related to death within 30 days. The relative risk of death was 2.4 (95% CI 1.3-4.2, p<0.01) in case of a minor increase in TnI (0.07-0.59 mcg/L), and 4.2 (95% CI 2.1-8.6, p<0.01) in case of a 10-fold increase or higher in TnI (≥0.60mcg/L) (Table 3). The AUROC of the model with only preoperative predictors was 0.75 (95% CI 0.68-0.83), compared to 0.78 (95% CI 0.71-0.85) of the model in which TnI was added. The integrated discrimination improvement index of the model including TnI was 0.02 (p < 0.001).

The median length of stay in the hospital was 10 days (IQR 12) in patients with
myocardial injury compared to 5 days (IQR 6) in patients without myocardial injury (p <0.01).

Ten of the 315 (3.2%) patients with troponin elevation had typical chest pain and ECG changes suggestive of new ischemia were found in 30 (9.5%) patients. One (0.3%) of these ECGs showed ST elevation (≥1 mm), 14 (4.4%) showed ST depression (≥ 1 mm) and 15 (4.8%) showed minimal ST depression (<1 mm) and/or repolarization changes.

A cardiologist was consulted in 110 of the 315 (34.9%) patients. In most of these 110 patients the clinical course was awaited without any intervention (N=67, 60.9%) and in 43 (39.1%) patients, cardiovascular medication was changed or added (statins and aspirin). Eight (7.3%) patients were transferred to a coronary care unit for continuous ECG monitoring.

Coronary angiography was performed in 7 (6.4%) patients, and significant coronary stenoses were found in 6 (5.4%) of these patients. A percutaneous coronary intervention was performed in 4 (3.6%) patients, one (0.9%) patient underwent coronary bypass surgery, and in one other patient (0.9%) a coronary intervention was considered not to be beneficial because of a poor clinical condition.

POMI according to the criteria of the universal definition was diagnosed in 10 of the 1,627 (0.6%) patients. This concerned a non-ST-elevation myocardial infarction (NSTEMI) in 9 patients (0.6%) and a STEMI in one (0.06%) patient. Because the STEMI was considered to have sustained more than six hours coronary angiography was not performed immediately. This patient was initially treated with medication, and percutaneous coronary intervention for a non-significant coronary stenosis was performed in an outpatient setting.

In order to determine whether the missing TnI measurements could be considered as missing at random, patients in whom TnI was measured were compared to those in whom it was not. Death occurred in 56 of the 1,627 (3.4%, 95% CI: 2.7-4.4) patients in whom troponin was
measured, compared to 20 of the 589 (3.4%, 95% CI: 2.2-5.2) patients in whom troponin was not measured (p=0.96). After imputation of the missing TnI values, multivariable regression analysis showed a comparable association between postoperative myocardial injury and death (Table 4).

**Discussion**

This cohort study estimated the incidence of myocardial injury after noncardiac surgery and its predictive value on the risk of death within 30 days, using data from routine postoperative monitoring of troponin. TnI was elevated in 19% of the patients and TnI elevation was an independent predictor of 30-day mortality. This association with the risk of death was dependent on the degree of the TnI elevation (RR between 2.4 and 4.2), but independent of preoperative factors known to be associated with postoperative death. As suggested previously, implementation of postoperative monitoring of troponin as standard of care is feasible and may improve risk stratification and reclassification of patients at risk for early postoperative death, even when daily care clinical protocols are not always followed.

This study is one of the first studies describing the results of the implementation of routine postoperative monitoring of troponin as part of a standard postoperative care protocol. The study has some obvious limitations. First, since we measured TnI only on the first three days after surgery, myocardial injury that may have occurred after that time interval has been missed. However, previous research has shown that myocardial injury mostly occurs within the first three postoperative days. Second, TnI was not measured in all patients due to the fact that it takes time to fully implement a new protocol in daily clinical practice. Patients in whom TnI was not measured seemed somewhat healthier at baseline and high risk surgery was less frequent in these patients. In contrast, these patients without TnI measurements underwent more often emergency surgery and reoperations with a higher incidence of death (Table 1). This apparent controversy
of healthier patients who were more likely to die may be explained by the fact that TnI measurements were more often (unintentionally) not ordered after emergency surgery. To check whether these baseline differences resulted in a biased association between myocardial injury and death, we compared the results of the complete case analysis to the results of a sensitivity analysis including all patients after multiple imputations of the missing TnI values. This analysis showed comparable results, indicating that imputation of missing data did not change the association between myocardial injury and short-term death. Third, as we did not measure TnI before surgery, we could not adjust the results for pre-existent TnI elevations. Pre-existent TnI elevations may occur in patients with renal failure or other cardiovascular conditions. The cause of the higher preoperative levels of cardiac biomarkers in these patients is not completely clear, but it is thought to be caused by subclinical cardiac damage from silent myocardial ischemia or microinfarction, mild heart failure, left ventricular hypertrophy, or increased cardiac apoptosis.21 We hypothesize that patients with a pre-existent TnI elevation may have an additional increase of TnI because of ischemia caused by surgical stress. Although some patients with a preoperative acute coronary syndrome in whom TnI levels decreased to normal values after surgery may have been missed, we do not expect that this has influenced the obtained results significantly. Moreover, although myocardial injury may already have occurred before surgery in some patients, postoperative troponin elevations may still predict short-term mortality.

