Relationship Between Postoperative Cardiac Troponin I Levels and Outcome of Cardiac Surgery

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Background—Cardiac surgery may be associated with significant perioperative and postoperative morbidity and mortality. Underlying pathology, surgical technique, and postoperative complications may all influence outcome. These factors may be reflected as a rise in postoperative troponin levels. Interpretation of troponin levels in this setting may therefore be complex. This study assessed the prognostic significance of such measurements, taking into account potential confounding variables.

Methods and Results—One thousand three hundred sixty-five patients undergoing cardiac surgery underwent measurement of cardiac troponin I (cTnI) at 2 and 24 hours after surgery. The relationship of these measurements to subsequent mortality was established. After taking into account all other variables, cTnI levels measured at 24 hours were independently predictive of mortality at 30 days (odds ratio [OR] 1.14 per 10 μg/L, 95% confidence interval [CI] 1.05 to 1.24, \( P = 0.002 \)), 1 year (OR 1.10 per 10 μg/L, 95% CI 1.03 to 1.18, \( P = 0.006 \)), and 3 years (OR 1.07 per 10 μg/L, 95% CI 1.00 to 1.15, \( P = 0.04 \)). Cardiac TnI levels in the highest quartile at 24 hours were associated with a particularly poor outcome.

Conclusions—cTnI levels measured 24 hours after cardiac surgery predict short-, medium-, and long-term mortality and remain independently predictive when adjusted for all other potentially confounding variables, including operation complexity. (Circulation. 2006;114:1468-1475.)

Key Words: surgery • cardiopulmonary bypass • coronary artery disease • survival • tests

Cardiac surgery is associated with a defined degree of perioperative and postoperative morbidity and mortality related not only to the underlying pathology but also to the procedures themselves.\(^1\) Identification of patients who are at higher risk may allow better targeting of investigation, monitoring, and treatment, ultimately leading to an improvement in patient outcome.

Clinical Perspective p 1475

Perioperative and postoperative myocardial ischemia, leading to myocardial damage and necrosis, can occur to varying degrees after cardiac surgery. It is not always easy to identify and classify with standard ECG techniques\(^3\) or biochemical markers.\(^5\) Cardiac troponin I (cTnI) and T (cTnT) are highly sensitive and specific markers of myocardial damage and have evolved as the “gold standard” for the diagnosis of myocardial infarction in patients presenting with an acute coronary syndrome.\(^6\) Troponin release after cardiac surgery is detectable in the majority of patients and was first described in 1991.\(^7\)\(^8\) The interpretation of such release, however, is complex because of the variety of potential underlying reasons. Several small studies have reported the prognostic significance of postoperative troponin measurements in relation to both short- and medium-term outcomes.\(^9\)\(^-\)\(^14\) Nevertheless, confusion remains with regard to what constitutes a “high-risk” troponin level and how to adjust for potential confounding variables such as the type of surgery performed, aortic cross-clamp time, and the timing of measurement.

In the present study, we have evaluated the significance of elevations in cTnI in a large cohort of consecutive patients undergoing cardiac surgery in relation to short-, medium-, and long-term outcome. In doing so, we have adjusted for potential confounding factors inherent in this patient cohort.

Methods

Ethical approval for the study was granted by the local Research Ethics Committee.

Patients and Measures

One thousand four hundred forty-two consecutive patients underwent cardiac surgery at Aberdeen Royal Infirmary between April 1, 2000, and September 30, 2002. Eighty-six patients were excluded: Twenty-three patients underwent congenital repairs, 51 underwent emergency surgery, 10 patients had suffered myocardial infarction in the 7 days before
surgery, and 2 patients died during the surgical procedure itself. The study cohort consisted of the remaining 1356 patients.

