

Perioperative myocardial damage and the incidence of type 2 myocardial infarction in patients with intermediate and high cardiovascular risk

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ABSTRACT

Objective: Perioperative myocardial infarction is a major cause of morbidity and mortality in patients undergoing surgical operations. We aimed to determine the incidence of perioperative myocardial infarction in patients with intermediate- or high-risk Framingham scores.

Methods: One hundred and one patients (62 males, 39 females) over 40 years of age (mean age 72±11 years) median 73 (65-81), min- max (46-96), with Framingham risk scores of 10% or higher, and scheduled for surgical interventions in the orthopedics and urology departments of our hospital were included in the study. Patient demographics, comorbidities, blood pressures, and biochemical data were recorded. Troponin values and electrocardiographic findings were obtained during the immediate preoperative period and on postoperative day 2 and then compared. Perioperative myocardial injury and infarction were diagnosed using the third universal definition of myocardial infarction.

Results: In 44 (43%) patients, postoperative troponin values were compared with the preoperative values. In 26 (25%) patients, the changes were consistent with myocardial ischemia or damage. Alterations in troponin values with significant electrocardiogram (ECG) changes were found in 6 patients (6%).

Conclusion: The risk of postoperative myocardial damage was high in our patients with intermediate or high-risk Framingham scores. This implies that close follow-up of these patients with abnormal ECG and troponin values during the pre- and postoperative period is required.

Keywords: Perioperative myocardial infarction, type 2 myocardial infarction, cardiovascular risk

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Introduction

Myocardial injury after non-cardiac surgery (MINS) is myocardial cell damage occurring during the first 30 days following non-cardiac surgery as a result of an ischemic insult. This means there is no evidence of a non-ischemic etiology, including sepsis, pulmonary embolism, rapid atrial fibrillation, chronic high troponin values, cardioversion, etc. It is independently associated with mortality. MINS is defined as MI occurring mostly in asymptomatic patients with elevated postoperative troponin levels, electrocardiographic abnormalities, or other criteria in-

cluded in the universal definition of MI, with no evidence of a non-ischemic etiology of the elevated troponin levels (1).

The incidence of MINS was reported as 8%–19%. MI accounts for approximately 40% of MINS when non-high-sensitivity cTn is evaluated, and about 20%–30% of MINS when high-sensitivity cTn (hs-cTn) is used (1, 2).

Myocardial necrosis occurs due to the imbalance between myocardial oxygen supply and/or demand in the absence of an acute atherothrombotic plaque disruption (3). Type 2 MI is one of the most common complications of non-cardiac surgeries, with a relatively poor prognosis (4). Therefore, in high-risk patients,

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HIGHLIGHTS

- Type 2 myocardial infarction due to perioperative myocardial damage is a common condition.
- This situation should be taken into consideration while making preoperative evaluation.

routine cardiac monitoring is recommended before and 48–72 hours after the operation (5). In this study, we aimed to assess the risk of perioperative myocardial infarction among patients with moderate- or high-risk Framingham scores.

Methods**Patients**

Patients who were admitted to orthopedics and urology departments of our hospital for elective surgeries were screened. Patients who were older than 40 years and whose Framingham scores were >10% were included in the study. Framingham scores of the patients (based on age, sex, blood pressure, LDL cholesterol, HDL cholesterol, history of smoking, and diabetic status) were calculated (6). The systolic and diastolic blood pressures of all patients were measured after at least 10 minutes of rest, using a suitable mercury blood sphygmomanometer from both arms based on Korotkoff phase I and phase V sounds. Local Ethics Committee approval was obtained from our hospital's Ethics Board (Date: 27.11.2012, Decision: 28/B) and written informed consent was obtained from each patient.

Blood analysis and electrocardiogram

Patients' fasting alanine transferase, aspartate transferase, LDL-C, HDL-C, sodium, potassium, urea, creatinine, preoperative hemogram, and troponin values were recorded. Since patients were usually discharged on postoperative day 3, troponin values were obtained during the preoperative period, and 48 hours after the operation. High-sensitivity (hs) cardiac troponin was used in the evaluation of the patients. The cut-off value for the test used in our laboratory was 0.034 ng/ml. Second-day postoperative troponin values and electrocardiogram (ECG) findings of the patients were also recorded. Preoperative and postoperative second-day ECG were taken. All the ECGs were assessed by an experienced cardiologist (S.B.).

Diagnosis of MI

The diagnosis of myocardial infarction was made by studying fluctuations in the troponin level and ECG changes according to the third universal definition of myocardial infarction (7).

