Clinical Study
Risk Stratification by Cardiac Biomarkers following Emergency Gastrointestinal Surgery

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Perioperative cardiac complications are a significant cause of death following emergency gastrointestinal surgery. Early diagnosis of subclinical myocardial injury and infarction may be improved by screening with cardiac biomarkers. The aim of this study was to assess the predictive value of troponin I (TnI) and B-type natriuretic peptide (BNP) in the early postoperative period after emergency gastrointestinal surgery. We prospectively recruited 48 patients undergoing major emergency surgery for gastrointestinal or colorectal pathology in a single district general hospital. The primary endpoint was mortality at 90 days following surgery. Overall survival was 81.3% (39/48), with 9 postoperative deaths. Elevated TnI (≥ 0.03 ng mL⁻¹) was the best predictor of mortality, associated with an odds ratio of death by 90 days of 14.3 (95% CI 1.50–337, \( P = 0.01 \)). A postoperative BNP concentration > 408.5 pg mL⁻¹ was associated with an odds ratio of death by 90 days of 13.6 (95% CI 2.03–106, \( P = 0.002 \)). A single measurement of postoperative BNP and TnI is a powerful predictor of short- to medium-term mortality in patients after emergency gastrointestinal surgery. Further work is required to demonstrate that cardiac biomarkers have independent predictive power and that patient outcomes can be improved.

1. Introduction

Perioperative cardiac complications are a major cause of death following emergency gastrointestinal surgery. Early diagnosis of subclinical myocardial injury and infarction may be improved by screening with cardiac biomarkers. The aim of this study was to assess the predictive value of troponin I (TnI) and B-type natriuretic peptide (BNP) in the early postoperative period after emergency gastrointestinal surgery. We prospectively recruited 48 patients undergoing major emergency surgery for gastrointestinal or colorectal pathology in a single district general hospital. The primary endpoint was mortality at 90 days following surgery. Overall survival was 81.3% (39/48), with 9 postoperative deaths. Elevated TnI (≥ 0.03 ng mL⁻¹) was the best predictor of mortality, associated with an odds ratio of death by 90 days of 14.3 (95% CI 1.50–337, \( P = 0.01 \)). A postoperative BNP concentration > 408.5 pg mL⁻¹ was associated with an odds ratio of death by 90 days of 13.6 (95% CI 2.03–106, \( P = 0.002 \)). A single measurement of postoperative BNP and TnI is a powerful predictor of short- to medium-term mortality in patients after emergency gastrointestinal surgery. Further work is required to demonstrate that cardiac biomarkers have independent predictive power and that patient outcomes can be improved.
emergency gastrointestinal surgery in the district general hospital setting.

2. Methods

2.1. Study Design and Recruitment. All patients over 18 years of age admitted for emergency major gastrointestinal and colorectal surgery were prospectively recruited over a nine-month period. It was postulated that patients with elevated biomarkers were 5-fold more likely to die (25%) compared to background rates of death that were 5% for emergency GI surgery, a sample size of 49 thus providing 80% power with a type I error of 0.05. Patients were excluded if they were unable to give informed written consent, died within 12 hours of surgery, or underwent abdominal surgery for non-gastrointestinal (e.g., vascular, hepatobiliary, urological, or gynaecological) indications. The study design was approved by the local research ethics committee.

2.2. Data Collection. Baseline clinical data were collected from patients and their medical records prior to surgery, along with routine bloods and a 12-lead ECG. All patients were subjected to routine anaesthetic procedure with standard management of perioperative fluid balance. All postoperative care (e.g., intensive care admission, oxygen therapy, fluid balance) was as per the normal practice of the surgical, anaesthetic, and intensive care teams.

Between 12 and 48 hours after surgery blood samples were drawn for TnI and BNP and a repeat 12-lead ECG was recorded, a time point demonstrated to detect almost 75% of cases of perioperative myocardial infarction [5]. All ECGs were batch analysed by two experienced cardiologists blinded to all clinical information. Patients were followed up for a minimum of 90 days via outpatient appointments, telephone contact or via their general practitioner. Survival status at 90 days was known for all patients.