Clinical details were collected prospectively by a full-time, experienced data collector. These included the European System for Cardiac Operative Risk Evaluation (EuroSCORE)\(^1,2\) and the glomerular filtration rate estimated from the Modification of Diet in Renal Disease equation.\(^3\) Preoperative and postoperative (at the time of hospital discharge or in-hospital death) medications were recorded by case note review. The ECGs performed immediately before surgery and those recorded on postoperative days 1 and 2 before discharge were retrospectively reviewed by a cardiologist blinded to all other data. The presence of new pathological Q waves was documented, as were any other changes consistent with perioperative ischemia/infarction. Vital status was determined with statistics obtained from the Scottish Register General Office. The main outcome measures were 30-day, 1-year, and 3-year all-cause mortality. In addition, the cause of death was verified prospectively based on medical records and written certificates as the principal cause or a major contributory factor. Serum levels of cardiac TnI were measured with the Bayer ADVIA Centaur automated immunoassay (Bayer Diagnostics, Tarrytown, NY). The 99th percentile value achieved at levels \(0.32 \mu g/L\), with a coefficient of variation of \(\leq 10\%\) achieved at levels \(\leq 0.32 \mu g/L\).\(^1,2\) Results were reported to the attending clinicians.

**Statistical Analysis**

Categorical data are expressed as number (%) and continuous variables as median (interquartile range). Differences in baseline characteristics between survivors and those who died were compared with the \(\chi^2\) test for categorical variables and the Mann-Whitney \(U\) or Kruskal-Wallis test for continuous data. Odds ratios (ORs) and 95% confidence intervals (CIs) for mortality were calculated. The effect of operation type on cTnI release was assessed with the Jonckheere-Terpstra test, and intervals (CIs) for mortality were calculated. The effect of operation type on cTnI release was assessed with the Jonckheere-Terpstra test, and intervals (CIs) for mortality were calculated. The correlation between duration of cardiopulmonary bypass and aortic cross-clamp times were determined with the Pearson correlation test. Survival was plotted by the Kaplan-Meier method, and comparisons were made with the log-rank test. The independent ability of clinical and demographic variables and cTnI to predict 30-day, 1-year, and 3-year mortality was assessed with logistic regression with backward stepwise selection. All statistical analyses were performed with SPSS version 13.0 for Windows (SPSS, Chicago, Ill).

The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

**Results**

Among a total of 1356 patients included in the study, 1041 underwent isolated coronary artery bypass grafting (CABG), with 59 patients having 1 vessel grafted, 346 having 2 vessels grafted, 533 having 3 vessels grafted, and 103 patients having \(>3\) vessels grafted. The remaining 315 patients had more complex procedures. These included 305 valve replacements/repairs (216 aortic valve replacements [3 with isolated surgery on the thoracic aorta and 79 with concomitant CABG]), 78 mitral valve replacements/repairs [27 with concomitant CABG], 10 combined aortic and mitral valve operations [1 with associated thoracic aortic surgery and 1 with concomitant CABG and tricuspid valve surgery], and 1 isolated tricuspid valve repair). The remaining 10 complex procedures consisted of CABG in combination with left ventricular aneurysmectomy (n=6), myxoma resection (n=2), aortic root surgery (n=1), and pericardiectomy (n=1).

Seventy-two patients (5%) did not have troponin analysis performed at 2 hours, whereas 58 (4%) did not have a measurement taken at 24 hours, in 7 cases because of death of the patient before this time point. These patients were excluded from analyses that involved cTnI at the respective time points. At 2 and 24 hours, 90% and 98% of patients, respectively, had a cTnI level above the locally used cutoff of 0.32 \(\mu g/L\).

**Univariate Predictors of Outcome**

The demographic, clinical, and biochemical characteristics of the study cohort are shown in Tables 1 and 2 along with related data comparing those who had died with survivors at 30 days and 1 year, respectively. A total of 31 patients (3%) died within the first 30 postoperative days, and this number increased to 65 (5%) at 1 year. All deaths within 30 days and 61 (94%) of those by 1 year were due at least in part to cardiovascular disease.

