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Postoperative troponin measurement as a screening tool for adverse cardiac events in adult patients undergoing moderate or major non-cardiac surgery

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Abstract

Elevated troponin levels within three days of surgery are strongly linked to major adverse cardiac events (MACE). However, the value of screening with troponin measurements is controversial. The extent to which this is done in routine practice is uncertain. We examined the medical records of all patients ≥45 years of age undergoing moderate or major non-cardiac surgery in our tertiary referral hospital over a six-month period. We determined how many patients had a troponin (TnT) measurement recorded in the first three days postoperatively, how many of these were abnormal, and the occurrence of MACE within 30 days. Two thousand and two hundred patients underwent 2,577 operations that met the study criteria. A postoperative TnT was measured after 4.5% of operations. Thirty-eight percent of patients with a recorded TnT measurement, and 44% of those with an abnormal measurement, experienced a MACE within 30 days. The sensitivity of an abnormal TnT to detect MACE was 86%. The specificity was low at 32% with a false positive rate of 56%. Patients with an abnormal TnT result had an increased risk of MACE (23%). The 'number needed to measure' to detect one patient with MACE was 4.4. In our institution, postoperative TnT levels were rarely measured and were used as a diagnostic rather than as a screening tool. The high false positive rate for MACE prediction limits its potential value as a screening tool. The test could be considered useful if it leads to further investigation, and may be best considered as one component of a multivariate approach to cardiac risk evaluation and diagnosis.

Keywords

surgery, troponin, measurement, screening, tool, adverse, cardiac, events, adult, patients, undergoing, moderate, major, non-cardiac, postoperative

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Postoperative troponin measurement as a screening tool for adverse cardiac events in adult patients undergoing moderate or major non-cardiac surgery

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Summary

Elevated troponin levels within three days of surgery are strongly linked to major adverse cardiac events (MACE). However the value of screening with troponin measurements is controversial. The extent to which this is done in routine practice is uncertain. We examined the medical records of all patients ≥45 years of age undergoing moderate or major non-cardiac surgery in our tertiary referral hospital over a six-month period. We determined how many patients had a troponin (TnT) measurement recorded in the first three days postoperatively, how many of these were abnormal, and the occurrence of MACE within 30 days. Two thousand and two hundred patients underwent 2,577 operations that met the study criteria. A postoperative TnT was measured after 4.5% of operations. Thirty-eight percent of patients with a recorded TnT measurement, and 44% of those with an abnormal measurement, experienced a MACE within 30 days. The sensitivity of an abnormal TnT to detect MACE was 86%. The specificity was low at 32% with a false positive rate of 56%. Patients with an abnormal TnT result had an increased risk of MACE (23%). The 'number needed to measure' to detect one patient with MACE was 4.4. In our institution, postoperative TnT levels were rarely measured and were used as a diagnostic rather than as a screening tool. The high false positive rate for MACE prediction limits its potential value as a screening tool. The test could be considered useful if it leads to further investigation, and may be best considered as one component of a multivariate approach to cardiac risk evaluation and diagnosis.

Key Words: troponin, postoperative complications, cardiovascular diseases, perioperative medicine

Adverse cardiac events after non-cardiac surgery are relatively common. One in twelve patients aged 45 and over sustains an ischaemic heart injury after non-cardiac surgery, and two-thirds of these events are asymptomatic[1-4]. Symptomatic and asymptomatic myocardial infarctions carry a similar risk of mortality[1]. Cardiac causes are responsible for up to half of deaths occurring within 30 days postoperatively[1,2,5]. They are also associated with substantially increased rates of complications, prolonged hospitalisation and increased costs[1].

Diagnosis of postoperative myocardial ischaemia is not straightforward and is often performed by detection of raised serum troponin (TnT) levels[2]. The availability of high-sensitivity fifth generation assays has further improved the specificity and sensitivity of this test[6]. Elevated TnT levels within three postoperative days are strongly linked to short- and longer-term mortality[5,7]. Without monitoring of perioperative TnT levels during the first few days after surgery in patients with known vascular disease or risk factors, the majority of myocardial infarctions and injuries will be undetected[1]. Early detection of myocardial ischaemia allows for rapid management and potentially improved postoperative outcomes[1,8-10].

