Background: The 30-day mortality following non-cardiac surgery ranges from 2% - 6%. Observational studies have suggested myocardial injury following non-cardiac surgery (MINS) and subsequent vascular events are partly responsible.

Methods: Postoperative high-sensitivity troponin I levels were recorded on in-patients undergoing non-cardiac surgery. Positive results (> 17 ng/L) were categorized by the associated pathophysiological process; “secondary” if associated with sepsis, significant perioperative bleeding or prolonged pathological atrial or ventricular tachyarrhythmias and “primary” if not. The 30-day and 6-month mortality data were collected. Multivariate Cox proportional hazard modeling determined independent predictors of 6-month mortality.

Results: Of 387 patients analyzed, 125 (32%) were over 75 years of age; 192 (50%) were male. The 30-day mortality (2.8%) was comparable to the VISION study (1.9%); 30-day mortality following an elevated postoperative troponin was 5.6%, all associated with sepsis. The 6-month mortality overall was 10%; 21% following any postoperative troponin elevation, 8.6% following “primary” events, 36% and 21% following “secondary” events associated with sepsis and bleeding respectively and 3.7% with normal post-operative troponin. 5% of deaths had vascular causes identified; none had an elevated postoperative troponin. Emergency presentation, sepsis, and abnormal renal function independently predicted 6-month mortality with the emergency presentation being the strongest predictor. Troponin levels > 1000 ng/l (highly suggestive of independently predicting 6-month mortality (P = 0.06)) occurred in 13 patients (3.4% of the entire cohort); the majority of these patients were emergency admissions requiring high-dependency or intensive care unit admission and 9 had evidence of perioperative sepsis. “Primary” elevated post-operative troponins were not independent predictors of mortality.

Conclusion: Postoperative high-sensitivity troponin elevation in patients undergoing non-cardiac surgery is associated with 30-day and 6-month mortality. However, early mortality in patients with elevated troponin was largely accounted for by other non-cardiac adverse events; we suggest a mixture of pathophysiological processes are at work rather than solely indicating new vascular events. (Funded by the Regional Innovation Fund of NHS England and the South Tees NHS Foundation Trust Research and Development Fund.)
Over 200 million people undergo major non-cardiac surgery worldwide every year (1). Mortality following such operations is estimated between 2% - 6% at 30 days (2, 3). The Vascular Events in Non-Cardiac Surgery Patient Cohort Evaluation (VISION) study recruited 15, 133 patients, routinely measuring post-operative troponins on all patients over the age of 45 years undergoing emergency or elective non-cardiac surgery with a length of stay more than 2 days (3). Raised troponin T was noted in 11.7% of patients and were associated with 30-day mortality, with increasing troponin levels adding additional prognostic significance.

The further analysis excluded non-ischemic etiology (sepsis, pulmonary embolism or undergoing cardioversion) and established diagnostic criteria for Myocardial Injury after Non-cardiac Surgery (MINS) events (4). Peak troponin T levels above 0.03 ng/L with or without ECG changes or ischemic symptoms were shown to be independently associated with elevated 30-day mortality. Such events were termed a MINS event, suggesting they marked cardiovascular events relating to undiagnosed or unstable atherosclerotic disease “triggered” by the stress of undergoing surgical intervention, hemodynamic fluctuations, and potentially physical maneuvering. MINS occurred without symptoms or ECG changes in 84% of patients. Routine post-operative troponin monitoring was recommended to maximize detection of such events; subsequent guidelines for perioperative cardiac risk assessment and management have adopted this strategy for selected patients felt to be at increased risk of cardiac events in the post-operative period although the optimal management of such events has not yet been established (5).

Our experience in day-to-day practice is that there is often no clear single shared mechanism that explains an elevated troponin following non-cardiac surgery, an important consideration when trying to determine therapeutic strategies. The introduction of high-sensitivity troponin assays will also dramatically increase the sensitivity for detecting myocardial injury although at the cost of reduced specificity. Through an in-depth analysis of our initial experience of post-operative high-sensitivity troponin monitoring, we aimed to further characterize the population of patients who experience raised postoperative troponins.