**Multivariate Analysis**

Analysis was performed with logistic regression with backward stepwise selection that incorporated all study variables. Cardiopulmonary bypass and cross-clamp time were strongly correlated (Pearson correlation coefficient 0.91, \(P<0.001\)), and therefore, only cross-clamp time was included in the regression models. Cardiac TnI levels measured 24 hours after surgery were independently predictive of mortality at all time points, even after adjustment for all other factors, including operation complexity and EuroSCORE (Table 3). The independent predictors of cardiovascular mortality at 3 years were similar to those that predicted all-cause mortality. Cardiac TnI at 24 hours remained an independent predictor of cardiac death (OR 1.08 per 10 \(\mu g/L\), \(P=0.03\)) after correction for all other variables.

**Cardiac TnI Quartile Analysis**

The Figure shows the Kaplan-Meier survival curves for patients grouped by quartile of troponin I at 2 (A) and 24 hours (B). Log-rank tests (Mantel-Cox, linear trend) were used to assess curve separation for cTnI levels at 2 hours (\(\chi^2 6.84, P=0.009\)) and 24 hours (\(\chi^2 16.78, P<0.001\)). The greatest risk was observed among patients with a cTnI level in the top quartile (2-hour cTnI levels: quartile 4 versus quartile 1, \(\chi^2 7.63, P=0.006\); quartile 4 versus quartile 2, \(\chi^2 6.31, P=0.01\); and quartile 4 versus quartile 3, \(\chi^2 10.99, P=0.001\); 24-hour cTnI...
The median cTnI levels at 2 hours in patients undergoing isolated CABG with a single graft was 0.22 μg/L, which rose as the complexity of surgery increased. cTnI levels: quartile 4 versus quartile 1, 2.97 to 7.64 μg/L (P<0.001); quartile 4 versus quartile 2, 2.11 to 9.43 μg/L (P=0.004); and quartile 4 versus quartile 3, 3.74 to 11.95 μg/L (P=0.001). This remained the case even after adjustment for EuroSCORE and operation type/complexity (Table 4).

Other Analyses
Cardiac TnI levels rose as the complexity of surgery increased. The median cTnI level at 2 hours in patients undergoing isolated CABG with a single graft was 0.22 μg/L (interquartile range: 0.00 to 1.04 μg/L); after 2 grafts, it was 1.53 μg/L (0.63 to 2.86 μg/L); after 3 grafts, it was 1.92 μg/L (0.99 to 3.31 μg/L); and in patients who had undergone complex surgery, it was 3.19 μg/L (1.63 to 5.76 μg/L; P<0.001). A similar pattern was apparent for 24-hour cTnI levels: 1 graft, 1.24 μg/L (0.29 to 2.75 μg/L); 2 grafts, 3.30 μg/L (1.53 to 7.05 μg/L); 3 grafts, 4.03 μg/L (2.11 to 7.64 μg/L); >3 grafts, 5.00 μg/L (3.47 to 9.43 μg/L); and after complex surgery, 6.35 μg/L (3.74 to 11.95 μg/L; P<0.001).

In patients who underwent isolated CABG (n=1041), cTnI levels at 24 hours were univariate predictors of death at 30 days (OR 1.18 per 10 μg/L, P=0.001), 1 year (OR 1.13 per 10 μg/L, P=0.005), and 3 years (OR 1.08 per 10 μg/L, P=0.04). In multivariate analyses with backward stepwise selection that incorporated all study variables, cTnI levels remained independent predictors of death at 30 days (OR 1.19 per 10 μg/L, P=0.003) but not at 1 or 3 years.

