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Association Between Postoperative Troponin Levels and 90 Days Mortality Among Patients Undergoing Non-Cardiac Surgery

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ABSTRACT

Background: Globally, the mortality of non-cardiac surgery patients within the first month is increasing. Monitoring troponin-I levels aids in early mortality risk identification. Hence, the objective of this study was to determine the association between increased postoperative troponin-I levels to 90-day mortality in non-cardiac surgery patients.

Methods: This prospective longitudinal study was conducted at Liaquat National Hospital's general surgery department from June to December 2018. A total of 188 patients aged 40-70 years receiving a general or regional anesthetic, and undergoing emergency/elective surgery with a ≥2 days hospital stays, a procedure time of ≥2 hours, or blood loss of more than 300ml were recruited using a non-probability consecutive sampling technique. Troponin-I levels were assessed 6 to 12 hours post-surgery, followed by a 90-day phone-based mortality check. Data was analyzed using SPSS v.22. The chi-square test and Fisher's exact test were applied with a p-value <0.05 considered significant.

Results: Among 188 patients, 11 (5.9%) had positive troponin-I levels, and 23(12.2%) had raised levels in the immediate postoperative period. In 90-day follow-up, 8(4.2%) patients expired, all within the first 5 days, with a significant association between mortality and surgery type (p=0.001). Post-operative troponin-I levels showed a strong association with mortality (p<0.001). The proportion of patients with raised or positive troponin I levels was significantly higher in emergency cases (p<0.001). No deaths occurred in patients with baseline troponin I levels.

Conclusion: Monitoring postoperative troponin I levels can help physicians intervene promptly, potentially reducing mortality in non-cardiac surgery patients.

Keywords: Troponin I, Mortality, Non-cardiac Surgery.

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INTRODUCTION

Troponin is a protein complex present in the cardiac and skeletal muscles of the body. Troponin exists in three subtypes: troponin I, T, and C each playing a role in actin and myosin binding by calcium in overall muscle contraction[1]. Troponin levels are remarkably elevated in myocardial ischemia or trauma and are a diagnostic biomarker for suspected cases of myocardial injury[2]. In recent times, a highly sensitive blood test can measure troponin levels rising in the blood even as low as a few ng/L but the challenging part is that troponin levels can rise in a patient without exhibiting any clinical signs or symptoms[3, 4]. In literature troponin I levels are considered to be more cardio-specific compared to the other two troponin subtypes[2, 5]. Troponin levels are suspected to be elevated in different conditions ranging from pulmonary embolism, COPD, end-stage renal disease, and post-exercise, increased stress, or post-operative sepsis with no association with any cardiac injury, hence enabling us to manage an asymptomatic patient at baseline before worsening of his condition[6].

Out of 200 million patients being operated on for non-cardiac surgeries globally, the estimated mortality rate within the first month for non-cardiac surgeries is reported to be more than 1 million[7]. Evaluating troponin levels after a suspected risky non-cardiac surgery is known to be related to early identification of patients who are at risk of high postoperative mortality[8]. Elevated troponin levels also provide physicians with information about the extent of myocardial necrosis, the development of heart failure, and the occurrence of major adverse cardiovascular events later in life such as the possibility of MI, angina, and cerebrovascular accident post-noncardiac surgery[8, 9]. Early measurement of troponin levels can improve outcomes by enabling rapid in-hospital triage, guiding post-discharge plans, and arranging advance care directives for high-risk patients. It allows physicians to promptly plan postoperative interventions according to guidelines[9].

A significant association between elevated cardiac troponin T levels and increasing risk in cardiac events including mortality has been identified as up to 6-fold greater risk whereas elevated cardiac troponin I levels increase the risk by 5-fold, despite the absence of any ischemic symptoms, electrocardiographic changes, or imaging evidence of myocardial ischemia[3, 10].