The improved risk discrimination of patients with mostly asymptomatic myocardial injury, together with the time interval between TnI elevation and death (median almost two weeks) may potentially allow physicians to modify prognosis. First, we showed that in most patients with postoperative TnI elevation, TnI was only slightly (up to tenfold) to moderately (up to hundredfold) increased, suggesting minor myocardial injury. In addition, only 3.2% of the
patients with TnI elevation had typical chest pain and in only 9.5% (minor) ECG changes suggestive for myocardial ischemia were found. Still, these patients with minor myocardial injury had a higher risk of death. This risk seems comparable to the detrimental risk on survival of spontaneous acute coronary syndrome, suggesting a comparable pathophysiological mechanism in patients with isolated troponin elevation after surgery. Given the numerous plaque destabilizing and thrombogenic factors that are present in the perioperative period, troponin elevation may be a consequence of coronary plaque rupture with distal embolization of thrombus or, alternatively, thrombosis of small coronary arteries.22-27 In these patients further myocardial damage may be prevented by adequate treatment during the time interval between troponin elevation and death. Although many studies have addressed prevention of postoperative myocardial injury and death, a major shortcoming is the insufficiently resolved pathophysiology of such myocardial injury and POMI.2-6 Myocardial injury may be caused by regional ischemia due to preexistent significant coronary artery disease or plaque rupture with thrombosis (acute coronary syndrome, type 1 MI), or as a consequence of diffuse myocardial ischemia due to an imbalance between myocardial oxygen supply and demand, caused by pre-existent stable coronary stenosis or non-coronary factors such as deep anemia or hemodynamic instability (type 2 MI).1 The treatment benefits and possible harms in patients with postoperative myocardial injury remain to be evaluated, particularly those harms associated with invasive treatment options. A recent study in which 70 patients with postoperative troponin elevation were randomized to cardiology care consisting of monitoring, investigations and changes to medications, versus standard ward treatment showed no difference in one year mortality.28 However, this study was performed in a limited number of patients.

The results of our evaluation of the data from routine postoperative monitoring of
troponin are comparable to those obtained under research circumstances. Until recently, research
was done in smaller cohorts of patients undergoing mainly vascular and other high risk but
elective surgical procedures, showing an incidence of postoperative myocardial injury of 8–52%.
Studies with a follow-up time of 12 months or less found a two- to twentyfold
increased mortality risk. Studies including emergency surgery reported an incidence of 33-53%
of postoperative myocardial injury, and four- to twelvefold increased mortality risk.40,41 We
found a similar association in our routine troponin measurement cohort including elective and
emergency patients. Like in previous studies, in most patients myocardial injury was found on
the first postoperative day.18-20 The recently published VISION study including over 15,000
patients reported that elevation of troponin T after non-cardiac surgery was strongly associated
with 30-day mortality, with adjusted Hazard Ratio’s comparable to the adjusted Relative Risks of
our protocol. The eligibility criteria of this study were comparable to those of our clinical
protocol, except for the age criterion above 45 years instead of 60 years in our protocol. Thus,
the predictive value of our standard of care postoperative troponin monitoring is markedly
concordant with that found in a large cohort of patients included in the VISION study. The
VISION investigators demonstrated that clinically relevant troponin thresholds existed below the
value that corresponded to a 10% co-efficient of variation of the troponin assay used. We
considered the sample size of our study not sufficient to confirm this finding. Nevertheless, the
strengths of our study are that it focused on patients at higher age and that patients from a single
center were included within a shorter time period. In addition, we made an attempt to validate
that the missing data were missing at random by imputation of missing troponin values.
Moreover, in our study we used troponin-I as compared to troponin-T in the VISION study.
Since troponin-I compared to troponin-T is less influenced by renal dysfunction42,43, the results
from our study may be more representative in patients with renal dysfunction. Finally, the
VISION study did not include renal failure in the multivariable analysis, while in our study the
association between postoperative myocardial injury and death was adjusted for preexistent renal
failure.