**MATERIALS AND METHODS**

**Data Collection and Study Population**

The James Cook University Hospital, Middlesbrough is a large NHS hospital with 250 surgical beds. It serves a population of over 1 million people in Teesside and County Durham as a regional trauma center and major cancer center. Sub-specialties include general, urological, major vascular, neuro- and orthopedic surgery (both trauma and elective) as well as plastics, otolaryngological and maxillofacial surgery.

Data were collected prospectively between September 2014 and May 2015 as part of a service evaluation project performed during this time period to gather data on the incidence of postoperative troponin elevation. Suitable elective cases were identified using the CaMIS patient identification system (EMIS Health © 2015) one month in advance. Pre-operative troponin I levels were performed on blood samples corresponding to the patient identifier if received on a pre-planned “Waiting List To-Come-In” (WL-TCI) date. Patients appeared on the TheatreMan operation record once they underwent surgery Patient Cohort Evaluation (VISION) study recruited 15, 133 patients, routinely measuring post-operative troponins on all patients over the age of 45 years undergoing emergency or elective non-cardiac surgery with a length of stay more than 2 days (3). Raised troponin T was noted in 11.7% of patients and were associated with 30-day mortality, with increasing troponin levels adding additional prognostic significance.

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**Postoperative Troponin Monitoring Following Noncardiac Surgery**

Emergency cases (that is, patients requiring in-hospital surgery after urgent or emergency admission) were identified by a daily download of the TheatreMan operation recording system indicating they had undergone surgery. Preoperative troponins were performed retrospectively on the blood sample obtained on admission. Postoperative troponins were performed as described for elective patients.

All troponins were performed using the ADI-VA Centaur Troponin I Ultra Assay (Siemens); this assay meets the International Federation of Clinical Chemistry and Laboratory Medicine (IF-CC) Task Force on Clinical Applications of Cardi-
ac Bio-markers recommendations with a coefficient of variation (CV) < 10\% at the 99th centile (40 ng/L) and demonstrates clinical equivalence to high-sensitivity troponin assay (6, 7). The lower limit of detection is 6 ng/L but our laboratory reports a minimum value of 17 ng/L and therefore values < 17 ng/L were deemed to be “undetectable”; to assess percentage change in troponin, < 17 ng/L was assigned the mid-range value of 8 ng/L. Assays were performed within 24 hours of phlebotomy to maximize accuracy.

Troponins requested by the clinical team for clinical reasons were available for view on our pathology reporting system. Troponins performed for the research study were withheld to prevent clinical care being affected, given the uncertain significance of the results.

According to local research protocols, the initial data collection process was deemed a service evaluation project with specific ethical approval not required. No ethical issues were raised by reviewers as part of the funding application to NHS England and our Trust R&D lead approved the project without any governance or ethical concerns.

Definitions

Clinical records were assessed retrospectively to determine the presence of events that may be associated with troponin release including sepsis, major perioperative bleeding, pulmonary embolism, cardioversion or prolonged tachyarrhythmia. Sepsis was defined as “the presence (probable or documented) of infection together with the systemic manifestation of infection” as per the 2012 sepsis guidelines (8). Major perioperative bleeding was defined as a fall in hemoglobin greater than 5 g/dL (9), or to a minimum level under 7 g/dL, considered a suitable threshold for transfusion using a restrictive transfusion policy in the 2015 NICE guidelines (10). This was chosen to identify patients at a high risk of significant or prolonged coronary under-perfusion. If a patient experienced significant bleeding but was rapidly transfused such that serial daily hemoglobins did not detect a fall in hemoglobin, this was not included in our definition. Prolonged tachyarrhythmias were defined as a pathological atrial or ventricular tachycardia excluding sinus tachycardia, documented either in the clinical notes or on 12-lead electrocardiography; the majority of patients were not monitored continuously so only those arrhythmias triggering clinical investigation or concerns were recorded.