2.3. Assays. BNP and TnI were measured by immunoassay on the Abbott Architect Ci8200 (Abbott Illinois USA). The detection limit of cardiac troponin I was 0.01 ng mL$^{-1}$, the upper measuring limit 50.4 ng mL$^{-1}$, the assay imprecision [%CV] 0.118 ng mL$^{-1}$ [5.4%]–12.83 ng mL$^{-1}$ [3.53%], the 10% coefficient of variation 0.023 ug L$^{-1}$, and the 99th centile 0.012 ug L$^{-1}$. The sensitivity of the BNP assay was 10 pg mL$^{-1}$ with an upper measuring limit 5000 pg mL$^{-1}$ and an assay imprecision [%CV] across the analytical range of 90 pg mL$^{-1}$ [4.5%]–3500 pg mL$^{-1}$ [2.5%].

2.4. Data Analysis. All-cause mortality at 90 days was chosen as the primary outcome measure. Categorical data were compared using the $\chi^2$ test with Yates correction. Univariate analyses were performed to identify risk factors predictive of survival and odds ratios presented with 95% confidence intervals. ROC curve by survival was constructed. Data were analysed using Stata 7.0 software (StataCorp, Texas, USA) and considered significant if $P < 0.05$. Multivariate analyses constructions were not conducted due to insufficient endpoints per variable [11].

3. Results

Over the study period a total of 55 patients were eligible for inclusion. One patient declined to give consent and six died within 12 hours of surgery and were excluded. The remaining 48 patients completed the study protocol and are included in the analysis.

The mean population age was 69.3 (range 20–98) years. 29 (60.4%) were male. Ten patients (20.8%) had a history of ischemic heart disease, although none had previously undergone revascularisation by percutaneous coronary intervention or bypass grafting. Eighteen patients (38.3%) had a history of hypertension and seven (14.9%) were current smokers. Seven (14.9%) were insulin-dependent diabetics and three (6.4%) had known congestive cardiac failure.

Indications for surgery were bowel obstruction (26 patients), perforation (13), ischemia (6), or other (3). 96% of surgical procedures were carried out by an open approach and 7 patients (14.6%) had a known or newly diagnosed gastrointestinal or colorectal malignancy.

Five patients (10.4%) had a perioperative myocardial infarction, as defined by elevated TnI level to above the 99th percentile of the upper limit of normal and one or more of ischaemic symptoms, ischemic changes or new pathologic Q waves on ECG, or evidence on MI on cardiac imaging [12]. In total, 18 patients (37.5%) had an elevated postoperative cardiac TnI.
Table 2: Univariate predictors of postoperative death at 90 days.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin I ≥ 0.03 ng mL⁻¹</td>
<td>14.3</td>
<td>1.50–337</td>
<td>0.01</td>
</tr>
<tr>
<td>BNP &gt; 408.5 pg mL⁻¹</td>
<td>13.6</td>
<td>2.03–106</td>
<td>0.002</td>
</tr>
<tr>
<td>Preop C-reactive protein &gt; 150 mg/L</td>
<td>7.00</td>
<td>1.16–47.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Lee revised cardiac index ≥ 3</td>
<td>0.64</td>
<td>0.08–4.27</td>
<td>Not significant</td>
</tr>
<tr>
<td>Bowel perforation</td>
<td>9.14</td>
<td>1.48–63.6</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Figure 1: Postoperative troponin I (a) and BNP (b) levels, grouped by 90-day survival.

Figure 2: BNP ROC curve for all-cause mortality at 90 days.

Figure 3: Kaplan-Meier survival curve according to BNP level.

Nine patients died in the 90-day follow-up period, of whom six had bowel perforation at presentation and three had suffered a perioperative myocardial infarction. Baseline characteristics according to patient survival at 3 months are shown in Table 1. In addition, baseline haemoglobin and blood pressure did not differ significantly between groups. The prevalence of ischemic heart disease or use of cardiac medications was not significantly different in patients who died in the follow-up period. The causes of death (four confirmed at autopsy) were bronchopneumonia (3 patients), abdominal sepsis (2), pancreatic carcinoma (1), ischaemic bowel (1), and unknown (2).