Retrospectively collected clinical data (preoperative and postoperative drug therapy and ECG findings) were available for...
TABLE 2. Univariate Predictors of Mortality at 1 Year

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n=1356)</th>
<th>Alive (n=1291)</th>
<th>Deceased (n=65)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors and medical history</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>66.2 (59.1–71.7)</td>
<td>65.8 (58.9–71.6)</td>
<td>70.6 (65.4–75.7)</td>
<td>1.07 (1.04–1.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>1014 (75)</td>
<td>965 (75)</td>
<td>49 (75)</td>
<td>1.04 (0.58–1.84)</td>
<td>0.91</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.4 (24.9–29.8)</td>
<td>27.4 (25.0–29.8)</td>
<td>26.3 (23.3–28.8)</td>
<td>0.91 (0.84–0.97)</td>
<td>0.004</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>140 (10)</td>
<td>129 (10)</td>
<td>11 (17)</td>
<td>1.84 (0.94–3.60)</td>
<td>0.08</td>
</tr>
<tr>
<td>Smoking*</td>
<td>933 (69)</td>
<td>889 (69)</td>
<td>44 (68)</td>
<td>0.99 (0.57–1.69)</td>
<td>0.96</td>
</tr>
<tr>
<td>Hypertension†</td>
<td>562 (41)</td>
<td>538 (42)</td>
<td>24 (37)</td>
<td>0.82 (0.49–1.37)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hypercholesterolemia‡</td>
<td>801 (59)</td>
<td>771 (60)</td>
<td>30 (46)</td>
<td>0.58 (0.35–0.95)</td>
<td>0.03</td>
</tr>
<tr>
<td>Previous MI (&gt;7 d)</td>
<td>507 (37)</td>
<td>482 (37)</td>
<td>25 (38)</td>
<td>1.05 (0.63–1.75)</td>
<td>0.86</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>39 (3)</td>
<td>34 (3)</td>
<td>5 (8)</td>
<td>3.08 (1.16–8.16)</td>
<td>0.02</td>
</tr>
<tr>
<td>NYHA functional class III/IV</td>
<td>895 (66)</td>
<td>850 (66)</td>
<td>45 (69)</td>
<td>1.17 (0.68–2.00)</td>
<td>0.57</td>
</tr>
<tr>
<td>Left main stem stenosis &gt;50%</td>
<td>234 (17)</td>
<td>222 (17)</td>
<td>12 (18)</td>
<td>1.10 (0.58–2.10)</td>
<td>0.77</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
<td>447 (33)</td>
<td>421 (33)</td>
<td>26 (40)</td>
<td>1.44 (0.86–2.41)</td>
<td>0.16</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L§</td>
<td>100 (89–113)</td>
<td>100 (89–113)</td>
<td>110 (98–126)</td>
<td>1.01 (1.00–1.01)</td>
<td>0.001</td>
</tr>
<tr>
<td>Estimated GFR, mL·min⁻¹·1.73 m⁻²</td>
<td>65 (55–74)</td>
<td>65 (56–74)</td>
<td>56 (46–70)</td>
<td>0.96 (0.95–0.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Perioperative/postoperative factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex surgery</td>
<td>315 (23)</td>
<td>276 (21)</td>
<td>39 (60)</td>
<td>5.52 (3.30–9.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bypass time, min</td>
<td>83 (65–100)</td>
<td>82 (65–100)</td>
<td>102 (89–160)</td>
<td>1.02 (1.01–1.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cross-clamp time, min</td>
<td>46 (35–66)</td>
<td>46 (35–64)</td>
<td>70 (47–106)</td>
<td>1.02 (1.01–1.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Off-pump surgery</td>
<td>103 (8)</td>
<td>101 (8)</td>
<td>2 (3)</td>
<td>0.37 (0.09–1.55)</td>
<td>0.18</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>4 (2–6)</td>
<td>4 (2–6)</td>
<td>7 (4–8)</td>
<td>1.40 (1.27–1.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative inotropes¶</td>
<td>337 (25)</td>
<td>291 (23)</td>
<td>46 (71)</td>
<td>8.30 (4.79–14.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative ventricular arrhythmia</td>
<td>42 (3)</td>
<td>33 (3)</td>
<td>9 (14)</td>
<td>6.13 (2.80–13.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative septicemia</td>
<td>34 (3)</td>
<td>24 (2)</td>
<td>10 (15)</td>
<td>9.60 (4.38–21.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cTnl at 2 h, μg/L</td>
<td>2.02 (1.02–3.72)</td>
<td>1.99 (1.00–3.57)</td>
<td>3.33 (1.49–7.52)</td>
<td>1.21 (1.02–1.42)#</td>
<td>0.02</td>
</tr>
<tr>
<td>cTnl at 24 h, μg/L</td>
<td>4.30 (2.19–8.48)</td>
<td>4.18 (2.16–8.11)</td>
<td>9.44 (5.37–21.51)</td>
<td>1.18 (1.09–1.27)#</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.
Data are expressed as median (interquartile range) or number (percentage) of patients.