Post-operative troponin elevations > 17 ng/L were sub-classified by associated clinical events to allow more detailed characterization of the underlying pathophysiological process at work. Primary events did not have an associated clinical event. Secondary events had a documented associated clinical event (i.e. sepsis, bleeding or arrhythmia as defined above).

Outcomes

The 30-day and 6-month mortality outcomes were obtained from the Office of National Statistics (ONS) along with a cause of death.

Statistical Analysis

Variables were separately assessed for association with mortality at 30 days and 6 months using a Cox Proportional Hazards univariate analysis with mortality as the dichotomous dependent variable, compared to a reference group without the variable (i.e. patients with sepsis versus patients without sepsis). Variables were also analyzed in combination with a positive troponin (e.g. patients with sepsis and a positive troponin (a “secondary MINS” event) versus all other patients). For all variables, we report a hazard ratio with 95\% confidence intervals and the associated P-value.

Abnormal renal function was evaluated by a variety of thresholds (eGFR > 60 mL/min vs < 60 mL/min, > 50 mL/min vs < 50 mL/min, etc.) to identify the most predictive threshold to use in subsequent multivariate analysis. Post-operative troponin level was tested as a dichotomous variable using values >17ng/L as positive. It was subsequently evaluated by a variety of thresholds (> 50 ng/L, > 100 ng/L, > 500 ng/L and every 100 ng/L to > 1000 ng/L) to identify the most predictive threshold to use in multivariate analysis.

A multivariate Cox Proportional Hazards model was then constructed to determine independent predictors of 6-month mortality. Forced simultaneous entry of all variables was used initially to determine significant variables compared to the univariate analysis. All variables with a P value less than 0.2 in either analysis...
were then entered into both a forward and backward stepwise selection model to determine the independent predictors of 6-month mortality.

Kaplan-Meier survival curves were constructed comparing mortality depending on post-operative troponin level, type of postoperative troponin elevation and outcomes for each pathological process associated with a “secondary” troponin elevation.

RESULTS

Of 1114 patients screened, 387 patients were identified for further analysis (Figure 1). All had a pre-operative and at least one post-operative troponin measurement; 460 (41%) patients had at least two post-operative troponin levels taken. The demographics can be seen in Table 1 with demographics from the VISION study for comparison.

Post-operative troponin elevations occurred in 141 (36%) patients; 61 patients had a postoperative troponin > 40 ng/L and 13 had a peak level > 1000 ng/L. Eighty-two (62%) of urgent/emergency patients and 59 (23%) of elective patients had an elevated post-operative troponin. Sepsis occurred in 71 (18%) patients, significant perioperative bleeding in 37 (9.6%) patients and prolonged pathological arrhythmia in 3 (0.8%) patients.

Mortality outcomes divided by underlying pathophysiology can be seen in Table 2; survival curves showing 30-day and 6-month mortality divided by normal troponin, “primary” and “secondary” troponins can be seen in Figure 2 and divided by peak post-operative troponin in Figure 3. For the whole cohort, 11 patients (2.8%) died within 30 days; eight had an elevated postoperative troponin all in the setting of peri-operative sepsis (11% of all patients with perioperative sepsis). Three deaths occurred in the 241 patients with a normal post-operative troponin. There were no early deaths amongst patients with “primary” troponin elevations or “secondary” troponin elevation in the setting of bleeding or tachycardia.

At 6 months, there were 39 deaths (10%); 29 deaths occurred following urgent/emergency surgery. Patients with a normal postoperative troponin had a mortality rate of 3.7% compared to 21% in patients with an elevated postoperative troponin. Patients with a “primary” troponin elevation suffered 8.7% mortality compared to 33% amongst patients with a “secondary” troponin elevation. The 6-month mortality was 36% and 21% following sepsis and bleeding respectively. Mortality following a “secondary” troponin elevation was significantly higher than a “primary” troponin elevation or normal postoperative troponin. There was no difference between mortality following “primary” troponin elevation and a normal postoperative troponin.