We found a strong association between postoperative myocardial injury, as measured by
TnI, and death in noncardiac surgery patients. We therefore conclude that patients at risk for
ey early death after noncardiac surgery are easily identified by routine postoperative troponin
measurements. The time interval between troponin elevation and death potentially allows
physicians to modify prognosis. Obviously, for this purpose the underlying pathophysiological
mechanisms of postoperative myocardial injury have to be explored. In addition, it has to be
elucidated whether there is a causal relationship between myocardial injury and mortality or
whether myocardial injury merely indicates a worse outcome, and next, whether patients with
myocardial injury may benefit from postoperative cardiovascular treatment.

Acknowledgements: The Cardiac Health After SurgEry (CHASE) investigators: University
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Hendrik M Nathoe, Cardiologist; Remco G Grobben, Resident in Cardiology. Department of
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Radiology: Tim Leiner, Radiologist. Department of Surgery: Gert Jan de Borst, Vascular
Surgeon; Loek PH Leenen, Professor of Trauma Surgery; Frans L Moll, Professor of Vascular
Surgery.
**Funding Sources:** This study was supported by a grant from the International Anesthesia Research Society (Clinical Scholar Research Award 2011 to dr. Van Klei), by a grant from the Friends of the University Medical Center Utrecht foundation / the Dirkzwager-Assink Fund to dr. Van Klei and by departmental sources.

**Conflict of Interest Disclosures:** None.

**References:**


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### Table 1. Baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Troponin measured N=1627</th>
<th>Troponin not measured N=589</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>844 (51.9)</td>
<td>303 (51.4)</td>
<td>0.86</td>
</tr>
<tr>
<td>Mean age (SD*)</td>
<td>71.0 (7.7)</td>
<td>70.2 (7.4)</td>
<td>0.02</td>
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<tr>
<td>RCRI† factors</td>
<td></td>
<td></td>
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<tr>
<td>High risk surgery</td>
<td>501 (30.8)</td>
<td>120 (20.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of ischemic heart disease</td>
<td>264 (16.2)</td>
<td>80 (13.6)</td>
<td>0.13</td>
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<tr>
<td>History of heart failure</td>
<td>35 (2.2)</td>
<td>16 (2.7)</td>
<td>0.43</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>242 (14.9)</td>
<td>88 (14.9)</td>
<td>0.97</td>
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<tr>
<td>Renal failure</td>
<td>166 (10.2)</td>
<td>68 (11.5)</td>
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</tr>
<tr>
<td>Preoperative insulin use</td>
<td>92 (5.7)</td>
<td>35 (5.9)</td>
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<tr>
<td>Smoking‡</td>
<td>286 (18.2)</td>
<td>97 (17.4)</td>
<td>0.68</td>
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<td>Hypertension</td>
<td>829 (51.0)</td>
<td>291 (49.4)</td>
<td>0.52</td>
</tr>
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<td>Diabetes</td>
<td>288 (17.7)</td>
<td>106 (18.0)</td>
<td>0.87</td>
</tr>
<tr>
<td>COPD</td>
<td>167 (10.3)</td>
<td>48 (8.1)</td>
<td>0.14</td>
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<td>Peripheral vascular disease</td>
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<td>ASA class§</td>
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<tr>
<td>1</td>
<td>197 (12.1)</td>
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<td>2</td>
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<td>357 (60.6)</td>
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<td>3</td>
<td>366 (22.5)</td>
<td>141 (23.9)</td>
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<td>4</td>
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<td>General anesthesia</td>
<td>1514 (93.1)</td>
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<td>Emergency surgery</td>
<td>306 (18.8)</td>
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<td>Re-operation within 30 days</td>
<td>163 (10.0)</td>
<td>49 (8.3)</td>
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<td>Surgical specialty</td>
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<tr>
<td>Plastic</td>
<td>37 (2.3)</td>
<td>23 (3.9)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Figures are numbers of patients (%), unless indicated otherwise.