*Previous or current smoker.
†Systolic ≥140 mm Hg or diastolic ≥90 mm Hg and/or undergoing antihypertensive treatment.
‡Total cholesterol ≥200 mg/dL and/or undergoing cholesterol-lowering drug therapy.
§1 mmol/L creatinine=1.136 mg/L.
¶See text for details.
¶Excludes “renal dose” (<5 μg·kg⁻¹·min⁻¹) dopamine.
#OR per 10 μg/L.

1213 patients (89%). Unfortunately, data were disproportionately missing for patients who had died during follow-up, because of destruction of their clinical records. Of the 117 patients who had died by 3 years, data relating to medication and ECG changes were available for 50 (47%) compared with 1164 (94%) of 1239 survivors. Preoperative treatment with aspirin and/or clopidogrel (used by 83%), β-blockers (69%), and statins (73%) was associated with a better 3-year survival (OR 0.51, P=0.04; OR 0.46, P=0.008; and OR 0.51, P=0.02, respectively). Preoperative use of an angiotensin-converting enzyme inhibitor and/or an angiotensin II receptor blocker (used by 39%) was not, however, predictive of 3-year outcome (OR 1.42, P=0.23). Of these agents, only the postoperative use of a statin (by 78% of patients) was predictive of outcome (OR 0.45, P=0.007). However, neither the development of postoperative ECG changes compatible with ischemia (33%) nor new Q waves (3%) were indicative of prognosis (OR 0.73, P=0.35 and OR 1.57, P=0.55, respectively). The incidence of postoperative ECG changes compatible with ischemia or new Q waves in patients with 24-hour cTnl levels in different quartiles is shown in Table 5, along with their postoperative (at discharge or in-hospital death) medical therapy. Patients with cTnl levels in the upper quartile had a higher prevalence of pathological Q waves. Likewise, those with levels above the median were less frequently treated with antiplatelet therapy and statins.

Discussion

Troponin measurement is routinely performed in many centers after cardiac surgery. Elevated levels are common, which can lead to diagnostic confusion. However, perhaps the most appro-
Levels of cTnI determined 2 hours after surgery were also commonly elevated. Their prognostic utility was, however, inferior to the 24-hour value, which suggests very early troponin values may not be as useful as measurements taken later after surgery. This is supported by other studies, which demonstrated that troponin levels in patients with good and bad outcomes did not separate well until 12 to 24 hours after surgery.\textsuperscript{9,10} It may be that early troponin release is due primarily to common factors, such as the surgery itself, whereas continued troponin release may also reflect perioperative/postoperative events, such as ongoing myocardial ischemia/necrosis, that affect subsequent outcome.

The type of operation is a significant confounder when one interprets postoperative troponin levels, with more complex surgery associated with greater elevations. This is likely related to several factors, including time on bypass and myocardial damage due to the surgery itself. A troponin level in the lowest quartile for valve surgery may have very different connotations if found in a patient after single-vessel CABG. The operation type, therefore, should be taken into account when values are interpreted.

