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The Correlation of Level of Surgical Risk with High Sensitivity Cardiac Troponin in Non-Cardiac Surgical Patients

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Kontext: Poškození myokardu po nekardiálním chirurgickém výkonu (myocardial injury after non-cardiac surgery, MINS) představuje závažný problém přímo související s mortalitou do 30 dnů po výkonu. V diagnostice poškození myokardu se přednostně používají hodnoty vysoce senzitivního srdečního troponinu (high-sensitivity cardiac troponin, hs troponin), protože se v současnosti jedná o nejcitlivější a nejspecifičtější srdeční biomarker vhodný pro zjišťování MINS. Cílem této studie je analyzovat vztah mezi změnami v hodnotách hs troponinu a riziky spojenými s chirurgickým výkonem u pacientů podstupujících nekardiální chirurgické výkony, které by ukazovaly na poškození myokardu.
Metoda: Naše studie je analytickou observační průřezovou studií, do níž byli zařazováni všichni pacienti podstupující nekardiální chirurgický výkon ve fakultní nemocnici Airlangga University Hospital. Krevní vzorky byly odebírány metodou náhodného vzorku (consecutive sampling) a hodnoty hs troponinu se stanovovaly před operací a 24 hodin po ní. Míra operačního rizika se hodnotila pomocí kritérií doporučených postupů ESAIC-ESC 2022. Statistická analýza se prováděla s použitím Spearmanova korelačního koeficientu.
Výsledky: Do studie bylo zařazeno 75 pacientů, 39 mužů a 36 žen, ve věku s mediánem 54 let. Výsledky prokázaly statisticky významnou korelaci mezi hodnotami hs troponinu a mírou operačního rizika, a to jak předoperačními hodnotami, tak i pooperačními a jejich změnami. Medián hodnoty (mezikvartilové rozpětí) hs troponinu při nízkém operačním riziku před operací vs. po operaci činil 1,2 ng/l (0,0), resp. 1,2 ng/l (0,0), s mediánem rozdílu 0,0 ng/l (0,0); $p < 0{,}001$. Medián hodnoty hs troponinu při středně vysokém operačním riziku před operací vs. po operaci byl 1,2 ng/l (0,0) vs. 1,2 ng/l (0,0), s mediánem rozdílu 0,0 ng/l (1,6); $p < 0{,}001$. Medián hodnoty hs troponinu při vysokém operačním riziku před operací vs. po operaci byl 1,7 ng/l (18,8) vs. 11,9 ng/l (27,6); medián rozdílu činil 5,3 ng/l (11,4); $p < 0{,}001$.
Závěr: Byla nalezena statisticky významná korelace mezi změnami hodnot hs troponinu a mírou operačního rizika a přítomností komplikací.

ABSTRACT

Background: Myocardial injury after non-cardiac surgery (MINS) is an important issue, directly related to the mortality rate within 30 days after surgery. High sensitivity cardiac troponin (HS troponin) is the preferred biomarker for diagnosing myocardial damage because it is the most sensitive and specific heart biomarker currently available, making it suitable for detecting MINS. The aim of this study is to analyse the relationship between changes in HS troponin levels and surgery-related risks in non-cardiac surgery patients as a marker of myocardial injury.
Method: This study is an analytical observational cross sectional study that included all patients who underwent non-cardiac surgery in the Airlangga University Hospital. Samples were taken using the consecutive sampling method. HS troponin values were measured before surgery and 24 hours after surgery. The level of surgical risk was assessed based on the criteria from ESAIC-ESC 2022. Statistical analysis used Spearman's correlation.

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Results: This study consisted of 75 samples, 39 men and 36 women, with a median age of 54 years. The results showed that there was a significant positive correlation between HS troponin levels and the level of surgical risk both from preoperative, postoperative values and changes in HS troponin levels. Median value (interquartile range) HS troponin with low risk level preoperatively vs. postoperatively 1.2 ng/L (0.0) vs. 1.2 ng/L (0.0), median difference 0.0 ng/L (0.0), $p < 0.001$. Median HS troponin value with moderate risk level preoperatively vs. postoperatively 1.2 ng/L (0.0) vs. 1.2 ng/L (0.0), median difference 0.0 ng/L (1.6), $p < 0.001$. Median HS troponin value with high risk level preoperatively vs. postoperatively 1.7 ng/L (18.8) vs. 11.9 ng/L (27.6), median difference 5.3 ng/L (11.4), $p < 0.001$.
Conclusion: There is a significant correlation between changes in HS troponin levels and the level of surgical risk and the presence of complications.