Statistical analysis

Statistical analysis was done with SPSS for Windows V.21.0 program. The normality of the distribution of variables was tested

using the Kolmogorov Smirnov test. Normally-distributed continuous variables were expressed as mean±standard deviation (SD), and those with non-normal distribution were expressed as median (interquartile range). Categorical data were analyzed using the Chi-square test, while quantitative data were analyzed by using Student's t-test and the Mann-Whitney U test. For the evaluation of preoperative and postoperative troponin changes, the Wilcoxon signed-rank test was used. Independent factors predicting postoperative troponin and ECG changes were determined through logistic regression analyses. P values <0.05 were considered significant.

Results

There were 62 male (61%) and 39 female (39%) patients. The demographic characteristics of the patients are shown in Table 1. In our study, the mean Framingham score of the patients was 17%. Postoperative ECG changes were seen in 45 (46%) patients (Table 2). While the most frequent ECG change was ST depression, T wave inversion, atrial and ventricular extrasystole, sinus tachycardia, newly-developed atrial fibrillation (AF), supraventricular tachycardia, and left and right bundle branch block were also observed (Table 3). Among these, ST depression, T wave inversion, LBBB, and newly-formed AF were considered as major ECG changes. In 26 patients, major ECG changes were observed.

In univariate analyses, female gender (OR=2.6, 95% CI, 1.1–5.9; p=0.022), presence of diabetes mellitus (OR=2.6, 95% CI, 1.2–6.1; p=0.024), and plasma glucose level (OR=1.0, 95% CI, 1.0–1.1; p=0.031) were significantly associated with postoperative ECG changes.

According to multiple regression analyses, female sex (OR=2.50, 95% CI, 1.04–6.01; p=0.041) and the presence of diabetes mellitus (OR=2.55, 95% CI; 1.06–4.11; p=0.030) were independent predictors of postoperative ECG changes (Table 4).

There was no difference in preoperative troponin values between the groups with and without postoperative ECG changes [0.1 (0.1–0.1) vs. 0.1 (0.1–0.2), p=0.651, respectively]. Similarly, there was no difference in the postoperative troponin values between the groups [0.2 (0.1–0.3) vs. 0.2 (0.1–0.3), p=0.861, respectively]. However, postoperative troponin values increased significantly in both groups (Table 5).

It was seen that the groups having moderate and high Framingham risk scores were similar in terms of ECG changes (p>0.05).

Postoperative troponin changes

Postoperative troponin changes were seen in 44 (43.5%) patients. In 19 patients, the troponin level was > 0.04. Patients with changes in the troponin level were significantly older (76±10 vs. 69±11, p=0.004) (Table 6). The risk of troponin change was 1.06 times higher in advanced-age patients than in younger patients (OR=1.06, 95% CI, 1.01–1.10, p=0.004). Age was the only factor predicting troponin change (p=0.01) (Table 7).

Table 1. Demographic characteristics of the patients

Parameters	Total (n=101)	Male (n=62)	Female (n=39)	P-value
Age (years)				
Mean±SD	72±11	70±11	75±11	0.022
Framingham score				
Median (IQR)	17 (12-24)	18 (14-27)	15 (11-19)	0.024
Smoking, n (%)	21 (20.8)	17 (27.4)	4 (10.3)	0.046
Systolic blood pressure (mm/Hg)				
Median (IQR)	140 (130-140)	140 (130-140)	140 (133-140)	0.251
LDL cholesterol (mg/dL)				
Median±SD	112±32	113±29	111±37	0.783
HDL cholesterol (mg/dL)				
Median±SD	43±14	43±16	43±12	0.979
Diabetes mellitus n (%)	35 (34.7)	20 (32.3)	15 (38.5)	0.529
Comorbidities, n (%)				
Ischemic heart disease	18 (17.8)	12 (19.4)	6 (15.4)	0.611
Atrial fibrillation	6 (5.9)	4 (6.5)	2 (5.1)	0.782
Hypothyroidism	3 (3.0)	1 (1.6)	2 (5.1)	0.554
Malignancy	1 (1.0)	1 (1.6)	-	-
Hypertension	93 (92.1)	55 (88.7)	38 (97.4)	0.142
Operation Type, n (%)				
Orthopedic surgery				
Femur fracture	56 (55.4)	28 (45.2)	28 (71.8)	
Gonarthrosis, osteoarthritis	5 (5.0)	-	5 (12.8)	
Coxarthrosis	3 (3.0)	1 (1.6)	1 (2.6)	
Foot amputation	1 (1.0)	1 (1.6)	-	
Urological surgery				
Prostatectomy	19 (18.8)	19 (30.6)	-	
Cystectomy	9 (8.9)	7 (11.3)	2 (5.1)	
Nephrectomy	4 (4.0)	3 (4.8)	1 (2.6)	
Nephrolithotomy	2 (2.0)	1 (1.6)	1 (2.6)	
Adrenalectomy	1 (1.0)	1 (1.6)	-	