In a recent study conducted in India, up to 17.5% of cases reported myocardial injury in the presence of peak troponin levels after a non-cardiac surgery out of which the 30-day mortality rate was alarmingly 11.7%[11]. The results of these studies indicate the importance of conducting research that would highlight the association between postoperative troponin levels and mortality. The literature so far only has results for 30-day mortality but no research in Pakistan has been done following patients for their 90-day mortality rate. The association between preoperative and perioperative troponin levels with mortality has been well established in Pakistan but post-operative troponin levels must be researched over to add more data to the research database[12 13]. Although troponin evaluation is not currently part of postoperative management, a single assessment of troponin I level after surgery will not significantly increase costs to the point of making treatment unaffordable for patients. Incorporating this test into post-operative care will enhance patient outcomes and help prevent future expenses associated with troponin-related complications that might arise if this condition is not detected early. Thus, the objective of this study was to determine the association between increased postoperative troponin I levels and 90-day mortality in patients undergoing non-cardiac surgery.

METHODS

This was a single-center, prospective longitudinal study. The study setting was the Department of General Surgery, Liaquat National Hospital. After the acceptance by the Liaquat National Hospital research and ethics committee (Ref: App#0653-2017 LNH ERC), this study was done from June 2018 to December 2018 with a study duration of 6 months. A non-probability consecutive sampling was used to recruit the patients. A sample size of 155 was estimated taking a 17.5% proportion of myocardial injury after non-cardiac surgery, at a 95% confidence interval and 6% margin of error[11]. However, for better results, this study included 188 patients. All patients had general surgical procedures either electively or as emergencies.

The inclusion criteria for patient selection were all patients having non-cardiac surgery, with an age limit of 40-70 years receiving a general or regional anesthetic, and undergoing emergency or elective surgery. All study subjects had a hospital stay of more than 2 days, a procedure time of more than 2 hours, or blood loss of more than 300ml. The study excluded all patients with known coronary artery or cardiac disease, patients who didn't require overnight hospital admission after surgery, and patients who did not consent to be a part of this study.

The Troponin I level of all non-cardiac surgery patients was sent within 6 to 12 hours postoperatively and a 90-day follow-up was done by contacting the patients over the phone to ascertain any mortality occurring within these patients. For this study, raised levels of Troponin I values were considered to be in the range of 0.1-0.3ng/dl whereas values above 0.3ng/dl were considered positive Troponin I levels. All positive troponin I findings were followed by bedside ECG to evaluate any changes. Baseline values were reported as <0.10 ng/dl.

The data was analyzed using the software IBM SPSS

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statistics version 22. For descriptive statistics, mean with standard deviation were used for continuous variables like hospital stay whereas frequencies and percentages were used for categorical variables like gender ratio. The chi-square test and Fisher's exact test were applied. P value <0.05 was considered as significant.

RESULTS

A total of 188 patients were recruited after the fulfillment of the inclusion criteria. Table 1 shows patient demographics. The mean age of patients was 53.7 ±8.4 years. The majority of the patients i.e., n=104 (55.3%) were males. From these recruits n=11 (5.9%) patients tested positive for troponin I levels in the immediate post-operative period, whereas n=23 (12.2%) patients had raised troponin I levels (>0.10ng/dl), making a total n=34 (18.1%) of patients with above baseline troponin I values. Table 1 shows the distribution of type of surgery (emergency vs., elective) with different age groups and gender. The majority of the patients, n=108 (57.4%) had elective procedures while the leftover, n=80 (42.6%) had emergency surgeries.

Table 1: Patients' demographic characteristics with the type of surgery.

Variables	n (%)	Emergency	Elective
Age groups (years)			
40-49	59 (31.4)	21 (35.6)	38 (64.4)
50-59	76 (40.4)	33 (43.4)	43 (56.6)
60 and above	53 (28.2)	26 (49.1)	27 (50.9)
p-value	0.348		
Gender			
Male	104 (55.3)	42 (40.4)	62 (59.6)
Female	84 (44.7)	38 (45.2)	46 (54.7)
p-value	0.503		

Figure 1 shows the distribution of Troponin I levels with age and gender, respectively.