Other factors also complicate attempts to establish universally acceptable cutoff levels for troponins. Surgical techniques and patient case mix may vary greatly between institutions. The additional variation depending on whether cTnI or cTnT is used, as well as the variety of different cTnI methods available, adds to the complexity, as does the lack of standardization of these assays. This means that the absolute values derived in the present study cannot be universally applied. Instead, it is more appropriate for individual centers to establish their own limits based on individual circumstances and analytical techniques.

### Previous Studies
Two large studies have assessed the relationship between creatine kinase-MB isoenzyme (CK-MB) and outcome from CABG.\textsuperscript{18,19} Among 496 patients assigned to CABG in the Arterial Revascularization Therapies Study,\textsuperscript{18} an elevated postoperative CK-MB (according to the local laboratory assay type and cutoff) was observed in 62% of patients. Patients with elevated levels had a higher 30-day and 1-year mortality, with the excess risk predominantly observed among patients with a $>5$ times increase. Likewise, CK-MB levels were an independent predictor of a composite end point of major adverse cardiac events at 1 year. In 2918 patients randomized to the CABG arm of the GUARD during Ischemia Against Necrosis (GUARDIAN) study,\textsuperscript{19} an elevated CK-MB ratio (peak CK-MB value/cutoff) was observed in 62% of patients. The operation type, however, should be taken into account when values are interpreted.

In contrast to the data pertaining to CK-MB, the studies assessing the prognostic utility of cardiac troponin levels after cardiac surgery have been relatively small with limited duration of follow-up. In a study of 224 consecutive patients undergoing a range of cardiac surgical procedures, Januzzi and colleagues\textsuperscript{12} have demonstrated that cardiac cTnT levels in the upper quintile interprets postoperative troponin levels, with more complex surgery associated with greater elevations. This is likely related to several factors, including time on bypass and myocardial damage due to the surgery itself. A troponin level in the lowest quartile for valve surgery may have very different connotations if found in a patient after single-vessel CABG. The operation type, therefore, should be taken into account when values are interpreted.

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hours was the strongest independent predictor of mortality (OR 5.45, 95% CI 4.5 to 232.5, \( P < 0.001 \)). The prognostic value of cTnT has also recently been reported in a cohort of 204 patients followed up for a mean of 28 months.\(^{10} \) In this study, a cTnT level \( > 0.46 \, \mu g/L \) (determined using receiver operating characteristic curve analysis) was an independent predictor of mortality (OR 4.93, 95% CI 1.02 to 23.9, \( P = 0.047 \)), though again there were few deaths on which to base this model (\( n = 14 \)).

In summary, therefore, the findings of the present study are comparable with prior data relating CK-MB and/or troponin levels after cardiac surgery to subsequent mortality but extend these by reporting the prognostic utility of cTnI in a large cohort followed up for longer. In addition, the size of the cohort allows us to adjust for potential confounding factors inherent in this patient cohort, and in particular the nature of the surgery performed.

**Potential Clinical Implications**
The current data suggest that troponin levels after cardiac surgery could be used to identify patients who are at consider-
ably increased risk. Identification of such individuals may allow more intensive monitoring and intervention and facilitate efficient use of clinical resources. Perhaps more important, if such patients can be identified at an early stage postoperatively, measures could be instituted to improve their outcome. These might include interventions proven to increase survival in other settings, such as treatment with β-blockers and agents that influence the renin-angiotensin-aldosterone system.

**Strengths and Limitations**

The strength of this study is that it assesses outcome in a large contemporary cohort of consecutive patients undergoing cardiac surgery in a regional cardiothoracic surgical center. The results are, therefore, likely to be widely applicable. The large cohort also ensures that all-cause mortality can be used as the primary end point. This has the advantage of being entirely objective.20 The absence of data on other important nonfatal outcomes such as recurrent myocardial infarction, postoperative heart failure, and stroke is a limitation, however, as is the absence of data regarding CK-MB and postoperative left ventricular systolic function.

