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Original research article

The relationship between troponin elevations and non-cardiac surgery

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Abstract

Introduction: Even slight increases in preoperative troponin levels have been demonstrated to be associated with worse outcomes. On the other hand, there are currently insufficient data on the connection between an elevated troponin level and the appropriate time for surgery.

Methods: We carried up a retrospective cohort analysis at a single institution on a total of 4575 patients, each of whom had a troponin measurement taken within the 30 days prior to undergoing a noncardiac surgical procedure. Subjects who had detectable levels of troponin were categorised into one of three terciles according to the magnitude of the value as well as the amount of time that had passed since this value before the surgery. Using bivariable and multivariable logistic regression, these 9 cohorts were compared with the group of patients whose preoperative troponin levels were undetectable. The comparison was made for those who were receiving non-emergency surgeries.

Results: In the group whose levels of troponin could not be detected, the thirty-day death rate was 4.7%, but it rose steadily with increasing concentrations, reaching rates of 8.9%, 12.7%, and 12.7% in the low, medium, and high tercile groups, respectively. Those patients who had the highest troponin levels and the shortest delay between the measurement and surgery had the highest unadjusted risk of 30-day death (odds ratio: 4.497; 95% confidence interval: 2.058-9.825). After taking into account the characteristics of the subjects, the association between troponin and 30-day mortality maintained in several groups, even those composed of people whose troponin levels were within the normal range.

Conclusions: Greater preoperative levels of cardiac troponin I were related with increased postoperative mortality, while persons with minor preoperative troponin increases who waited longer before undergoing surgery appeared to have a reduced risk of dying after surgery. There is a pressing need for prospective research to evaluate whether or not postponing surgery in individuals who have elevated preoperative troponin levels results in better postoperative outcomes.

Keywords: Preoperative, troponin elevations, postoperative mortality, non-cardiac surgery

Introduction

Damage to cells can be caused by inadequate perfusion of the coronary arteries, which can then lead to the release of intracellular components into the circulation [1-3]. Some of these proteins, such as cardiac troponin (cTn), have isoforms that are distinct from those present in the muscles of the body's other organs. cTn is an essential component in the diagnosis of acute coronary syndrome due to the high degree of specificity it possesses (ACS). In addition, the degree to which cTn is elevated in ACS has been shown to have a correlation with the likelihood of short-term death [4]. Patients who are considered to be at risk have their cTn concentrations evaluated frequently due to the significance of early identification and therapy. As the sensitivity of clinically applicable assays continues to increase, it is becoming increasingly apparent that a significant number of patients, even in the absence of ACS, have serum cTn levels that are low but nonetheless detectable. Elevations of cTn that are indicative of cardiac strain or injury, but are not associated with coronary atherosclerosis, can be caused by a wide variety of factors [5, 6]. These factors include per myocarditis, endocarditis, takotsubo cardiomyopathy, radiofrequency catheter ablation, cardiac contusion, strenuous exercise and sympathomimetic drugs, among others. These elevations are related with unfavourable outcomes, despite the fact that they are not created by myocardial ischemia or ACS. This fact is established by a number of studies, despite the fact that it is sometimes dismissed as nothing more than a troponin leak [7]. Although having a preoperative myocardial infarction is a known risk factor for adverse outcomes, there is less information available on patients who have a preoperative elevation of cTn that is not associated with ACS. Since of this, physicians are placed in a difficult position because not only have appropriate therapy techniques not been determined, but it is also difficult to quantify the risk of moving through with surgery [8]. This condition creates a perilous situation for medical professionals. For instance, even though a preoperative cTnT level of more than 14 ng/L was associated with increased postoperative mortality, we do not know

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whether the risk of postoperative mortality is proportional to the magnitude of cTn elevation, whether there is a risk for smaller elevations, or whether this risk decreases with longer time between peak cTn measurement and the time of surgery [9, 10]. This is because we do not know whether the risk decreases with longer time between peak cTn measurement and the time In order to find the answers to these issues, we carried out a retrospective cohort research on patients who were due to have noncardiac surgery and who had cTnI testing done before to the operation. In addition to looking at the influence of concentration, we also looked at the amount of time that passed between the highest levels of cTnI and the surgery. We expected that an increased risk of postoperative death was related with both high cTnI levels and a short delay between the peak level and surgery [11, 12].