The 6-month mortality in patients with perioperative sepsis regardless of troponin was 31% (4.8% in elective patients, 42% in emergency patients); in patients with a normal post-operative troponin, this was 6.7%, 0% and 11% in the three cohorts compared to 38%, 6.7%, and 49% if an elevated troponin was present. Patients without perioperative sepsis had 6-month mortality rates of 5.4%, 3.8%, and 9.8%. Kaplan-Meier survival curves comparing 6-month mortality in patients without peri-operative sepsis, with perioperative sepsis but with a normal post-operative troponin and sepsis with an elevated postoperative troponin are shown in Figure 4.

Perioperative Troponin Trends

Perioperative trends in troponin can be seen in Table 3. Preoperative troponin exceeded peak postoperative troponin levels in 37 (9.6%) patients; one (2.7%) patient suffered 30-day mortality and eight (22%) suffered 6-month mortality. A positive preoperative troponin fell to a negative troponin in 17 (6.9%) patients; one (5.9%) suffered 6-month mortality.

The percentage change in troponin was < 20% in 63% of patients; mortality in this group was 0.8% at 30-days and 2.9% at 6-months. Large changes (> 1000%) occurred in 7% of patients; mortality was 19% at 30-days and 26% at 6-months.

Univariate and Multivariate Analysis

Univariate analysis of perioperative variables can be seen in Table 4. An urgent / emergency surgical presentation, perioperative sepsis, and postoperative troponin elevation were associated with both 30-day and 6-month mortality. Renal function was a significant predictor at all tested...
thresholds with a minimum P value obtained for eGFR < 60 mmol/L (P = 0.003, HR 7.338 (1.947 - 27.661)); this was therefore used as the threshold in subsequent analyses. Significant peri-operative blood loss was not associated with 30-day mortality (P = 0.706, HR 1.485 (0.190 - 11.596) but was associated with 6-month mortality (P = 0.003 HR 3.412 (1.506 - 7.731)). Age at presentation was not associated with 30-day mortality but age over 75 years was associated with 6-month mortality.

The “Secondary” troponin elevations associated with sepsis and bleeding exhibit a higher hazard ratio than sepsis alone for 30-day and 6-month mortality, suggesting raised troponin as a marker of risk. The “Primary” troponin elevations were not statistically associated with 30-day or 6-month mortality (P = 0.325 HR 0.036 (0.0 - 26.807)).

Multivariate analysis with simultaneous entry of all variables confirmed these findings. Stepwise regression modeling determined that urgent/
Various troponin thresholds were tested; only troponin > 1000 ng/L was suggestive of independently predicting 6-month mortality (HR 2.425 (0.967 - 6.079) P = 0.06). This degree of troponin elevation occurred in 13 patients (3.4% of the entire cohort); 12 were emergency admissions, 11 required admissions to high-dependency or intensive care units and 9 had evidence of perioperative sepsis with / without multi-organ failure. One patient was documented as suffering a “likely type 1 myocardial infarction” prior to admission which was managed conservatively.

2. “Secondary” troponin elevations in the setting of postoperative clinical events have a significantly higher mortality than “primary” troponin elevations at both 30-day and 6-months.

3. Troponin elevation adds prognostic significance to post-operative complications that already carry significant mortality.

4. There is no significant difference in mortality between patients experiencing an isolated low-to-medium postoperative troponin elevation and a normal postoperative troponin.

The role of postoperative troponin monitoring using contemporary troponin assays has been explored in several studies previously. Landesberg and colleagues demonstrated even small elevations in postoperative cardiac biomarkers were predictive of adverse outcomes in patients undergoing major vascular surgery (11). Beattie and colleagues performed a single-center cohort analysis of over 10,000 patients undergoing major non-cardiac surgery; an elevated postoperative troponin I > 0.07 ng/mL, found in 11% of patients, was independently associated with 30-day postoperative mortality (2.1% overall, 24.3% with elevated postoperative troponin) with incremental increases of troponin strengthening this
Van Waes and colleagues found an elevated troponin I (> 0.06 ng/mL) in 19% of patients undergoing intermediate or high-risk non-cardiac surgery with all-cause 30-day mortality of 3% (13). Elevated postoperative troponin again independently predicted 30-day mortality after non-cardiac surgery although myocardial infarction was only diagnosed in 10 (0.6%) patients.