* Standard Deviation
† Revised Cardiac Risk Index
‡ N=1568 and 556 respectively, due to some missing values for smoking status.
§ Physical status classification by the American Society of Anesthesiologists.
|| Ear Nose Throat
Table 2. Baseline characteristics of patients in each category of troponin elevation.

<table>
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<tr>
<th></th>
<th>Troponin ≤ 0.06 mcg/L N=1312</th>
<th>Troponin 0.07-0.59 mcg/L N=258</th>
<th>Troponin ≥ 0.60 mcg/L N=57</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>660 (50.3)</td>
<td>148 (57.4)</td>
<td>36 (63.2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Mean age (SD*)</td>
<td>70.6 7.5</td>
<td>72.7 8.0</td>
<td>73.1 8.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RCRI† factors</td>
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<td></td>
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<td></td>
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<tr>
<td>High risk surgery</td>
<td>372 (28.4)</td>
<td>103 (39.9)</td>
<td>26 (45.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of ischemic heart disease</td>
<td>192 (14.6)</td>
<td>53 (20.5)</td>
<td>19 (33.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>21 (1.6)</td>
<td>11 (4.3)</td>
<td>3 (5.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>182 (13.9)</td>
<td>47 (18.2)</td>
<td>13 (22.8)</td>
<td>0.05</td>
</tr>
<tr>
<td>Renal failure</td>
<td>104 (7.9)</td>
<td>39 (15.1)</td>
<td>23 (40.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Preoperative insulin use</td>
<td>66 (5.0)</td>
<td>18 (7.0)</td>
<td>8 (14.0)</td>
<td>0.01</td>
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<tr>
<td>Smoking‡</td>
<td>226 (17.8)</td>
<td>50 (20.4)</td>
<td>10 (19.2)</td>
<td>0.61</td>
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<tr>
<td>Hypertension</td>
<td>649 (49.5)</td>
<td>148 (57.4)</td>
<td>32 (56.1)</td>
<td>0.05</td>
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<tr>
<td>Diabetes</td>
<td>221 (16.8)</td>
<td>51 (19.8)</td>
<td>16 (28.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>COPD</td>
<td>134 (10.2)</td>
<td>28 (10.9)</td>
<td>5 (8.8)</td>
<td>0.89</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>133 (10.1)</td>
<td>35 (13.6)</td>
<td>12 (21.1)</td>
<td>0.01</td>
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<tr>
<td>ASA class§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>174 (13.3)</td>
<td>21 (8.1)</td>
<td>2 (3.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2</td>
<td>858 (65.4)</td>
<td>158 (61.2)</td>
<td>27 (47.4)</td>
<td>0.01</td>
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<tr>
<td>3</td>
<td>270 (20.6)</td>
<td>73 (28.3)</td>
<td>23 (40.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>4</td>
<td>10 (0.8)</td>
<td>6 (2.3)</td>
<td>5 (8.8)</td>
<td>&lt;0.01</td>
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<tr>
<td>General anesthesia</td>
<td>1211 (92.3)</td>
<td>246 (95.3)</td>
<td>57 (100.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>215 (16.4)</td>
<td>69 (26.7)</td>
<td>22 (38.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Re-operation within 30 days</td>
<td>112 (8.5)</td>
<td>39 (15.1)</td>
<td>12 (21.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Surgical specialty</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>276 (21.0)</td>
<td>79 (30.6)</td>
<td>14 (24.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Neuro</td>
<td>302 (23.0)</td>
<td>44 (17.1)</td>
<td>9 (15.8)</td>
<td>0.06</td>
</tr>
<tr>
<td>Vascular</td>
<td>186 (14.2)</td>
<td>47 (18.2)</td>
<td>22 (38.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ENT</td>
<td></td>
<td>and dental</td>
<td>169 (12.9)</td>
<td>33 (12.8)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>154 (11.7)</td>
<td>33 (12.8)</td>
<td>6 (10.5)</td>
<td>0.85</td>
</tr>
<tr>
<td>Gynaecology</td>
<td>116 (8.8)</td>
<td>10 (3.9)</td>
<td>2 (3.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Urologic</td>
<td>73 (5.6)</td>
<td>11 (4.3)</td>
<td>0 (0)</td>
<td>0.14</td>
</tr>
<tr>
<td>Plastic</td>
<td>36 (2.7)</td>
<td>1 (0.4)</td>
<td>0 (0)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Figures are numbers of patients (%), unless indicated otherwise.
* Standard Deviation
† Revised Cardiac Risk Index
‡ N=1271, N=245 and N=52 respectively, due to some missing values for smoking status.
§ Physical status classification by the American Society of Anesthesiologists.
|| Ear Nose Throat

DOI: 10.1161/CIRCULATIONAHA.113.002128
**Table 3.** Association of postoperative troponin and 30 day mortality, adjusted for age, sex, emergency surgery and preoperative renal failure.