One previous report noted that in inpatients ≥45 years of age having non-cardiac surgery, the number necessary to screen to detect myocardial injury that would otherwise be missed, is only about 15 patients[2]. One international collaboration recommends routine monitoring of cardiac biomarkers in high-risk patients after major surgery, with TnT as the preferred marker[11]. Others have suggested that it is not valuable as a screening tool[12]. TnT measurement is not currently established as a standard postoperative screening measure.

We performed a retrospective audit to explore how TnT measurements were used in routine clinical practice in our institution. We first determined how many patients aged ≥45 years undergoing moderate to major non-cardiac surgery who stayed at least one postoperative night in our tertiary referral hospital had a TnT measurement recorded in the first three days postoperatively. We then explored the utility of this measurement in the prediction of major adverse cardiac events (MACE) at 30 days postoperatively.

Methods

This retrospective audit was registered as a quality improvement project with The Wollongong Hospital Clinical

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Governance Unit (4/5/2016). We examined the electronic medical records of all surgical patients ≥45 years of age who spent at least one night in hospital postoperatively in a six-month study period from April to September 2016. Both scheduled (elective) and unscheduled (emergency) procedures were included. The Wollongong Hospital is an outer metropolitan tertiary referral centre with 500 beds. Approximately 12,500 operations are performed each year with all types of surgery excluding cardiothoracic and complex paediatric procedures. The electronic medical record includes complete information on most aspects of inpatient care including pathology, radiology, consultations, perioperative records, ward progress records and discharge information.

Data were extracted for all study patients who had at least one measurement of high-sensitivity TnT (hs-TnT) on postoperative days 0 to 3. We followed local New South Wales (NSW) pathology guidelines that defined hs-TnT <14.0 ng/l as normal, with 14.0 ng/l and above as abnormal. Electronic medical records (eMR) were accessed through PowerChart® (Cerner, North Sydney, NSW) and manually searched to obtain demographic and outcome data on each patient. The clinical reasoning behind the ordering of any individual TnT measurement was not recorded in the eMR, so could not be audited.

MACE within 30 days of surgery was defined according to previous literature to include cardiac arrest, acute coronary syndrome (ACS), new onset heart failure or pulmonary oedema, new arrhythmia, cerebrovascular accident (CVA), and death due to a vascular cause[5,13]. All deaths due to non-vascular causes were also recorded, as were unplanned postoperative intensive care unit (ICU) admissions. Data were entered into Microsoft Excel (Microsoft® Office Professional Plus 2013, Redmond, WA, USA) and analyses were computed using IBM SPSS 24.0 (IBM, Armonk, NY, USA).

The statistical approach to determining the predictive value of a marker depends on the purpose of the test and the clinical context in which it is performed[14]. If the purpose of a test is to screen for a disease state (MACE in this situation), the test should have a high sensitivity so that few true cases are missed. If the purpose is to make a diagnosis, then a test should have a high degree of specificity, so that few patients are misclassified as having the disease. A trade-off between sensitivity and specificity always exists. The acceptability of the balance between a high sensitivity and a high false positive rate depends on the clinical context[14]. In our situation, a high rate of false positives would mean that more patients would be concerned about and investigated for MACE than was necessary, whereas a high false negative rate would suggest that a number of patients would suffer missed or delayed diagnosis and intervention. It has been noted that the best prediction model for an individual patient is likely to involve multiple variables rather than a single test, and that to be useful, any single test should improve the predictive ability of established models[15].

Results

A total of 6,372 operations were performed in the six-month study period. Of these, 2,577 operations were performed in 2,200 patients aged ≥45 years who stayed in hospital for at least one postoperative night. Of these, 116 patients (5.3%) had at least one TnT measurement on days 0 to 3 postoperatively. This cohort of 116 patients had a total of 121 operations in the study period. The 116 TnT measurements occurred after 4.5% of the 2,577 operations (Table 1).