Introduction

Myocardial injury after noncardiac surgery (MINS) is defined as the presence of at least one postoperative cardiac troponin (cTn) concentration that exceeds the upper reference limit at the 99th percentile of the cTn assay, resulting from a suspected ischemic mechanism (such as supply-demand mismatch or atherothrombosis) without any clear non-ischemic cause. Myocardial injury after noncardiac surgery is a common occurrence.[1]

In the VISION study (Vascular Events in Noncardiac Surgery Patients Cohort Evaluation) of 21,842 inpatients aged ≥40 years undergoing non-cardiac surgery with systematic hsTnT measurements, 18% experienced MINS.[2] High-sensitivity cardiac troponin (HS-cTn) has been introduced into routine clinical practice to detect myocardial injury. The upper reference limit at the 99th percentile threshold is the diagnostic cutoff for myocardial injury. HS-cTn measurement has improved the accuracy and speed of diagnosing MINS.[3,4] While most MINS occur during surgery or in the immediate postoperative period, where the patient is still under anesthesia and/or high doses of analgesics, approximately 90% of patients with MINS do not report typical symptoms and are therefore missed in routine clinical examination. This is a major concern, as the risk of death associated with MINS is also high in asymptomatic patients. Additionally, the risk of death from MINS is also high in patients without typical ECG and/or imaging evidence of myocardial ischemia. Overall, 30-day mortality in patients experiencing MINS is ~10%.[5–7]

The risk factors for MINS are associated with the type of surgery performed. According to the 2022 ESC Guidelines on Cardiovascular assessment and management of patients undergoing non-cardiac surgery, the surgical risk estimation is categorized based on the type and duration of surgery, as well as the urgency of the procedure or intervention. The type of anesthesia and anesthetic agents can also affect the risk of complications in patients with moderate to high cardiac risk undergoing noncardiac surgery. The guidelines recommend the use of cTn in patients at high risk in two situations: first, for preoperative risk stratification, and second, for detecting perioperative cardiac injury using an active monitoring strategy involving serial cTn measurements, starting before the surgery and continuing on postoperative days 1 and 2. The aim of this study is to analyze the relationship between delta hs-cTn and the level of surgery-related risk in non-cardiac surgical patients.

Material and methods

Design and population

This study is an analytical observational study with a cross-sectional design conducted in the inpatient ward of Airlangga University Hospital in Surabaya during the period of December 2023 to January 2024. The population in this study consists of patients who will undergo non-cardiac surgical procedures at Airlangga University Hospital and are willing to participate in the study by signing an informed consent form. Blood samples will be taken to assess the levels of high-sensitivity troponin before surgery and 24 hours after surgery.

The subjects used in this study are non-cardiac surgical patients selected through non-probability sampling, specifically consecutive sampling. The total sample size is 75 patients who meet the inclusion criteria. The inclusion criteria include all non-cardiac surgical patients aged over 40 who have been treated for at least 24 hours after the non-cardiac surgical procedure at the hospital. The exclusion criteria include patients with unstable cardiac conditions and patients with comorbidities that could cause non-ischemic cardiac complications such as sepsis, kidney failure, fluid overload, heart valve disease, and pulmonary embolism.

The data obtained in this study are secondary data collected from medical records, biochemical data, and echocardiography examinations of non-cardiac surgical patients to obtain data on gender, age, surgical risk level, high-sensitivity troponin biomarker, comorbidities, body mass index, and blood pressure. The high-sensitivity troponin variable is a numerical variable, while the surgical risk level variable categorized as low, moderate, and high is a nominal variable.

Statistical analysis

The research data were processed using SPSS version 26.0. The data obtained were analyzed through univariate and bivariate analyses. Descriptive analyses were performed for demographic data and clinical characteristics, presented as frequencies and percentages. Numerical data are displayed in mean/median form according to the results of the data normality test. Analysis of the relationship between surgery-related risks in non-cardiac surgical patients and delta hs-cTn was carried out using: Spearman's correlation (rs). Meaning is determined based on p-value < 0.05.

Results

Baseline characteristic

Demographic data for the research sample are listed in **Table 1**. The total sample included in the study were 75 patients with a median age of 54 years and predominantly male. The most common comorbidity found is hypertension. ECG examination of patients found that almost all patients did not have heart rhythm disorders. The ejection fraction of the sample has a median value above the limit for reducing the ejection fraction value. In this study, the complication rate was 27.0%. Findings referred to as complications in this study included hypotension and bradycardia.