Methods and Subjects

This retrospective study was given the go-ahead, and the requirement for informed consent was eliminated because the only data included had been deidentified and obtained in the past. Patients who were at least 18 years old and who had a cTnI measurement done at the Department of General Surgery, CAIMS, Karimnagar, Telangana, India within the preceding 30 days of a noncardiac surgical operation were considered for inclusion in the study (Figure 1). Individuals who had undergone a preoperative percutaneous coronary intervention were identified with the help of current procedural nomenclature codes, and this group was omitted from the analysis. The time frame that was taken into consideration was from July 2022 to June 2023.

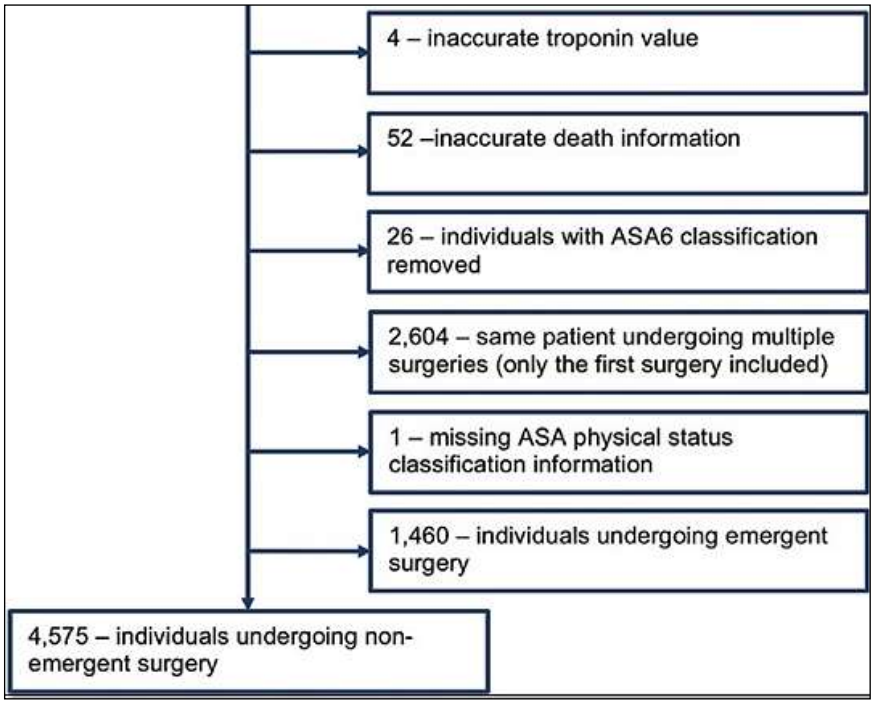

Fig 1: Diagram showing population origins. The original list of eligible participants was identified by looking for non-cardiac surgical cases with a troponin level assessed 30 days before the surgery

The start date was selected as the first day on which all the data in our electronic medical record were dependable, and the end date as the final day before submission. The controlling service had the discretion to measure preoperative cTnI concentration based on clinical considerations because this research was retrospective in nature. Chest discomfort, hemodynamic instability, and irregular electrocardiograms are typical warning signs. Our institution measures cTnI and reports readings as low as 0.10 ng/mL. The reference range's upper limit of 0.30 ng/mL remained consistent over the course of the investigation. The hospital laboratory does not report decreased troponin levels, despite the fact that this assay can find them. Instead, it is reported that they went undiscovered. Using terciles of cTnI concentrations and terciles of time between this measurement and surgery, subjects with identified cTnI concentrations were grouped into 9 cohorts. The controls were patients with undetectable cTnI levels. Patients who received a nonemergent, noncardiac surgical procedure and had their preoperative troponin level assessed during the previous 30 days were included in the research. Emergent surgical operations were excluded from the analysis. Additionally, data on the subjects' age, sex, ASA physical status, length of surgery, and a number of laboratory values were gathered (bicarbonate, creatinine, total bilirubin, lactate, and brain natriuretic peptide). Body mass index and laboratory results both had missing data. The main outcome of this study was 30-day postoperative mortality, which was imputed using IVE ware version 2.0, with 10 iterations per imputation.