Overall, the median (IQR) postoperative BNP level was significantly higher in patients who died over the follow-up period compared to those who did not (420 (178–802) pg mL⁻¹, P < 0.01). Median (IQR) troponin was also significantly higher in patients who died (0.16 (0.08–0.58) versus 0.01 (0.0–0.07) ng mL⁻¹, P = 0.001) (Figure 1).

ROC curves were constructed to identify the optimum cutoff for BNP for prediction of 90-day mortality and for
comparison of TnI with BNP (Figure 2). A BNP level of 408.5 pg mL$^{-1}$ had the optimal balance of sensitivity (66.7%) and specificity (87.2%) for prediction of 90-day mortality. For BNP, the AUC was 0.7934 (95% CI 0.6437 to 0.9432, \( P < 0.01 \)). For troponin, the AUC was 0.8494 (95% CI 0.7315 to 0.9673, \( P = \) 0.001). Kaplan-Meier survival curves, dichotomised by BNP result, are shown in Figure 3. Univariate predictors of all-cause death within 90 days of surgery are shown in Table 2. Multivariate analysis was not performed due to insufficient endpoints per variable [11].

4. Discussion

The principal finding of our study is that elevated cardiac biomarkers following emergency gastrointestinal surgery identify patients with increased all-cause mortality at 90 days. Our work follows a number of studies indicating that elevated postoperative TnI predicts adverse outcomes in a range of non-cardiac surgery, including orthopaedic [13], vascular [14], cardiac [15], and emergency [16] surgery, confirmed by meta-analysis [7]. Both pre- and postoperative levels of BNP predict outcomes in patients undergoing non-cardiac surgery [10, 17].

Screening with biomarkers offers the potential to intervene before the window for cardiac salvage has been missed [18, 19]. In our emergency GI surgical population, we found TnI to provide stronger predictive power compared with BNP, as measured by the area under the ROC curve. Improved outcome through postoperative cardiac biomarker screening has yet to be definitively demonstrated, however.

Optimal therapy for myocardial injury and infarction in the postoperative period is not well established [20]. The apparent benefit of beta-blockers [21] has been subject to significant uncertainty following the publication of the POISE trial, which demonstrated a reduction in cardiac risk but worse overall survival and increased risk of stroke [22, 23]. Risk stratification and balancing the advantages of antiplatelet and antithrombotic therapy with the risk of bleeding is difficult. DECREASE-VII is a randomised controlled trial designed to assess the efficacy of adding clopidogrel to patients with an asymptomatic troponin T rise following major vascular surgery [24].

Further work remains to determine the role of postoperative cardiac biomarkers. There is uncertainty relating to what cut-off should be used for BNP in different surgical populations and the optimal timing and frequency of measurement is unclear. A combined scoring system incorporating pre- and postoperative cardiac biomarkers and traditional cardiac risk factors might be derived and prospectively validated.

5. Limitations

Our study has several limitations inherent of a small-sized, hypothesis-generating study. No specific protocols existed for fluid or anaesthetic management beyond routine practice. Despite this, BNP and TnI values held important predictive information. Preoperative or serial biomarker levels were not collected, therefore the value of preoperative TnI and BNP cannot be assessed, and it is possible that some subclinical delayed infarcts were missed. Finally, the independent value of BNP and TnI remains to be confirmed in a larger study supporting multivariate analysis.

6. Conclusions

We have identified a correlation between cardiac biomarkers and medium-term outcomes in patients undergoing emergency gastrointestinal surgery. Our study strengthens the argument for postoperative screening by cardiac biomarkers, in order to diagnose cardiac ischemia or dysfunction early and target specialist and high-dependency resources. In the first instance, these preliminary data will inform future studies of the value and thresholds of BNP testing in the non-cardiac surgical setting.

Authors’ Contribution

T. J. Cahill, P. Bowes, M. Ward and A. Bakhai conceived and designed the study. All authors participated in collection and analysis of data. T. J. Cahill and A. Bakhai drafted the manuscript, which was edited, read, and approved by all authors.

Conflict of Interests

BNP reagents were provided at the request of the investigators for research purposes to Dr. Ameet Bakhai who has received honoraria for educational activities with Abbott Diagnostics Limited.

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References


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