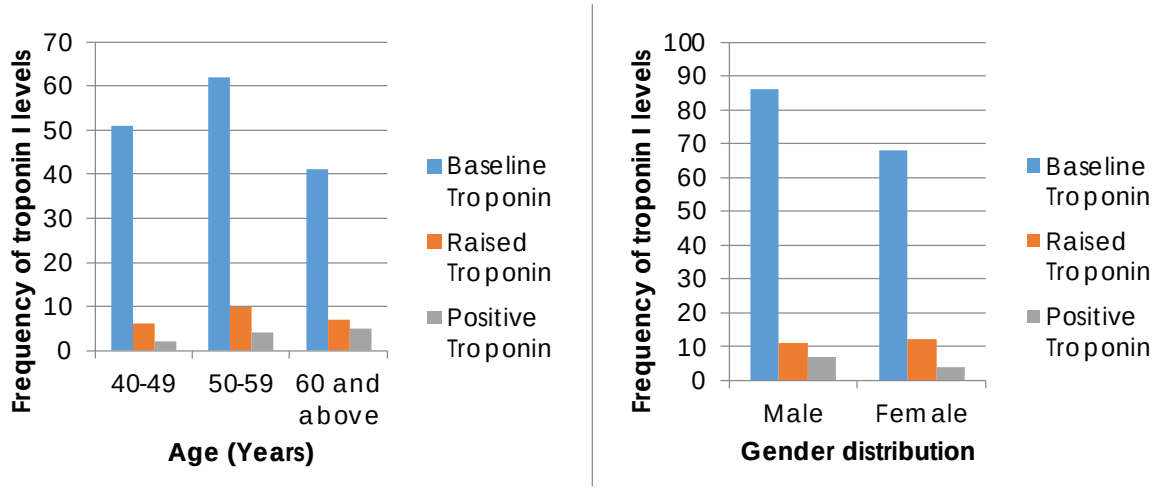

Figure 1: Distribution of Troponin I level with age and gender.

In 90 days, of follow-up, a total of 8 mortalities were recorded which is calculated to be 4.2% of total recruits. All of these mortalities occurred in the first 5 days. All of the mortalities occurred during post-operative hospitalization and the cause of death in all these patients was myocardial infarction. The proportion of patients with raised or positive troponin I level postoperatively was significantly higher in emergency cases as compared to elective procedures [n=26 (32.5%) vs. n=8 (7.4 %), p<0.001].

Table 2 displays a comparison of patient's demographics and surgery type with 90 days mortality. There was a significant association between 90 days of mortality and type of surgery (p=0.001). All of the reported mortalities were seen in emergency surgeries. A strong association was also found between post-operative troponin I levels and mortality (p<0.001). The proportion of expired patients with positive troponin I levels was higher than those with raised troponin I levels [n=6 (54.5%) vs. n=2 (8.7%)]. No mortalities were seen in patients with baseline troponin I levels. No association was seen between age and gender with the troponin I level (p=0.687) (p=0. 655), respectively. No significant association was observed between age and gender with 90 days of mortality in patients (Table 2).

Table 2: Comparison of patients' demographics and surgery type with 90 days mortality

Variables	Groups	90 days mortality		p-value
		Mortality n (%)	Recovered n (%)	
Age	40-49	1 (1.7)	58 (98.3)	0.302
	50-59	3 (3.9)	73 (96.1)	
	60 and above	4 (7.5)	49 (92.5)	
Gender	Male	5 (4.8)	99 (95.2)	0.733
	Female	3 (3.6)	81 (96.4)	
Type of surgery	Elective	0 (0)	108 (100)	0.001
	Emergency	8 (10)	72 (90)	
Troponin I level	Baseline Troponin	0 (0)	154 (100)	<0.001
	Raised Troponin	2 (8.7)	21 (91.3)	
	Positive Troponin	6 (54.5)	5 (45.5)	

p<0.05 was considered significant.

Earliest mortality was recorded at 8 hours postoperatively and the maximum duration was recorded at 120 hours (5 days) (Figure 2). The mean duration came out to be 60.3 ±41.8 hours (2.5 days).

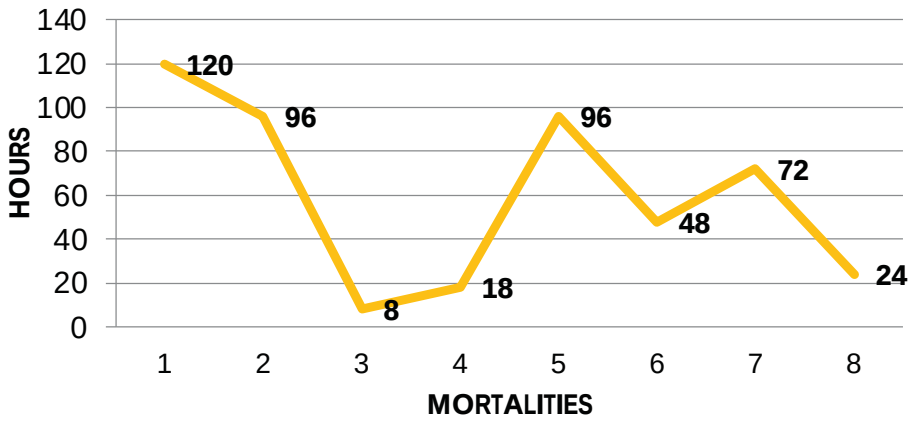

Figure 2: Patient mortality distribution (hours).