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Statistics

The data were reported using means and standard deviations for features that followed a normal distribution, and the median and interquartile range for variables that did not follow a normal distribution. For the purpose of determining whether or not there was a shift in risk among the various cohorts, the Cochran-Armitage trend test was carried out. The incidence of 30-day mortality was compared across groups using bivariable and multivariable logistic regressions. This was done in order to account for the differences in risk variables. In the multivariable models, every piece of preoperative patient information that was available (Table 1) was factored in, regardless of whether or not it had a univariable connection with 30-day mortality. When describing the magnitude and precision of relationships, the odds ratio (OR) and the 95% confidence interval (CI) were also useful tools. In each and every statistical test, the threshold for determining statistical significance was set at a P value of less than 0.05. R Core Team was utilised in order to carry out the statistical analysis.

Table 1: Patient Demographics Prior to Surgery

Sr. No.	Parameters	*n* (%)
1.	30-day mortality	281 (6.1)
2.	Male	2531 (55.3)
3.	Troponin >0.10 ng/mL	986 (21.6)
	Procedure type	
4.	General	1014 (22.2)
5.	Neurosurgery	488 (10.7)
6.	Obstetrics/gynecology	106 (2.3)
7.	Oral/maxillofacial	237 (5.2)
8.	Orthopedics	735 (16.1)
9.	Otolaryngology	387 (8.5)
10.	Plastics	209 (4.6)
11.	Thoracic	341 (7.5)
12.	Transplant	267 (5.8)
13.	Urology	340 (7.4)
14.	Vascular	451 (9.9)
15.	Age (y)	63 (52, 73)

Results

During the course of the trial, a total of 4575 individuals had blood obtained within 30 days prior to a noncardiac surgical operation to determine their cTnI levels. The majority of them were of middle age, and they suffered from a wide range of co-morbid conditions (Table 1). 986 of these patients had cTnI levels that were higher than 0.10 ng/mL (Figure 2), and 281 of these patients (6.1%) passed away during the first 30 days. The mortality rate was 4.7% for those whose preoperative troponin levels were undetectable and 11.4% for those whose troponin levels were detectable.

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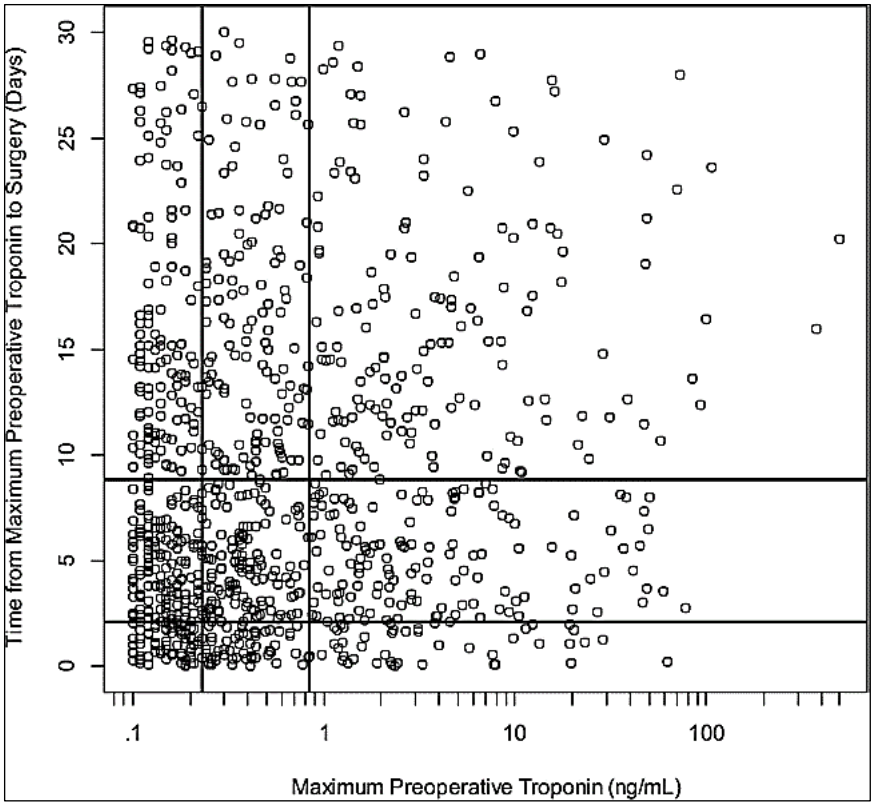

Fig 2: Scatterplot showing preoperative troponin concentrations and time between highest measured value and operation for study population with detectable preoperative troponin levels