Troponin levels were not assayed before surgery. Thus, although all patients undergoing emergency surgery or with an acute myocardial infarction in the week before surgery were excluded, it is possible that some subjects had minor preoperative elevations. In addition, cTnI levels were available to the clinicians attending the patients. These may have prompted interventions that could have influenced outcome. To address this in part, we retrospectively collected data relating to postoperative drug therapy. Unfortunately, these data were incomplete, limiting the conclusions that can be drawn. Nevertheless, those data that were available suggest that use of secondary preventative therapies such as aspirin and statins was less common among patients with cTnI levels in the highest quartile(s), though this may reflect a higher prevalence of valvular heart disease.

The range of cTnI levels, particularly within the upper quartile, is wide. This is not unexpected given the multiple potential causes of troponin release in this setting. These may include direct, surgery-related tissue damage, ischemia/reperfusion injury, suboptimal cardiac protection, perioperative myocardial infarction, and preoperative factors such as the extent of underlying coronary artery disease and the presence of left ventricular hypertrophy. The current study does not address the important issue of the mechanism of cTnI elevation.

**Conclusions**

Cardiac TnI levels are frequently elevated after cardiac surgery, with the degree of elevation influenced by the nature of the operation. However, after accounting for the complexity of the surgery and other potential confounding factors, cTnI levels at

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**TABLE 4. Quartiles of 24-Hour Troponin Levels and Subsequent Mortality**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Quartile 1 (0–2.19 μg/L), n = 327</th>
<th>Quartile 2 (2.20–4.30 μg/L), n = 325</th>
<th>Quartile 3 (4.31–8.48 μg/L), n = 322</th>
<th>Quartile 4 (8.49–350.81 μg/L), n = 326</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-Day mortality, n (%)</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
<td>6 (1.9)</td>
<td>15 (4.6)</td>
</tr>
<tr>
<td>Unadjusted OR (95% CI)</td>
<td>1</td>
<td>0.33 (0.03–3.22)</td>
<td>2.05 (0.51–8.27)</td>
<td>5.21 (1.49–18.17)</td>
</tr>
<tr>
<td>OR adjusted for EuroSCORE and operation type* (95% CI)</td>
<td>1</td>
<td>0.24 (0.02–2.31)</td>
<td>1.05 (0.25–4.52)</td>
<td>2.37 (0.63–8.85)</td>
</tr>
<tr>
<td>1-Year Mortality, n (%)</td>
<td>6 (1.8)</td>
<td>7 (2.2)</td>
<td>13 (4.0)</td>
<td>32 (9.8)</td>
</tr>
<tr>
<td>Unadjusted OR (95% CI)</td>
<td>1</td>
<td>1.18 (0.39–3.54)</td>
<td>2.25 (0.85–6.00)</td>
<td>5.82 (2.40–14.13)</td>
</tr>
<tr>
<td>OR adjusted for EuroSCORE and operation type* (95% CI)</td>
<td>1</td>
<td>0.86 (0.28–2.62)</td>
<td>1.14 (0.41–3.21)</td>
<td>2.94 (1.16–7.45)</td>
</tr>
<tr>
<td>3-Year Mortality, n (%)</td>
<td>15 (4.6)</td>
<td>21 (6.5)</td>
<td>28 (8.7)</td>
<td>42 (12.9)</td>
</tr>
<tr>
<td>Unadjusted OR (95% CI)</td>
<td>1</td>
<td>1.44 (0.73–2.84)</td>
<td>1.98 (1.04–3.78)</td>
<td>3.08 (1.67–5.67)</td>
</tr>
<tr>
<td>OR adjusted for EuroSCORE and operation type* (95% CI)</td>
<td>1</td>
<td>1.12 (0.55–2.26)</td>
<td>1.37 (0.69–2.73)</td>
<td>1.94 (1.01–3.72)</td>
</tr>
</tbody>
</table>

*One, 2, 3, or >3 grafts or complex surgery (see text for details).