The VISION study also demonstrated that even smaller elevations in troponin I (>0.01 ng/mL) present in 11.7% of patients were associated with adverse outcomes. Features required to meet the Universal Definition of myocardial infarction, such as ECG changes or ischemic symptoms were often absent. Routine postoperative troponin monitoring was recommended as the majority of myocardial injury and troponin release occurred in the first 72 postoperative hours (14, 15). The recent BASEL-PMI study supported these findings in a higher risk cohort (patients over 65 years of age or over 45 with a history of vascular disease; perioperative troponin elevation was associated with higher mortality and was largely asymptomatic (16). Low-risk patients, comprising 56% of the VISION cohort and 50% of patients stud-
ied by Beattie et al were at low risk of adverse outcomes regardless of postoperative troponin. Of note, both VISION and BASEL-PMI report high non-cardiovascular mortality at 30-days (45% vs 55% (VISION), 41% vs 59% (BASEL-PMI) and 12-months (32% vs 68% (BASEL-PMI)).

Our cohort experienced comparable 30-day mortality rates (2.8%) to the above studies; there is no published 6-month mortality data for comparison. Incidence of an elevated postoperative troponin was higher (37% vs 11.6% in VISION/11% in Beattie et al./19% in Van Waes et al.); the low threshold combined with the higher-sensitivity troponin assay used will increase detection rates and recent analysis of 21,842 patients by the VISION investigators using a fifth-generation high-sensitivity troponin assay did demonstrate higher detection rates of postoperative troponin exceeding the 99th centile (35.5% vs 19% in our study) (17). Significantly raised troponins > 1000 ng/L were less common in VISION compared to our study (0.2% vs 3.4%) reflecting the lower risk patient cohort studied but experienced similarly high 30-day mortality (29.6% vs 31%). The low proportion of minor surgery and high proportion of emergency admission compared to the original VISION study (9% vs 41% and 40% vs 14% respectively) and high-sensitivity troponin VISION study (9% vs 36% and 40% vs 7.4% respectively) reflects our institution’s role as a major trauma center and will select a higher surgical risk population, potentially increasing the incidence and prognostic value of an elevated postoperative troponin.

Our cohort experienced significantly higher rates of sepsis compared to the original VISION (20% vs 5.4%), likely due to the differing definitions between the two studies. The VISION trial definition of sepsis selected patients more likely to have more severe sepsis with hemodynamic compromise. Our definition, based on blood results, positive blood cultures and clinical documentation instead of hemodynamic parameters, may include less severe infective states hence the higher incidence. However, the systemic inflammatory response associated will still be present along the possibility of associated elevations in troponin and we note that the presence of troponin significantly increases 6-month mortality in all cohorts compared to patients with sepsis but a normal post-operative troponin.

**MINS – Multiple Pathophysiological Processes?**

The detailed patient-level analysis permitted by our smaller study suggests that postoperative troponin elevations may represent a complex mix of multiple pathophysiological processes rather than a single disease state.

Troponin elevation may occur due to type 1 myocardial infarctions, triggered by acute coro-
Table 3. Incidence and Mortality by Peak Postoperative Troponin.

| Postoperative troponin | Number of patients | 30-day mortality | 6-month mortality |
|------------------------|--------------------|------------------|------------------|
| < 17 ng/L              | 245 (63%)          | 3 / 245 (0.1%)   | 8 / 245 (3.3%)   |
| 17 – 40 ng/L           | 69 (18%)           | 2 / 69 (2.9%)    | 11 / 69 (16%)    |
| 40 – 1000 ng/L         | 60 (16%)           | 2 / 60 (3.3%)    | 7 / 60 (12%)     |
| >1000 ng/L             | 13 (3.4%)          | 4 / 13 (31%)     | 6 / 13 (46%)     |