*SD stands for standard deviation and IQR stands for interquartile range

In 6% (6/101) of the patients, ischemic ECG changes (1 LBBB, 2 ST depression, and 3 T wave inversion) were accompanied by significant changes in troponin values. No death occurred in this subgroup.

Discussion

In this study, among patients with moderate or high cardiovascular risk who underwent moderate-risk surgical operations, approximately one third had postoperative ECG findings associated with myocardial ischemia or damage, and approximately half of the patients had troponin level change. Carol et al. reported in their study, which included 187 patients who were aged ≥60 and underwent emergency orthopedic operations, postoperative ECG changes were observed in approximately

18.4% of the patients. Also, 40% of the ECG changes were accompanied by troponin change. On the other hand, in 13% of the patients with postoperative ECG changes, troponin values were normal (8). In our study, the estimated risk of postoperative ECG change was 43.5%. Among these changes, the most common one was ST depression (31%), seen in 14 patients. In 6 of the 24 patients whose ECGs showed ischemic changes, simultaneous troponin changes were also noticed. On average, in one out of every 16 patients, postoperative myocardial infarction was observed. These findings showed that troponin level changes after orthopedic and urologic operations were common, although ECG changes accompanied only half of these cases. In patients with preoperative ECG abnormalities, postoperative troponin follow-up is instrumental for the evaluation of postoperative ECG changes. In previous studies, postoperative ischemic ECG changes were reported in only half of the patients with postop-

Table 2. The factors predicting postoperative ECG changes, univariable analysis

	ECG changes (+) (n=45)	ECG changes (-) (n=56)	OR (95% CI)	P-value
Age (years)				
Mean±SD	73±12	72±11	1.0 (0.9-1.0)	0.551
Female, n (%)	23 (51.1)	16 (28.5)	2.6 (1.1-5.9)	0.022
Framingham score				
Median (IQR)	17 (12-24)	17.5 (11.5-23)	0.9 (0.9-1.0)	0.742
Comorbidities, n (%)				
Ischemic heart disease	5 (11.1)	13 (23.2)	0.4 (0.1-1.2)	0.121
Atrial fibrillation	2 (4.4)	4 (7.1)	0.6 (0.1-3.4)	0.569
Diabetes mellitus	21 (46.7)	14 (25.0)	2.6 (1.2-6.1)	0.024
Hypertension	42 (93.3)	51 (91.1)	1.3 (0.3-6.0)	0.675
Femur fracture, n (%)	25 (55.6)	31 (55.4)	1.0 (0.4-2.2)	0.981
Prostatectomy, n (%)	8 (17.8)	11 (19.6)	0.8 (0.3-2.4)	0.812
Glucose mg/dL				
Median (IQR)	123 (104-163)	114 (100-136)	1.0 (1.0-1.1)	0.031
Preoperative troponin				
Median (IQR)	0.1 (0.1-0.1)	0.1 (0.1-0.2)	0.04 (0-58)	0.390
Postoperative troponin				
Median (IQR)	0.2 (0.1-0.3)	0.2 (0.1-0.3)	3.1 (0.1-72)	0.471
Hemoglobin, g/dL				
Mean±SD	11.5±1.9	11.8±1.9	0.9 (0.7-1.1)	0.381
Creatinine, mg/dL	0.98 (0.84-1.17)	1.03 (0.81-1.38)	0.6 (0.2-1.4)	0.282

*SD stands for standard deviation and IQR stands for interquartile range, ECG - electrocardiogram