Data on the level of surgery and the level of surgical risk are listed in **Table 1**. Only a small percentage of patients require surgery urgently. There were 30 patients included in operations with a low level of risk, 28 patients included in operations with a medium risk level, and 17 patients included in operations with a high level of risk.

The types and amounts of anesthetic drugs are listed in **Table 1**. In this study it was found that the majority of patients received general anesthesia and only a small portion received spinal anesthesia (subarachnoid spinal block). This study also showed that the majority of patients required two anesthetic drugs during the surgical procedure.

HS troponin data for the entire sample are listed in **Table 1**. In this study, preoperative and postoperative HS troponin levels had the same median value, namely 1.20 ng/mL with changes in HS troponin levels having a median value of 0 ng/mL. This is due to the limitations of the troponin level calculator which is only able to detect troponin levels as low as 1.20 ng/mL so that all patients with troponin levels below this value only show low troponin levels or <1.20 ng/mL. In this study, all patients with low troponin levels were stated to have troponin levels of 1.20 ng/mL.

Table 1 – Baseline clinical demographics, surgical variables, anesthesia variables, and HS troponin levels in the entire sample

Variable	Mark
Demographics clinical base	
Total sample	75
Age, median (RIK)	54.0 (18.25)
Gender, n (%)	
Woman	36 (48.0)
Man	39 (52.0)
BMI, mean ± SB	23.84 ± 3.71
Obesity, n (%)	8 (10.7)
Hypertension, n (%)	31 (41.3)
Diabetes mellitus	13 (17.3)
Smoker active	6 (8.0)
History of illness in family, n (%)	2 (2.7)
Findings, n (%)	
Sinus rhythm	72 (96.0)
Bundle-branch block / Bradycardia	3 (4.0)
Fraction ejection, median (RIK)	0.63 (0.03)
Patient with complications, n (%)	20 (27.0)
Variable operation	
Operation type, n (%)	
Elective	61 (81.3)
Urgent	14 (18.7)
Risk operations, n (%)	
Low	30 (40.0)
Currently	28 (37.3)
Tall	17 (22.7)
Variable anesthesia	
Type of anesthesia, n (%)	
Subarachnoid spinal block	19 (21.3)
General anesthesia	56 (74.7)
Amount drug anesthesia, n (%)	
One drug	20 (27.0)
Two drugs	43 (58.1)
Three drugs	12 (14.9)
HS troponin levels	
Preoperative HS troponin, median (RIK)	1.20 (0.0)
Postoperative HS troponin, median (RIK)	1.20 (1.25)
Change in HS troponin levels, median (RIK)	0.0 (1.18)

ECG – electrocardiogram; BMI – body mass index; RIK – range interquartile.

The correlation between the level of surgical risk and changes in HS troponin levels

The correlation between the level of surgical risk and HS troponin levels is listed in **Table 2**. This study shows that there is a significant positive correlation between HS troponin levels and the level of surgical risk both from preoperative, postoperative values, and changes in HS troponin levels. These findings indicate that the higher the level of surgical risk, the higher the HS troponin levels and the number of changes.

The correlation between type of anesthesia and changes in HS troponin levels

The correlation between the type of anesthesia and HS troponin levels is listed in **Table 3**. This study shows that there was no significant relationship found between HS troponin levels both preoperatively, postoperatively, and changes depending on the type of anesthesia used.

The correlation between changes in HS troponin levels and the incidence of complications

The correlation between the incidence of complications and HS troponin levels is listed in **Table 4**. This study shows that patients with complications will have HS troponin values both preoperatively, postoperatively, and changes that are higher than patients without complications.

Table 2 – Correlation between surgical risk level and HS troponin value

Risk level operation	HS troponin levels								
	Preoperative			Postoperative			Change		
	Mark	r	*p*	Mark	r	*p*	Mark	r	*p*
Low	1.20 (0.0)	0.509	< 0.001*	1.20 (0.0)	0.648	< 0.001*	0.0 (0.0)	0.643	< 0.001*
Currently	1.20 (0.0)			1.20 (0.0)			0.0 (1.6)		
Tall	1.70 (18.8)			11.9 (27.6)			5.30 (11.4)		

The value is displayed in median (RIK); r = coefficient Spearman's correlation.
**P*-value is significant (< 0.05).

Table 3 – Correlation between type of anesthesia and HS troponin values

Types of anesthesia	HS troponin levels					
	Preoperative		Postoperative		Change	
	Mark	*p*	Mark	*p*	Mark	*p*
SAB	1.20 (0.0)	0.572	1.20 (1.5)	0.771	0.0 (1.50)	0.804
GA	1.20 (0.0)		1.20 (2.1)		0	

The value is displayed in median (RIK); *p* is obtained from the Mann-Whitney test.