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted analysis</th>
<th></th>
<th>Adjusted analysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR*</td>
<td>95% CI†</td>
<td>p-value</td>
<td>RR*</td>
</tr>
<tr>
<td>Age (per year increase)</td>
<td>1.04</td>
<td>1.01 – 1.07</td>
<td>&lt;0.01</td>
<td>1.01</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.08</td>
<td>0.64 – 1.80</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>5.76</td>
<td>3.44 – 9.63</td>
<td>&lt;0.01</td>
<td>4.46</td>
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<tr>
<td>Renal failure (preoperative)</td>
<td>2.67</td>
<td>1.46 – 4.85</td>
<td>&lt;0.01</td>
<td>1.37</td>
</tr>
<tr>
<td>Troponin elevation, categorical</td>
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</tr>
<tr>
<td>Troponin ≤ 0.06 mcg/L</td>
<td>ref</td>
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<td></td>
<td>ref</td>
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<tr>
<td>Troponin 0.07-0.59 mcg/L</td>
<td>2.98</td>
<td>1.66 – 5.34</td>
<td>&lt;0.01</td>
<td>2.36</td>
</tr>
<tr>
<td>Troponin ≥ 0.60 mcg/L</td>
<td>7.94</td>
<td>4.07 – 15.5</td>
<td>&lt;0.01</td>
<td>4.19</td>
</tr>
</tbody>
</table>

* Relative Risk  
† Confidence interval

**Table 4.** Association of postoperative troponin and 30 day mortality after multiple imputation of missing troponin values and adjusted for age, sex, emergency surgery and preoperative renal failure.

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted analysis</th>
<th></th>
<th>Adjusted analysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR*</td>
<td>95% CI†</td>
<td>p-value</td>
<td>RR*</td>
</tr>
<tr>
<td>Age (per year increase)</td>
<td>1.05</td>
<td>1.02 – 1.07</td>
<td>&lt;0.01</td>
<td>1.02</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.02</td>
<td>0.65 – 1.58</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>6.87</td>
<td>4.34 – 10.9</td>
<td>&lt;0.01</td>
<td>5.06</td>
</tr>
<tr>
<td>Renal failure (preoperative)</td>
<td>2.63</td>
<td>1.58 – 4.38</td>
<td>&lt;0.01</td>
<td>1.33</td>
</tr>
<tr>
<td>Troponin elevation, categorical</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Troponin ≤ 0.06 mcg/L</td>
<td>ref</td>
<td></td>
<td></td>
<td>ref</td>
</tr>
<tr>
<td>Troponin 0.07-0.59 mcg/L</td>
<td>2.98</td>
<td>1.66 – 5.34</td>
<td>&lt;0.01</td>
<td>1.93</td>
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<tr>
<td>Troponin ≥ 0.60 mcg/L</td>
<td>7.94</td>
<td>4.07 – 15.5</td>
<td>&lt;0.01</td>
<td>3.47</td>
</tr>
</tbody>
</table>

* Relative Risk  
† Confidence interval
Figure Legends:

**Figure 1.** Distribution of the first troponin elevations over the first three postoperative days.

**Figure 2.** Distribution of myocardial injury over age.

**Figure 3.** Survival curve of each category of TnI elevation.
Figure 1
Figure 2

<table>
<thead>
<tr>
<th>Age</th>
<th>% Patients</th>
<th>No. patients</th>
<th>TnI elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69</td>
<td>10%</td>
<td>777</td>
<td>121</td>
</tr>
<tr>
<td>70-79</td>
<td>20%</td>
<td>595</td>
<td>121</td>
</tr>
<tr>
<td>≥ 80</td>
<td>30%</td>
<td>255</td>
<td>73</td>
</tr>
</tbody>
</table>
Figure 3
Myocardial Injury after Noncardiac Surgery and its Association with Short-Term Mortality
on behalf of the CHASE investigators

Circulation. published online May 10, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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http://circ.ahajournals.org/content/early/2013/05/10/CIRCULATIONAHA.113.002128

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