| % Troponin change preop to peak postop | Number of patients | 30-day mortality | 6-month mortality |
|---------------------------------------|--------------------|------------------|------------------|
| < 20%                                 | 242 (63%)          | 2 / 242 (0.8%)   | 7 / 242 (2.9%)   |
| 20 – 100%                             | 49 (13%)           | 2 / 49 (4.1%)    | 10 / 49 (20%)    |
| 100 – 1000%                           | 69 (18%)           | 2 / 69 (2.9%)    | 8 / 69 (12%)     |
| >1000%                                | 27 (7.0%)          | 5 / 27 (19%)     | 7 / 27 (26%)     |

| Type of event | Falling troponin trend (of total number events) | 30-day mortality (with falling troponin trend) | 6-month mortality (with falling troponin trend) |
|--------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| All troponin elevations (i.e. > 17 ng/L) | 20 / 141 (14%) | 1 / 20 (5%) | 7 / 20 (35%) |
| Primary troponin elevations | 12 / 69 (17%) | 0 / 12 | 2 / 12 (17%) |
| Secondary troponin elevations | 8 / 72 (11%) | 1 / 8 (13%) | 5 / 8 (60%) |
| Associated with sepsis | 5 / 55 (9.1%) | 1 / 5 (20%) | 3 / 5 (60%) |
| Associated with bleeding | 1 / 14 (7.1%) | 0 / 1 (0%) | 1 / 1 (100%) |
| Associated with tachycardia | 2 / 3 (67%) | 0 / 2 (0%) | 1 / 3 (33%) |
| No troponin elevation | 17 / 246 (6.9%) | 0 / 17 (0%) | 1 / 17 (5.9%) |

The % change between preoperative and postoperative level and associated pathophysiology with a falling troponin trend.
Table 4. Univariate Analysis of Variables for Associations with 30-day and 6-month Mortality.

| Variables                                      | 30-day Mortality | 6-month Mortality |
|------------------------------------------------|------------------|-------------------|
|                                                | Hazard Ratio     | P value           | Hazard Ratio | P value |
| Age                                            |                  |                   |              |         |
| 45 - 65                                        | 1 (Reference)    |                   | 1 (Reference)|         |
| 65 – 74                                        | 2.294 (0.445 – 11.823) | P = 0.321 | 1.880 (0.759 – 0.466) | P = 0.173 |
| >75                                            | 2.030 (0.372 – 11.082) | P = 0.414 | 2.652 (1.108 – 6.350) | P = 0.029 |
| Male vs. Female                                | 1.229 (0.375 – 4.029) | P = 0.733 | 0.778 (0.413 – 1.466) | P = 0.438 |
| Abnormal renal function                        |                  |                   |              |         |
| eGFR < 60                                      | 7.338 (1.947 – 27.661) | P = 0.003 | 4.734 (2.482 – 9.026) | P < 0.001 |
| eGFR < 50                                      | 3.498 (1.067 – 11.462) | P = 0.039 | 4.789 (2.555 – 8.976) | P < 0.001 |
| eGFR < 40                                      | 5.869 (1.791 – 19.233) | P = 0.003 | 6.030 (3.200 – 11.363) | P < 0.001 |
| eGFR < 30                                      | 4.157 (1.103 – 15.671) | P = 0.035 | 3.562 (1.691 – 7.505) | P = 0.001 |
| eGFR < 20                                      | 4.207 (0.909 – 19.473) | P = 0.066 | 4.599 (2.029 – 10.424) | P < 0.001 |
| Abnormal renal function with elevated postoperative troponin | 6.725 (2.052 – 22.041) | P = 0.002 | 7.430 (3.595 – 13.957) | P < 0.001 |
| Emergency admission                            | 19.9 (2.55 – 155) | P = 0.004 | 6.350 (3.081 – 12.982) | P < 0.001 |
| Emergency admission with elevated post-operative troponin | 10.034 (2.733 – 38.845) | P < 0.001 | 6.986 (3.662 – 13.325) | P < 0.001 |
| Sepsis                                         | 11.375 (3.017 – 42.880) | P < 0.001 | 6.255 (3.319 – 11.790) | P < 0.001 |
| Sepsis with elevated post-operative troponin    | 15.596 (4.243 – 60.308) | P < 0.001 | 7.856 (4.188 – 14.739) | P < 0.001 |
| Bleeding with elevated post-operative troponin  | 1.485 (0.190 – 11.596) | P = 0.706 | 3.412 (1.502 – 7.708) | p = 0.003 |
| Tachycardia                                    | 0                | P = 0.799 | 2.224 (0.305 – 16.198) | P = 0.430 |
| Tachycardia with elevated post-operative troponin | 0                | P = 0.820 | 4.196 (0.576 – 30.585) | P = 0.157 |
| All post-operative troponin elevations         | 4.695 (1.246 – 17.7) | P = 0.022 | 6.275 (2.979 – 13.219) | P < 0.001 |
| Primary post-operative troponin elevation      | 0.036 (0 – 26.807) | P = 0.325 | 0.802 (0.336 – 1.914) | P = 0.619 |