Eighty-seven of the initial postoperative TnT levels were abnormal (75%), with 29 (24%) within the normal range. In the total of 116 patients, 44 (38%) experienced a MACE within 30 days of surgery (Table 2). Data from patients who underwent more than one operation were analysed in relation to the first operation. The large majority of MACE events (38/44, 86%) occurred in the patients with an abnormal TnT. The incidence of MACE in the abnormal TnT group was twice that of the normal TnT group (44% versus

Table 1

Demographics of patients with troponin measurements

	Overall	Abnormal TnT	Normal TnT
Age, mean (SD)	73.1 (11.1)	74.7 (11.2)	68.2 (9.5)
Gender, n (%)	F 55 (47.4%) M 61 (52.6%)	F 42 (48.3%) M 45 (51.7%)	F 13 (44.8%) M 16 (55.2%)
Emerg v elective, n (%)	Emerg 78 (64.5%) Elective 43 (35.5%)	Emerg 62 (67.4%) Elective 30 (32.6%)	Emerg 16 (55.2%) Elective 13 (44.8%)
Procedure type, n (%)			
Vascular	19 (15.7%)	14	5
General	31 (25.6%)	27	4
HNENT	8 (6.6%)	8	0
Neurosurgery	6 (5.0%)	3	3
Orthopaedic	35 (28.9%)	24	11
Other	22 (18.2%)	16	6

TnT, troponin; Emerg, emergency operation; SD, standard deviation; HNENT, head and neck and ear, nose, and throat surgery.

Table 2

Frequencies of abnormal troponins and major adverse cardiac events

	MACE		
TnT	Yes	No	Total
Abnormal	38	49	87
Normal	6	23	29
Total	44	72	116

TnT, troponin; MACE, major adverse cardiac event.

Table 3

Analysis of troponin levels and major cardiac events

Index	Value	Interpretation
Sensitivity	0.864	86% of patients with a MACE were correctly detected by the TnT.
Specificity	0.319	32% of patients without a MACE were correctly labelled by the TnT.
Positive predictive value	0.437	Of those labelled by the TnT as "abnormal", 44% had a MACE. 56% of positive TnT results were false positives.
Negative predictive value	0.793	Of those labelled by the TnT as "normal", 79% did not have a MACE. 21% of negative TnT results were false negatives.
Likelihood ratio^{+}	1.269	A positive TnT result (i.e., labelled as "abnormal") was slightly more likely in those who had a MACE.
Likelihood ratio^{-}	2.343	A negative TnT result (i.e., labelled as "normal") was two times as likely to have come from a person without a MACE.
Odds ratio	2.97	The odds of having a MACE were 3 times higher with an abnormal TnT.
Risk difference	0.23	Patients with a positive TnT result had an increased risk for MACE of 23%.
Numbers needed to screen	4.4	4.4 patients must be labelled by the TnT as "abnormal" to detect 1 patient with a MACE.

TnT, troponin; MACE, major adverse cardiac event.

21%). Table 3 presents the predictive statistical analysis. Patients with an abnormal TnT result had an increased risk of MACE (23%) with a number needed to measure to predict MACE of 4.4 patients.

A receiver operating characteristic analysis was performed. This showed an area under the curve of 0.699 (95% confidence interval, 0.597 to 0.801). The accuracy of tests with areas under the curve between 0.50 and 0.70 is generally considered as low; between 0.70 and 0.90 as moderate; and over 0.90 as high[16].

A total of 62 MACEs were found in 44 patients, with many individuals experiencing more than one type of MACE (Table 4). Furthermore, 20 of the 25 (80%) unplanned postoperative ICU admissions in the study patients were in those with abnormal TnT levels. Eight deaths occurred within 30 days of surgery in the study population. All deaths occurred in patients with an abnormal TnT level, and all occurred in patients who presented for emergency surgery.