DISCUSSION

Postoperative myocardial infarction causes a high fraction of deaths annually. Strategies for early diagnosis of cardiac injury and timely intervention are important to reduce the high risk of mortality in these patients. For such reasons, our primary objective focuses on the association between raised levels of troponin I and postoperative mortality. Currently, new guidelines suggest that diagnosis of MI requires additional criteria beyond biomarkers only, such as the presence of cardiac symptoms, electrocardiographic changes, and use of noninvasive and invasive diagnostic imag-

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ing, we have been careful not to characterize these troponin elevations as MI as these patients could not evaluate according to diagnostic criteria[14, 15]. Based on a study published in 2023, the positive relationship between the two variables i.e. troponin I levels and mortality was identified, therefore, this study evaluated the risk of mortality only using troponin I levels[16]. Although increased troponin I levels are associated with different diseases, in our research positive troponin I levels showed mortality due to MI only. If the same research was replicated on a larger scale, the results may differ because, in a larger sample size, different people may have different comorbidities hence other causes of mortality were not seen in our study due to the limited sample size and limited mortalities i.e., 8 patients only.

Most of the previous studies took a sample size of more than 1,000 individuals whereas our study was limited to a smaller sample size of 188 patients only[11, 17]. Despite having a smaller sample size the ratio of recruited genders was close to the international VISION study i.e., 49.1% female recruitment compared to our study with 44.7% of female patients[17]. Our study is the only study that highlights the division of total surgeries into electives and emergency surgeries. The inclusion of this variable was an important confounder as stress situations (emergencies) are also known to raise troponin I levels[6]. In a recent study with a sample size of 3288 patients, 22.7% had troponin I elevations post-operatively, however, despite having a smaller sample size, our results were comparatively similar with a total of 18.1% patients with postoperative troponin I levels above baseline[18].

The results of our study showed a significantly higher mortality percentage in patients with above baseline troponin I levels postoperatively in comparison with other studies that reported lower mortality rates of 16.7% and 4.2%, respectively [18, 19]. Despite this difference, our results were similar to these studies as no significant association was observed between genders and mortality rate postoperatively. Our results found a significant association between above-baseline troponin I levels post-operatively and 90-day mortality which is comparable to the evidence provided via the international VISION study[17]. Other researchers also concluded a strong association between elevated troponin levels after surgery with short- and long-term mortality[20,21]. Despite having similar outcomes, our study differentiates from the VISION study as we used troponin I levels instead of troponin T levels as the former is less likely to be influenced by renal dysfunction and superior in accuracy hence revealing a more accurate value of the test for patients undergoing non-cardiac surgery [22,23,24]. A similar study was done in India using troponin I level as the biomarker with the same cut-off value (≥ 0.03 ng/dl) suggestive of positive troponin I levels but they concluded a less significant relation between mortality and post-operative troponin I levels11. The mean number of days in which mortality occurred was 3 days in our study whereas another study reported a mean of less than 3 days[3, 25].

Our study has a few limitations. This study shared the experience of a single center with a limited sample size. Moreover, we did not explore comorbidities, surgical specialty, and use of medications impacting troponin I levels, baseline evaluation of cardiac markers, and sequential monitoring of troponin I levels following surgery. Because of these limitations, the study findings cannot be generalized to the entire population. Thus, it is suggested to conduct a larger study to address the limitations of the current study and validate our findings.

CONCLUSION

Among patients undergoing non-cardiac surgery, postoperative troponin I levels were significantly associated with 90-day mortality. All reported mortalities were seen during the first 5 postoperative days, either in patients with raised or positive troponin I levels. The study also concluded an association between postoperative troponin I levels and surgery type, as troponin I levels above baseline were seen more in emergency cases as compared to elective procedures, indicating the need to measure early troponin I levels in patients postoperatively. This can prompt timely intervention, enhancing patient outcomes and reducing mortality rates.