---

**TABLE 5. Relationship Between Quartiles of cTnI at 24 Hours and Postoperative ECG Changes and Medical Therapy**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Quartile 1 (0–2.19 μg/L)</th>
<th>Quartile 2 (2.20–4.30 μg/L)</th>
<th>Quartile 3 (4.31–8.48 μg/L)</th>
<th>Quartile 4 (8.49–350.81 μg/L)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative ischemic ECG changes</td>
<td>99 (33)</td>
<td>84 (29)</td>
<td>110 (38)</td>
<td>85 (32)</td>
<td>0.57</td>
</tr>
<tr>
<td>New postoperative pathological Q waves</td>
<td>9 (3)</td>
<td>3 (1)</td>
<td>7 (2)</td>
<td>15 (6)</td>
<td>0.05</td>
</tr>
<tr>
<td>Postoperative treatment with inotropes†</td>
<td>61 (19)</td>
<td>61 (19)</td>
<td>80 (25)</td>
<td>120 (37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative treatment with aspirin/clopidogrel</td>
<td>286 (93)</td>
<td>263 (88)</td>
<td>242 (85)</td>
<td>233 (84)</td>
<td>0.001</td>
</tr>
<tr>
<td>Postoperative treatment with β-blocker</td>
<td>130 (42)</td>
<td>132 (44)</td>
<td>128 (45)</td>
<td>124 (45)</td>
<td>0.49</td>
</tr>
<tr>
<td>Postoperative treatment with statin</td>
<td>257 (83)</td>
<td>240 (81)</td>
<td>202 (71)</td>
<td>215 (78)</td>
<td>0.01</td>
</tr>
<tr>
<td>Postoperative treatment with ACE inhibitor/ARB</td>
<td>99 (32)</td>
<td>122 (41)</td>
<td>105 (37)</td>
<td>91 (33)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

Data are expressed as number (percentage) of patients with data available.

*p* test for trend.

†Excludes “renal dose” (<5 mg·kg⁻¹·min⁻¹) dopamine.
24 hours remain independent predictors of short, medium, and long-term outcome. Patients with cTnI levels in the highest quartile are at particular risk. These data suggest that routine measurement of troponin levels after cardiac surgery may be clinically useful and can identify a group of patients at increased risk of death. These individuals might benefit from more intensive investigation and treatment, though this remains to be tested.

Acknowledgments
We are grateful to staff in the Departments of Clinical Biochemistry and Cardiothoracic Surgery, Aberdeen Royal Infirmary for their assistance in this study.

Disclosures
None.

References

CLINICAL PERSPECTIVE
Almost all patients undergoing cardiac surgery will have elevated cardiac troponin levels postoperatively. This may be a result of a number of factors, including the underlying pathology, surgical technique, and perioperative complications. The interpretation of troponin measurements in this setting is therefore complex, and the clinical significance of elevated levels is uncertain. The present study assessed the prognostic importance of cardiac troponin I (cTnI) in 1365 patients undergoing cardiac surgery who were followed up at 30 days, 1 year, and 3 years after surgery. It confirms that cTnI levels are frequently elevated, with 98% of patients having levels above the locally used cutoff of 0.32 µg/L by 24 hours after surgery. Independent of other factors, including conventional cardiac risk factors, the nature and duration of surgery, and the European System for Cardiac Operative Risk Evaluation (EuroSCORE), cTnI levels 24 hours after surgery are powerful predictors of both short- and medium-term all-cause mortality. Patients with cTnI levels in the highest quartile are at particular risk, even after adjustment for operation type and EuroSCORE. These data suggest that routine measurement of cTnI levels after cardiac surgery may be clinically useful and can detect patients who are more likely to die. Identification of these individuals at an early stage postoperatively may allow measures to be taken to improve their outcome. This, however, remains to be tested.
Relationship Between Postoperative Cardiac Troponin I Levels and Outcome of Cardiac Surgery

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