Table 4

Types and frequencies of major cardiac adverse events

Event	Abnormal TnT n (%)	Normal TnT n (%)	Total
ACS	16 (100%)	0	16
Acute PO	8 (100%)	0	8
New CCF	1 (100%)	0	1
New arrhythmia	22 (85%)	4 (15%)	26
Cardiac arrest	5 (83%)	1 (17%)	6
CVA	4 (80%)	1 (20%)	5

Note: more than one type of MACE in an individual patient was common. MACE, major adverse cardiac event, TnT, troponin; ACS, acute coronary syndrome; PO, pulmonary oedema; CCF, congestive cardiac failure; CVA, cerebrovascular accident.

Discussion

In a large cohort of patients aged ≥45 years having moderate or major surgery in our institution, TnT measurements were rarely performed. When performed, 75% of tests were abnormal. The low frequency and high detection rates suggest that TnT measurements were being performed more as a diagnostic than as a screening tool. Predictive analysis suggests at best a moderate value for abnormal TnT as a tool to predict postoperative MACE. The test had a high sensitivity of 86% but its utility based on our results would be limited mainly by the low specificity, with a high false positive rate of 56% and low positive predictive value of 44%.

The 116 patients in this study who had a TnT measured were presumably a higher risk group than the rest of the sample in whom measurements were not performed. We were unable to assess the reasoning behind TnT requests but postulate that they were at least to some degree performed according to clinical indicators at the discretion of the treating teams. The type of clinical findings that triggered a TnT measurement could not be determined. Our findings therefore represent the potential utility of TnT measurements in a group with postoperative suspicion of myocardial ischaemia based on other parameters. For patients without this clinical suspicion, the incidence of postoperative ischaemia is likely to be lower and the TnT test positive and negative predictive values are likely to be less convincing.

The high sensitivity of the test (86%) is encouraging and is close to that suggested for screening tools. Patients with a high TnT had double the incidence of MACE compared to those with a normal TnT level. Almost half of the patients with an abnormal TnT level suffered at least one type of MACE. Eighty percent of unplanned ICU admissions and all deaths occurred in the abnormal TnT group of patients. This approach to the data suggests that identifying a group of patients at higher risk may be valuable if an abnormal TnT level results in closer medical observation and treatment.

The optimal treatment to improve patient outcomes after postoperative myocardial ischaemia is not yet established. Treatment options include aspirin, beta-blockers, angiotensin converting enzyme inhibitor drugs, statins, early reperfusion strategies, and more comprehensive evaluation such as angiography and echocardiography, but definitive outcome studies are awaited[2,8]. Lack of established treatment guidelines may limit the usefulness of early identification.

In the real clinical world, aggressive treatment is unlikely to be initiated after a single abnormal level without other confirming factors such as serial measurements or other abnormal test results. TnT measurement may be best considered as one part of a multivariate risk prediction model, rather than as a single measure with a definitive binary outcome. Other potential benefits of early identification of abnormal TnT levels include alerting patients to their risk of future myocardial events, improving hypertension control, and taking advantage of a teachable moment to promote lifestyle changes, including smoking cessation[2].

The question of whether TnT measurements should be performed in higher risk surgical populations as a routine screening tool or only as a diagnostic tool has not yet been conclusively answered. The most recent American College of Cardiology/American Heart Association Guideline recommends measurement of postoperative TnT levels only in the setting of signs or symptoms suggestive of myocardial ischaemia[12]. The current study suggests that clinical practice in our institution reflects this guideline. Postoperative screening in high-risk patients without signs or symptoms suggestive of myocardial ischaemia is considered to have uncertain value due to the absence of validated treatment strategies to attenuate the risk of an abnormal TnT[8]. Routine postoperative screening for directing perioperative management is not recommended in this guideline. Obtaining an electrocardiogram (ECG) was given the same weighting as performing TnT measurements[12].