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None.

CONFLICT OF INTEREST

There is no conflict of interest.

ETHICAL APPROVAL

Approval was taken from the Liaquat National Hospital ethics committee (Ref: App#0653-2017 LNH ERC).

PATIENT CONSENT

Informed consent was taken from the patients.

AUTHOR'S CONTRIBUTION

FS conceptualized the study. MH, FS, and MAB designed the study protocol. AA and MH were involved in data collection and performed data analysis, result write-up, and interpretation. AA, MH, and MAB wrote the initial draft of the study. FS and MAB, AAB critically reviewed and revised the initial draft. All authors read and approved the manuscript.

REFERENCES

1. Martini L, Mandoli GE, Pastore MC, Pagliaro A, Bernazzali S, Maccherini M, et al. Heart transplantation and biomarkers: a review about their usefulness in clinical practice. Front Cardiovasc Med. 2024;11:

1336011. doi: 10.3389/fcvm.2024.1336011.
2. Wu Y, Pan N, An Y, Xu M, Tan L, Zhang L. Diagnostic and Prognostic Biomarkers for Myocardial Infarction. Front Cardiovasc Med. 2021;7:617277. doi: 10.3389/fcvm.2020.617277.
3. Ruetzler K, Smilowitz NR, Berger JS, Devereaux PJ, Maron BA, Newby LK, et al. Diagnosis and Management of Patients With Myocardial Injury After Noncardiac Surgery: A Scientific Statement From the American Heart Association. Circulation. 2021;144:e287–e305. doi: 10.1161/CIR.0000000000001024.
4. Potter JM, Hickman PE, Cullen L. Troponins in myocardial infarction and injury. Aust Prescr. 2022;45(2):53-57. doi: 10.18773/austprescr.2022.006.
5. Welsh P, Preiss D, Hayward C, Shah ASV, McAllister D, Briggs A, et al. Cardiac Troponin T and Troponin I in the General Population: Comparing and Contrasting Their Genetic Determinants and Associations With Outcomes. Circulation. 2019;139:2754–2764. doi: https://doi.org/10.1161/CIRCULATIONAHA.118.038529.
6. Chaulin A. Modern View on the Role of Sex-Specific Levels of High-Sensitive Cardiospecific Troponins T and I in the Diagnosis of Myocardial Infarction. Cardiol Res. 2023;14(1):22-31. doi: 10.14740/cr1450.
7. Mazzarello S, McIsaac DI, Montroy J, et al. Postoperative shared-care for patients undergoing non-cardiac surgery: a systematic review and meta-analysis. Can J Anesth. 2019;66(11):1095–1105. doi: https://doi.org/10.1007/s12630-019-01433-5.
8. Mol KHJM, Hoeks SE, Liem VGB, Stolker RJ, Lier FV. Postoperative troponin release is associated with major adverse cardiovascular events in the first year after noncardiac surgery. International Journal of Cardiology. 2019; 280; 8–13. doi: 10.1016/j.ijcard.2019.01.035.
9. McIlvennan CK, Urra M, Helmkamp L, et al. Magnitude of troponin elevation in patients with biomarker evidence of myocardial injury: relative frequency and outcomes in a cohort study across a large healthcare system. BMC Cardiovasc Disord. 2023;23(1):151. doi: https://doi.org/10.1186/s12872-023-03168-0.
10. Zhang LJ, Li N, Li Y, Zeng XT, Liu MY. Cardiac Biomarkers Predicting MACE in Patients Undergoing Noncardiac Surgery: A Meta-Analysis. Front Physiol. 2019;9:1923. doi: 10.3389/fphys.2018.01923.
11. George R, Menon VP, Edathadathil F, Balachandran S, Moni M, Sathyapalan D et al. Myocardial injury after noncardiac surgery—incidence and predictors from a prospective observational cohort study at an Indian tertiary care centre. Medicine (Baltimore). 2018; 97(19): e0402. doi: 10.1097/MD.0000000000010402.
12. Zhu Y, Bi Y, Yu Q, Liu B, et al. Assessment of the prognostic value of preoperative high-sensitive troponin T for myocardial injury and long-term mortality for groups at high risk for cardiovascular events following noncardiac surgery: a retrospective cohort study. Front Med. 2023;10:1135786. DOI: https://doi.org/10.3389/fmed.2023.1135786.