Table 4 – Correlation between postoperative complications and HS troponin values

Complications	HS troponin levels					
	Preoperative		Postoperative		Change	
	Mark	*p*	Mark	*p*	Mark	*p*
No	1.20 (0.0)	0.001*	1.20 (0.0)	0.002*	0.0 (0.0)	0.005*
Yes	1.20 (15.5)		1.70 (19.5)		0.5 (9.0)	

The value is displayed in median (RIK); *p* is obtained from the Mann-Whitney test.
**P*-value is significant (< 0.05).

Discussion

HS troponin as a marker of myocardial injury

This research studied the relationship between changes in high sensitivity (HS) troponin levels and types of surgical risk in patients undergoing non-cardiac surgery. The results of this study showed that there was a positive correlation between increased changes in HS troponin and increased risk of surgery. Apart from that, this study also shows a significant relationship between changes in HS troponin levels and the incidence of complications in the form of postoperative hypotension and bradycardia. Changes in HS troponin levels may be associated with the occurrence of non-cardiac postoperative myocardial injury.[8,9] Elevated HS troponin levels have been widely used as a laboratory test to indicate myocardial damage because this compound is released from the cytoplasm of myocardial cells immediately after hypoxia occurs in the tissue.[10] The upper reference limit of the 99th percentile is the threshold for the diagnosis of myocardial injury. The 99th percentile upper reference limit is sex specific, with women typically having a lower 99th percentile than men.[4] A retrospective cohort study reported by Orji et al. showed that an increase in HS troponin according to the definition above the 99th percentile had a high sensitivity of 92.8% and a high negative predictive value (NPV) of 97.8%.[11]

Cardiac troponin surveillance in non-cardiac surgical processes consists of two steps: The first step involves preoperative hs-cTn measurement, accompanied by preoperative risk stratification, benefiting patients at high cardiovascular risk. The goal of the first step is to identify patients at a high risk of acute postoperative myocardial injury, major adverse cardiovascular events, and death. The addition of biomarkers such as N-terminal B-type natriuretic peptide (NT-proBNP) and hscTns may improve preoperative risk stratification.[12] Preoperative cTn concentration is not only a reference point for assessing perioperative changes, but also has predictive value for the prediction of fatal or non-fatal cardiac complications of non-cardiac surgery.[13,14]

HS troponin and a level of surgical risk

This study confirms that the condition of the myocardium will tend to worsen with an increasing risk of non-cardiac surgery. It should be noted that in this study a positive

correlation was also found between preoperative HS troponin levels and the level of surgical risk. In this study, the surgical risk level was determined based on the risk of cardiovascular death, myocardial infarction and stroke from each surgical procedure based on guidelines from the European Society of Anaesthesiology and Intensive Care (ESAIC) and the European Society of Cardiology (ESC) in 2022. Risk level in this guide, it is determined to be divided into two, namely patient-related risks and surgery-related risks. The risk associated with the patient is related to the patient's age, cardiac comorbidities, and frailty conditions. The risks associated with surgery are related to the duration, type, and amount of anesthesia required, and the location of the organ being operated on.[9,15] This study showed that patients with surgical risk levels had higher preoperative HS troponin levels than patients with low risk levels. Looking at the list of surgical procedures in each surgical risk category released by the 2022 ESAIC-ESC guidelines, higher HS troponin levels in high surgical risk patients may be caused by the patient's initial clinical condition which causes the indication for surgery. For example, HS troponin levels are known to increase in patients with ALI, especially high degrees, which are indicated for open surgery, which is a high-risk operation.[16]

Although preoperative HS troponin levels were higher in patients with a high surgical risk level, this study also showed a higher change in HS troponin levels along with increasing surgical risk.[5] This research shows that apart from the worse condition of the myocardium in patients who require high-risk surgery, there is also greater myocardial damage after these patients undergo high-risk surgery. This finding can occur because operations that are classified as high risk are quite closely related to the heart and cardiovascular system. Some of the high-risk surgical procedures include major aortic and vascular surgery, open surgery for ALI, open surgery for pneumothorax, and lung or liver transplantation.[16] Higher changes in HS troponin levels indicate greater myocardial damage, potentially causing myocardial injury after non-cardiac surgery (MINS). The relationship between MINS and the level of surgical risk was reported by several previous studies. Gonzales-Tallada et al. in their observational study reported the incidence of MINS in high-risk patients undergoing thoracic surgery, which is a high-risk operation. In this study, the incidence of MINS would increase in patients undergoing surgery related to lobectomy, pneumonectomy, and pericardial incision, three procedures that are often performed in high-risk operations.[17] Apart from that, a study by Sunny also reported similar findings. In this study, it was found that the proportion of patients undergoing high-risk surgery was higher in patients who experienced MINS than in patients without MINS (89.9% vs. 28.2; $p = 0.02$).[18]