On the other hand, abnormal postoperative TnT levels have been found to be an independent predictive measure for both MACE and mortality at various timepoints from 30 days to three years and in various surgical populations in an increasing number of studies[5,7,17-23]. Most of these studies report hazard ratios, odds ratios and logistic regression analysis as their method of risk prediction. There have been several recent reviews supporting routine TnT measurement postoperatively and the field now contains a strong body of evidence[1,2,13]. Without monitoring of perioperative TnT levels during the first few days after surgery in patients with known vascular disease or risk factors, the majority of myocardial infarctions and injuries will be undetected[1]. A troponin measurement, when added to other postoperative blood tests, currently costs A$19.69 in our institution. At this cost, with a number needed to measure of 4.4 patients, a decision to use the test as a screening tool could well be considered to be cost-effective and beneficial to individual patients. On the other hand, it could lead to unnecessary concern and unnecessary further investigations for many patients if not interpreted correctly.

The background prevalence of MACE and the definition of a 'high-risk' patient are clearly important factors in this discussion. Some authorities consider a background incidence of myocardial injury of 8% in patients aged over 45 having moderate or major surgery sufficient to consider the entirety of this group as high-risk, particularly as this is such an important clinical problem[2]. Others require the presence of other cardiac risk factors, or signs and symptoms, to define a high-risk group. Thirty-eight percent of our population with a measured TnT experienced a MACE. It could be reasonably supposed that clinical suspicion of myocardial injury selected a higher risk cohort amongst our patient sample. As a theoretical calculation, if our population in whom a TnT was not measured, numbering 2,084 individuals, had experienced a rate of MACE of the background 8% figure, then potentially 166 patients in the unmeasured group were at risk. A broader use of TnT measurements may have detected more of these patients at an early stage.

The decision about the manner in which to use the test revolves around the intended purpose, the clinical context, and the balance between false positives and negatives. One could argue clinically that a high detection rate is the priority, as treatment is only likely to occur after other more confirmatory findings and because myocardial ischaemia is a very important patient event. Our study suggests that almost half of patients with a high postoperative TnT in a high-risk group with clinical suspicion will have a MACE. The VISION study reported that inclusion of the peak TnT in the first three days postoperatively added incremental prognostic value to predict 30-day mortality compared to models not including TnT measurement[5]. The monetary cost of the test is low. Clinical concerns including the time and cost of investigating false positives need to be considered and balanced against the risk of missing or delaying diagnosis and intervention.

This is a single-centre study, and although large numbers were included, it may not be representative of or generalisable to other institutions. The retrospective nature means that we could not influence patient events or outcomes in any way. Outcome timepoints of longer than 30 days may yield further information and be even more relevant to patients. We did not collect detailed data on the vast majority of surgical patients in this period for whom a TnT was not measured. Therefore, we cannot comment on the rate of MACE in the rest of the surgical population. Other variables that could theoretically be important in predicting outcomes include preoperative factors such as presence of cardiovascular comorbidities and type of medications, intraoperative factors such as duration and blood loss, and postoperative factors such as level of care[1]. Our study was not designed or able to investigate the potential impact of such other variables, but these are important considerations for overall risk reduction.

Conclusion

In conclusion, in this large pragmatic observational study, we investigated the actual practice of postoperative TnT measurement in a large tertiary referral hospital in Australia.

We report that in our institution, this simple and inexpensive measure is currently being used as a diagnostic rather than as a screening tool. We confirm that in the setting of postoperative surgical patients with a clinical suspicion of myocardial ischaemia, TnT measurement can identify patients at high risk of significantly poor outcomes, including death, with a number needed to measure of 4.4. Our data suggest that some of these patients may be missed if screening measurements are not performed. The cost of the test is low, and the cost of missing the diagnosis of postoperative myocardial ischaemia is high. Predictive statistical analyses suggest a low–moderate value of an elevated TnT to predict MACE in this situation. It may have some utility in a high-risk population depending on the definition of high risk and the clinical context. The test could be considered useful as an early warning sign if it leads to further investigation before aggressive treatment is undertaken and therefore may be best considered as one component of a multivariate approach to cardiac risk evaluation.

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