13. Chew MS, Saugel B, Lurati-Buse G. Perioperative troponin surveillance in major noncardiac surgery: a narrative review. Br J Anaesth. 2022. doi: 10.1016/j.bja-.2022.08.041.
14. Domienik KJ, Kupczyńska K, Michalski B, Kapłon-Cieślicka A, Darocha S, Dobrowolski P, et al. Fourth universal definition of myocardial infarction. Selected messages from the European Society of Cardiology document and lessons learned from the new guidelines on ST-segment elevation myocardial infarction and non-ST-segment elevation-acute coronary syndrome. Cardiol J. 2021;28(2):195-201. doi: 10.5603/CJ.a2021.0036.
15. Sandoval Y, Thygesen K, Jaffe AS. The Universal Definition of Myocardial Infarction: Present and Future. Circulation. 2020;141:1434–1436. doi: 10.1161/CIRCULATIONAHA.120.045708.
16. Hinton J, Mariathas MN, Gabara L, et al. Association between troponin level and medium-term mortality in 20,000 hospital patients. Heart. 2023;109(5 Pt A):heartjnl-2023-322463. doi: 10.1136/heartjnl-2023-322463.
17. Writing Committee for the VISION Study Investigators; Devereaux PJ, Biccard BM, Sigamani A, Xavier D, Chan MTV, Srinathan SK, et al. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. JAMA. 2017;317(16):1642-1651. doi: 10.1001/jama.2017.4360.
18. Reed GW, Horr S, Young L, Clevenger J, Malik U, Ellis SG, Lincoff AM, Nissen SE, Menon V. Associations Between Cardiac Troponin, Mechanism of Myocardial Injury, and Long-Term Mortality After Noncardiac Vascular Surgery. J Am Heart Assoc. 2017;6:e005672. doi: 10.1161/JAHA.117.005672.
19. Machado MN, Rodrigues FB, Nakazone MA, Martin DF, Sabbag ATR, Grigolo IH, Silva-Júnior OL, Maia LN, Jaffe AS. Prediction of Death After Noncardiac Surgery: Potential Advantage of Using High-Sensitivity Troponin T as a Continuous Variable. J Am Heart Assoc. 2021;10:e018008. doi: 10.1161/JAHA.120.018008.
20. Caruana CB, Jackson SM, Khuong JN, Campbell R, Liu Z, Ramson DM, et al. Systematic review and meta-analysis of postoperative troponin as a predictor of mortality and major adverse cardiac events after vascular surgery. J Vasc Surg. 2020;72(3):1132-1143.e1. doi: https://doi.org/10.1016/j.jvs.2020.03.039.
21. Landesberg G, Jaffe AS. 'Paradox' of troponin elevations after non-cardiac surgery. BJA: British Journal of Anaesthesia. 2015;114(6):863-865. doi: https://doi.org/10.1093/bja/aev068.
22. Chesnaye NC, Szummer K, Bárány P, Heimbürger O, Magin H, Almquist T, Uhlin F, Dekker FW, Wanner C, Jager KJ, Evans M, EQUAL Study Investigators. Association Between Renal Function and Troponin T Over Time in Stable Chronic Kidney Disease Patients. J Am Heart Assoc. 2019;8:e013091. doi: 10.1161/JAHA.119.013091.
23. Braghieri L, Badwan OZ, Skoza W, Fares M, Menon V. Evaluating troponin elevation in patients with chronic kidney disease and suspected acute coronary syndrome. Cleveland Clinic Journal of Medicine.

2023;90(8):483-489. doi: https://doi.org/10.3949/ccjm.90a.23012.
24. Morgan H, Ezad SM, Rahman H, De Silva K, Partridge JSL, Perera D. Assessment and Management of Ischaemic Heart Disease in Non-Cardiac Surgery. Heart International. 2023;17(2):19-26. doi: https://doi.org/10.17925/HI.2023.17.2.19.
25. Conti D, Ballo P, Ruggiano P, Boccalini R, Pavoni V, Sarti A. Very early postoperative troponin increase and clinical outcome in patients admitted to the recovery room after noncardiac surgery with suspected cardiac events. Indian Heart J. 2020;72(3):197-199. doi: 10.1016/j.ihj.2020.05.013.