Any rise in cTnI that was greater than the level that was reported (0.10 ng/dL) was associated with an increased risk of dying during the first 30 days. This risk increased from 4.7% in the group whose cTnI was undetectable to 12.7% in the group whose cTnI was in the upper tercile. When compared to those whose levels were undetectable, the odds ratio (OR) of death within 30 days gradually climbed from 1.98 in the low tercile of cTnI to 2.95 in the high tercile of the variable. The risk was comparable to that of patients who did not have elevation in their cTnI levels when they underwent surgery 8.86 days after their cTnI levels had been elevated. Except for the medium-troponin/short-time group, which exhibited an OR similar to that of the control group, the unadjusted OR of 30-day mortality was higher for patients who had more widespread cTnI elevations than in the control group. The examination of this risk across time terciles found a connection between reduced mortality and longer time between the peak cTnI concentration and surgery for the low cTnI cohort, but not for the medium or high cTnI cohorts. This trend was only seen in the low cTnI cohort. After adjusting for surgical specialisation, demographics, comorbidities, and other laboratory results using multivariable logistic regression, preoperative cTnI values remained linked with 30-day mortality for three of the nine groups (Table 2). Additional logistic regression models were created with these interaction terms included as a sensitivity analysis in order to evaluate the interactions that occurred between the troponin/time categories and the other important variables. Although there were a few interactions that had statistical significance for individual troponin/time categories, none of them were consistent regardless of the troponin concentration or the amount of time. In addition, likelihood ratio tests comparing the models that included the interactions to those that did not include the interactions did not produce significant results. Because of this, these interaction terms were ultimately left out of the final model.

Discussion

In spite of the fact that an elevated cTn level is most commonly considered to be a biomarker of ACS, research has shown that it is important in other contexts as well. The circumstance in which these biomarkers are released from the heart in the absence of coronary artery obstruction is referred to as secondary unstable angina, myocardial damage, and troponin leak, all of which are terms that are used to characterise the situation. This situation has been documented in multiple settings, such as sepsis, pulmonary embolism, renal failure, and stroke, and these non-ACS cTn elevations are associated with increased risk for mortality even in the general population [13-15]. Although some of our patients may have suffered from a classic case of myocardial infarction, more than one-third of them-including the entire low tercile and some of the medium tercile of troponin values-were classified as having normal troponin values by our laboratory, despite the fact that they were at an increased risk of 30-day mortality. This leads us to believe that the parameters used in our laboratory to determine what constitutes normal

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troponin levels in this cohort need to be changed. Additionally, research is required to understand whether or not levels of troponin below our threshold for detection are connected with an elevated risk. This study adds to our understanding of how the levels of cTn affect surgical risk for patients undergoing procedures that do not involve the heart [16]. In a prior study, Weber and colleagues demonstrated that high-sensitivity cTnT values contribute extra predictive information to the information that is provided by the updated cardiac risk index in a high-risk population that is undergoing non-cardiac surgery.

Table 2: Multivariable Regression

Sr. No.	Parameters	OR	95% CI	P
1.	**Troponin/time categories**			
2.	Low/short	2.78	1.38-5.61	0.0044
3.	Low/medium	1.13	0.60-2.13	0.7143
4.	Low/long	0.58	0.25-1.31	0.1897
5.	Medium/short	1.06	0.37-3.05	0.9153
6.	Medium/medium	1.75	0.95-3.22	0.0707
7.	Medium/long	2.05	1.19-3.54	0.0099
8.	High/short	3.16	1.36-7.33	0.0075
9.	High/medium	1.40	0.80-2.45	0.2437
10.	High/long	1.24	0.68-2.25	0.4806
11.	Age	1.03	1.02-1.04	<0.0001
12.	Case duration	1.00	1.00-1.00	0.0703
13.	Serum bicarbonate	0.97	0.94-1.00	0.0370
14.	Creatinine	1.26	1.03-1.53	0.0221
15.	Total bilirubin	1.19	1.09-1.30	0.0001
16.	Serum bicarbonate squared	1.00	1.00-1.00	0.0347
17.	Creatinine squared	0.97	0.93-1.01	0.1215
18.	Total bilirubin squared	1.00	0.99-1.00	0.0095
19.	Gender	1.15	0.88-1.51	0.2983
20.	ASA physical status			
21.	III	3.83	1.66-8.82	0.0016
22.	IV	9.43	4.06-21.90	<0.0001
23.	V	19.02	4.47-80.80	0.0001
	Procedure type			
	General (reference)			
24.	Oral/maxillofacial	3.51	2.17-5.69	<0.0001
25.	Orthopedics	0.89	0.55-1.44	0.6350
26.	Otolaryngology	1.82	1.12-2.96	0.0150
27.	Plastics	0.62	0.24-1.62	0.3308
28.	Thoracic	2.82	1.76-4.54	<0.0001
29.	Transplant	0.46	0.22-0.97	0.0402
30.	Vascular	0.83	0.49-1.41	0.4908