Table 3. Type of postoperative ECG changes (n=45)

	n	(%)
ST depression	14	31.1
T wave inversion	8	17.8
Atrial extrasystole	7	15.6
Ventricular extrasystole	4	8.9
Sinus tachycardia	6	13.3
Newly-formed atrial fibrillation	2	4.4
Supraventricular tachycardia	1	2.2
Left bundle branch block	2	4.4
Right bundle branch block	1	2.2
Total	45	100

erative MI. For this reason, it is thought that in order to assess MI, the evaluation of ECG without troponin values is not sufficiently sensitive. The findings of perioperative MI established in the previous studies were: non-ST elevated MI, non-Q MI, mild ECG changes, and ST depression. In our study, like in other studies, ST elevation was not frequent. As stated in the Fourth Universal Definition of Myocardial Infarction, these findings could be interpreted as the imbalance between oxygen supply and/or demand, seen in situations like perioperative hypotension. The

prevalence and incidence of coronary heart disease increases exponentially with age (9, 10). Although perioperative myocardial infarction can occur due to various reasons in younger patients, perioperative cardiac mortality and morbidity is a more common problem in advanced-age patients experiencing non-cardiac operations (11). In a study by Naughton and Feneck (12), surgical procedures were performed on elderly patients four times more than the rest of the population. Although we do not have the exact number of patients who underwent surgical operations in Europe, it is thought that this number would increase by 25%, with a 50% increase in the elderly population as of 2020 (13). In our study, the mean age of the patients was 72±11 years, and a majority of patients were of advanced age.

The Framingham Heart Study was the pioneer project to assess the risk of coronary artery disease. The study predicts the ten-year risk of coronary heart disease as follows: <10% was low risk, 10%–20% was moderate risk, and >20% was high risk (14). While most of the patients (70%) who were included in the study belonged to the moderate-risk group, the proportion of high-risk patients was 30%. However, no significant difference was found between postoperative ECG and troponin changes in the moderate- and high-risk patients included in the study. In the last 30 years, various risk indices showing the relationship between clinical features and perioperative cardiac mortality

Table 4. The factors predicting postoperative ECG changes, multiple logistic regression analysis

	OR	95% CI		P-value
		Lower limit	Upper limit	
Age	1.01	0.96	1.04	0.841
Sex, female	2.50	1.04	6.01	0.041
The presence of diabetes mellitus	2.55	1.06	6.11	0.030
The presence of CAD	0.43	0.13	1.41	0.161

CAD - coronary artery disease

Table 5. Postoperative ECG and troponin changes

	All patients (n=101)	ECG changes (+) (n=45)	ECG changes (-) (n=56)	P-value
Preoperative troponin Median (IQR)	0.1 (0.1-0.2)	0.1 (0.1-0.1)	0.1 (0.1-0.2)	0.651
Postoperative troponin Median (IQR)	0.2 (0.1-0.3)	0.2 (0.1-0.3)	0.2 (0.1-0.3)	0.861
P-value*	<0.001	0.005	0.005	

*IQR stands for interquartile range, ECG - electrocardiogram

Table 6. Postoperative troponin changes

Parameters	Troponin change (+) (n=44)	Troponin change (-) (n=57)	OR (95% CI)	P-value
Age (years)				
Mean±SD	76±10	69±11	1.06 (1.01-1.10)	0.004
Female, n (%)	19 (43.2)	20 (35.1)	1.4 (0.6-3.1)	0.411
Framingham score				
Median (IQR)	18 (11-26)	17 (12-22)	1.0 (0.9-1.1)	0.791
Comorbidities, n (%)				
Ischemic heart disease	7 (15.9)	11 (19.3)	0.8 (0.3-2.2)	0.660
Atrial fibrillation	2 (4.5)	4 (7.0)	0.6 (0.1-3.6)	0.611
Diabetes mellitus	18 (40.9)	17 (29.8)	1.6 (0.7-3.7)	0.240
Hypertension	42 (95.5)	51 (89.5)	2.4 (0.4-12.8)	0.284
Femur fracture, n (%)	28 (63.6)	28 (49.1)	1.8 (0.8-4.0)	0.145
Prostatectomy, n (%)	8 (18.2)	11 (19.3)	0.9 (0.3-2.5)	0.882
Glucose mg/dL				
Median (IQR)	122 (106-139)	117 (100-153)	0.9 (0.9-1.0)	0.821
Postoperative ECG changes, n (%)	19 (43.2)	26 (45.6)	0.9 (0.4-2.0)	0.812
Hemoglobin, g/dL				
Mean±SD	11.8±1.4	11.5±2.1	1.0 (0.8-1.3)	0.483
Creatinine, mg/dL				
Median (IQR)	0.93 (0.79-1.19)	1.07 (0.85-1.30)	0.8 (0.4-1.6)	0.541

*SD stands for standard deviation and IQR stands for interquartile range

and morbidity were developed, based on multivariate analyses of observational data. In the Lee index (1999), five independent clinical determinants of major perioperative cardiac events

were stated. These were: history of ischemic heart disease, history of cerebrovascular disease, history of heart failure, presence of diabetes, and impaired renal function (15). It was report-