We note that the CCS guidelines recommend postoperative troponin monitoring in patients with “significant obstructive cardiac disease” (5); this definition includes severe obstructive valvular disease, hypertrophic cardiomyopathy, and pulmonary hypertension, all of which will have detectable cardiac troponin through differing non-cardiac mechanisms. To further complicate matters, sepsis and the associated systemic inflammatory response (considered a “non-ischemic" mechanism by the MINS criteria) may trigger acute plaque rupture events (33, 34).

Trials investigating therapeutic options targeting antiplatelet and anti-ischemic medications on the basis that such events represent type 1 ischemia have been negative to date (35, 36). The MANAGE trial has shown treatment with dabigatran reduces major vascular events but demonstrated no reduction in vascular or all-cause mortality with event reduction driven by less non-hemorrhagic stroke rather than the myocardial ischemic event (37). Ausset et al. noted that optimizing factors associated with type 2 myocardial injury (hypoxemia, anemia, hypotension, tachycardia, and hyperglycemia) resulted in a 56% reduction of postoperative myocardial injury and a 75% reduction in MACE at 1 year (38).

It is not known whether elevated postoperative troponin events are more common in patients with a known obstructive coronary disease, nor whether it is worth investigating patients for...
this possibility once they are stable enough postoperatively for evaluation. The investigation into the coronary anatomy of patients, either invasively or using CT coronary angiography, may determine the underlying incidence of unstable or significant coronary disease that is present in these patients and allow nuanced interpretation of these rises in troponin.

**Strengths**

Our sample represents an all-comer real-world population with few exclusion criteria. All suitable patients were potentially included in the study regardless of past medical history, pre-test likelihood of a positive result or nature of surgery performed.

**Limitations**

Our sample is much smaller than the VISION study. Data collection and troponin measurement for elective patients required a fixed operative date to trigger the process; any patients who canceled, changed their date or whose operation as delayed were lost. The retrospective nature of screening for emergency operations made data collection easier; however, patients presenting at a weekend were not included as the troponins could not be added on within 24 hours of admission and as such were not included. As such, our sample is a non-consecutive convenience sample.

As our troponin assays were performed on routinely collected blood samples, troponins were not recorded at precise intervals following surgery. Our assessment of troponin trends uses the assumption that troponins < 17 ng/L have the value of 8 ng/L. This prevents accurate calculation of trends for small values; as such, we did not include troponin trend in the univariate or multivariate analysis.

**CONCLUSION**

Postoperative high-sensitive troponins are associated with 30-day and 6-month mortality following non-cardiac surgery. However the picture is complex, and using troponin in isolation to guide treatment would ignore significant non-vascular pathophysiological processes that carry their own risk of mortality and require alternative therapeutic interventions. Therapeutic maneuvers aimed at atherosclerotic disease or thrombosis may have limited benefit and better methods are needed to determine which patients may benefit from conventional secondary prevention strategies. Strategies to avoid and manage both infection and renal dysfunction may have an important role to play in reducing the high mortality of these patients.

This study was supported by grants from the the Regional Innovation Fund of NHS England and internally by the South Tays NHS Foundation Trust Research and Development Fund. The authors have no other potential conflicts of interest for this work.

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