HS troponin and its relationship with the type of anesthesia and cardiac complications

This study also shows that there is a higher rate of cardiac complications in patients with higher HS troponin levels. The conditions determined as complications in this study were hypotension and bradycardia, two conditions associated with massive myocardial damage. The correlation between myocardial injury after non-cardiac surgery (MINS) and hypotension was also reported by Salmasi et al. in 2017. In this study, MINS increased the risk of hypotension which was defined as a mean arterial pressure (MAP) value below 65 mmHg or a decrease in MAP above 20%.[19]

This study shows that there is no relationship between the type of anesthesia and the amount of anesthetic drug required and changes in HS troponin levels. This finding is in line with previous research by George et al. in 2018. In this study, there was no difference in the proportion of patients who received GA and SAB between patients who experienced MINS and those who did not.[20] Clinical trial research conducted by Buse et al. (2012) also found no difference in the incidence of MINS and major adverse cardiac events in patients undergoing GA with propofol when compared with Sovoflurane.[21]

Limitation

There are two important limitations that need to be considered in interpreting the results of this study. The first limitation is that although this study shows that myocardial tissue damage is greater in high-risk operations, this study has limitations because it does not examine the influence of the level of surgical risk on the incidence of myocardial injury after non-cardiac surgery (MINS). According to the MINS definition, a patient will be said to have suffered a cardiac injury if they experience an increase in HS troponin above 14 ng/mL compared to the preoperative HS troponin value.[1] Researchers decided not to analyze MINS incidents due to limited tools and time. In the data collection process, HS troponin levels were examined 24 hours after surgery which resulted in the finding of at least an increase in HS troponin levels >14 ng/mL. Data from this study showed that only two patients experienced an increase in HS troponin levels above this value so this number was not enough to produce statistically valid findings. However, it was still found that there was a significant positive correlation between the level of surgical risk and the increase in HS troponin levels. This research can be the basis for further research by looking at changes in HS troponin levels over a wider period of time or carried out serially. One time point that can be taken is three days after surgery. One cohort study showed that there was a 7-fold increase in the risk of major cardiac events and cardiovascular mortality within 30 days in patients with peak HS troponin levels ≥60 ng/L.[22]

The second limitation in the study was that the sensitivity of the equipment used was not able to detect HS troponin levels below 1.2 ng/mL. This causes all patients with HS troponin levels below 1.2 ng/mL to only produce low output on the device. To overcome this, the researchers decided to assign all patients with low levels to have an HS troponin value of 1.2 ng/mL. As a result, the results found in this study may slightly underestimate the effect of changes in actual HS troponin levels because the lowest value obtained only reached 1.2 ng/mL. On the other hand, this condition causes the correlation of preoperative HS troponin with the level of surgical risk and cardiac complications to be slightly overestimated because

it increases the average HS troponin value in the entire sample.

Conclusion

This research shows that there is a significant positive correlation between changes in HS troponin levels and the level of surgical risk. This study shows that patients with a high level of surgical risk experienced a higher increase in HS troponin levels compared to patients who underwent surgery with a low and medium risk level.

Conflict of interests
The authors declare that they have no conflict of interest in the conduct and reporting of this study.

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None to declare.

Ethical statement
This study was conducted with the approval of the Research Ethics Committee of Universitas Airlangga Hospital, under the protocol number UA-01-23237 under the name of Mochamad Yusuf Alsagaff as the Principle Investigator. Ethical considerations were meticulously adhered to, ensuring compliance with international standards for research involving human subjects.

Informed consent
All participants provided written informed consent prior to participating in the study, without identifiable data. The consent form documented the aims, nature, procedure, benefits and risks of the study. Anonymity and confidentiality were strictly maintained.

Author's contribution
DKSCP, MYA, and BSP conceptualized and designed the study framework and methodology. DKSCP, MYA, and BSP were responsible for the data collection, curation, and visualization. All authors (DKSCP, MYA, BSP, and MRF) contributed to the drafting and revising of the manuscript and approved the final version to be published. Each author agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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