Their investigation demonstrated a relationship between minor changes in cTnT concentrations and mortality, with values >14 ng/L linked to a 160% increase in death risk. Our study shows a dose-response association between the time between a tiny peak troponin value and survival, especially in those with lower troponin levels. A longer interval from peak cTnI to surgery reduces the risk of death for people with minor preoperative troponin elevations. Time between peak cTnI levels and surgery has not been explored. Our retrospective analysis can't prove a direct link, but it implies that delaying surgery after cTn rise may reduce 30-day mortality in some patients [17]. We don't know why intermediate cTnI patients had a different time-to-surgery trend than small and big cTnI patients. Why a comparable trend wasn't noticed in all troponin concentration groups? Possible explanations include a different disease process with different features, prolonged troponin rise times, or different patient management. Time between peak cTnI levels and surgery has not been explored. Our retrospective study implies that waiting longer after cTn increase before surgery may minimise 30-day mortality. Unfortunately, our study does not provide any information on preoperative management, such as-blockers and antiplatelet medicines, or intraoperative management, such as various arterial blood pressure and heart rate targets. Understanding the biology of cTn release and how it relates to cardiac injury and death will lead to measures to limit its occurrence and association with surgical mortality.

Longer time between cTn elevation and surgery was associated with lower risk of death before adjusting for other patient characteristics. Additional studies are needed to determine if surgery should be delayed for individuals with a recent troponin elevation and, if so, to what level troponin values should be decreased. Our data imply this may be more than a month given that some individuals remained at greater risk. Myocardial damage after radiofrequency ablation provides some guidance. Higher cTn levels were related with longer-lasting inflammation, which increased the chance of recurrence. Patients remain at heightened risk for 3 months following an ablation procedure, therefore this may be a

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reasonable interval to wait after myocardial injury before undergoing surgery until further research provide greater clarity. Our findings have limitations. This study was retrospective, therefore unmeasured factors may have confounded the results. Given the high mortality rate of those with and without detectable troponin, our study cohort is skewed toward those with a high baseline mortality risk. These findings may not apply to people not at risk for myocardial ischemia. Since blood troponins aren't usually utilised as a screening test before noncardiac surgery, this selection bias doesn't affect the study's findings. Second, changes in clinical practise between institutions may limit our capacity to transfer our findings to places that measure cTn. Third, our lab only publishes concentrations >0.10 ng/mL; these data don't include lower values. We don't know the surgery's purpose or timeframe. We corrected for surgical specialisation, but we don't know the specific surgeries. Patients with higher troponin levels may have had more complicated operations within each speciality. Emergency surgery may not be delayed, therefore patients and doctors must weigh the dangers of an elevated cTn. Because we don't know the reason of the cTn elevation or the cause of death, we don't know if the myocardial injury evidenced by the higher cTnI contributed to death or if the underlying pathology that led to the myocardial injury and cTnI elevation contributed to death. We need further research.

Conclusion

We were able to analyse a large group of patients thanks to the use of an electronic medical record, which provided us with sufficient statistical power to determine the relationship between cTnI level and the amount of time that had passed since the last surgery and the risk of mortality. This was the primary strength of our study. Our findings are most applicable to patients with disease entities involving presumed coronary blood flow-demand imbalance rather than type 1 myocardial infarction because we excluded subjects who underwent preoperative percutaneous coronary intervention. This was done to ensure that the results would be valid. In conclusion, we came to the conclusion that the mortality risk is proportional to both the amount of the danger and the length of time. It was found that greater levels of preoperative cTnI were related with increased postoperative mortality, and that waiting longer before surgery tended to minimise this risk for those who had minor preoperative troponin increases. There is a need for prospective studies to assess whether or not postponing surgery in patients whose preoperative troponin levels were already elevated results in better postoperative outcomes.

Conflict of interest: None.

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