Table 7. The factors predicting postoperative troponin change-Multiple logistic regression analysis

Parameters	OR	95% CI		P-value
		Lower limit	Upper limit	
Age	1.07	1.01	1.13	0.010
Sex, female	1.11	0.43	2.88	0.811
Femur fracture	0.88	0.25	3.07	0.840
Ischemic heart disease	0.85	0.28	2.56	0.772
Prostatectomy	1.66	0.41	6.72	0.471
Hypertension	2.07	0.37	11.5	0.412
Diabetes mellitus	1.88	0.76	4.64	0.171

ed that hospitalization time and the use of healthcare resources were more frequent, and the perioperative mortality was higher in patients with diabetes mellitus. Recently, attention has been focused on newly-developed hyperglycemia in diabetic patients. In patients with known diabetes, newly-developed hyperglycemia was related to a higher risk for adverse results when compared with present hyperglycemia (16). In our study, the proportion of diabetes was high in patients showing postoperative ECG changes in accordance with the literature. However, as for postoperative troponin changes, there was no significant difference between diabetics and non-diabetics. On the other hand, plasma glucose levels were higher in patients with postoperative ECG changes than in those without such ECG changes. In the perioperative period, the prognosis of patients with stable coronary artery disease having high functional capacity is good (17). Preoperative ECGs provide important prognostic data, and are predictors of perioperative ischemia in patients with ischemic heart disease (18).

Study limitations

There were several limitations in this study. The number of events was not enough to establish underlying risk factors for six patients whose ECG changes were accompanied by significant changes in troponin values. Postoperative ECG and troponin values were evaluated only on the second postoperative day. Serial monitoring and longer follow-up were not done. Another limitation was that information about the functional capacity of the subjects and the presence of heart failure and/or renal failure were not present in the data.

Conclusion

In conclusion, the occurrence of postoperative myocardial infarction in 1 out of every 16 patients who with high- or moderate-risk scores is significant. The evaluation of preoperative cardiovascular disease risk profiles and close follow-up, especially of high- and moderate-risk patients through ECG and troponin values is important.

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References

1. Botto F, Alonso-Coello P, Chan MT, Villar JC, Xavier D, Srinathan S, et al.; Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology* 2014; 120: 564–78.
2. Writing Committee for the VISION Study Investigators, Devereaux PJ, Bicccard BM, Sigamani A, Xavier D, Chan MTV, et al. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA* 2017; 317: 1642–51.
3. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al.; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation* 2018; 138: e618–51.
4. Devereaux PJ, Xavier D, Pogue J, Guyatt G, Sigamani A, Garutti I, et al.; POISE (PeriOperative ISchemic Evaluation) Investigators. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. *Ann Intern Med* 2011; 154: 523–8.
5. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators, Devereaux PJ, Chan MT, Coello PA, Walsh M, Berwanger Otavio, Villar JC, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; 307: 2295–304.
6. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; 97: 1837–47.

7. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. *Glob Heart* 2012; 7: 275-95.
8. Chong CP, van Gaal WJ, Profitis K, Ryan JE, Savige J, Lim WK. Electrocardiograph changes, troponin levels and cardiac complications after orthopaedic surgery. *Ann Acad Med Singap* 2013; 42: 24-32.
9. McDermott MM. The international pandemic of chronic cardiovascular disease. *JAMA* 2007; 297: 1253-5.
10. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2007; 115: e69-71.
11. Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery; European Society of Cardiology (ESC), Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. *Eur Heart J* 2009; 30: 2769-812.
12. Naughton C, Feneck RO. The impact of age on 6-month survival in patients with cardiovascular risk factors undergoing elective non-cardiac surgery. *Int J Clin Pract* 2007; 61: 768-76.
13. Mangano DT. Perioperative medicine: NHLBI working group deliberations and recommendations. *J Cardiothorac Vasc Anesth* 2004; 18: 1-6.
14. Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham Study. *Am J Cardiol* 1976; 38: 46-51.
15. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; 100: 1043-9.
16. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 2002; 87: 978-82.
17. Morris CK, Ueshima K, Kawaguchi T, Hideg A, Froelicher VF. The prognostic value of exercise capacity: a review of the literature. *Am Heart J* 1991; 122: 1423-31.
18. Jeger RV, Probst C, Arsenic R, Lippuner T, Pfisterer ME, Seeberger MD, et al. Long-term prognostic value of the preoperative 12-lead electrocardiogram before major noncardiac surgery in coronary artery disease. *Am Heart J* 2006; 151: 508-13.