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Increased neutrophil to lymphocyte ratio predicts myocardial injury in patients undergoing non-cardiac surgery

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ABSTRACT

Background: The neutrophil to lymphocyte ratio (NLR), has been proposed as potential indicator of cardiovascular events. Our aim was to determine the relationship between NLR and development of myocardial injury after non-cardiac surgery (MINS).
Methods: This observational cohort study included 255 consecutive noncardiac surgery patients aged ≥45 years. Electrocardiography recordings and high sensitivity cardiac troponin T (hscTnT) levels of the patients were obtained for a period of 3 days postoperatively.
Results: MINS was detected in 30 (11.8%) patients using the cut-off level of ≥14 ng/L for hscTnT. In the MINS group NLR (3.79 ± 0.7 vs. 2.69 ± 0.6, $p < 0.000$) values were higher than non-NLR group. The NLR to be independently associated with the development of MINS (OR: 11.690; CI: 4.619–29.585, $p < 0.000$).
Conclusions: NLR seems to be a simple, easy and cheap tool to predict the development of MINS in patient undergoing non-cardiac surgery.

Introduction

Nearly 1 million people die from non-cardiac surgery worldwide every year[1,2] and the most common reason for this is myocardial ischemia.[3,4] According to the American Heart Association and the European Society of Cardiology, acute myocardial infarction (AMI) is defined as ischemic symptoms and/or echocardiographic and electrocardiographic findings together with increase in levels of cardiac biomarkers (preferably troponin).[5] However, ischemic symptoms are not apparent because patients are often under analgesia and/or sedation and are connected to mechanical ventilation in the postoperative period.[4] ECG findings may be short-term, transient, or completely faint.[5] For these reasons, myocardial damage, which is determined by elevation of troponin after non-cardiac surgery, does not usually meet AMI criteria (especially in the first 72 hours).[6] On the other hand, as shown in the VISION study, "myocardial injury after non-cardiac surgery" (MINS) is a common clinical condition which is an independent indicator of increased mortality risk.[4] Therefore, simple and cheap markers are needed to determine the risk of developing postoperative myocardial injury.

Studies on atherosclerotic lesions have shown that the inflammation is important in both the onset and progression of the pathogenesis of atherosclerosis.[7] It is known that increased inflammatory markers are closely associated with increased incidence of cardiovascular events.[8] The neutrophil to lymphocyte ratio (NLR), which indicates the level of inflammatory activity, is also used as a predictor of coronary artery disease (CAD).[9] Many studies found that high NLR is associated with progression of atherosclerotic plaques, increased cardiac event rate in acute coronary syndrome, and prevalence of CAD.[10–12] Our aim is to examine the relationship between NLR and development of MINS.

Methods

Patient group

This observational cohort study included consecutive patients aged ≥45 years who underwent noncardiac surgery under general or spinal anesthesia. Those who underwent emergency surgery or reoperation, who were expected to be discharged within 24 hours, who had elevated high-sensitivity troponin cardiac troponin T (hs-cTnT) levels in the preoperative period, and who had a non-sinus rhythm on ECG or a conduction defect that can mask ischemic changes were not included in the study. Those who had chronic obstructive pulmonary disease or chronic renal failure (glomerular

Abbreviations: MINS, myocardial injury after non-cardiac surgery; NLR, neutrophil to lymphocyte ratio; hs-cTnT, high-sensitivity troponin cardiac troponin T.

Conflicts of interest: There is no conflict of interest regarding the publication of this article.

The study was performed in Haseki Education And Research Hospital.

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filtration rate (GFR) < 60 ml/min/1.73 m2), who had abnormal liver function (transaminase levels higher than 1.5 times normal), who had inflammatory disease, cancer, thromboembolic and hematological disease, who had a recent history of infection or clinical evidence of infection, who used drugs (oral contraceptives and anti-inflammatory drugs) that may affect NLR, who had abnormal thyroid function test, who had a white blood cell (WBC) count >12,000 or <4000 cells/μL, who had a recent history of cerebrovascular event, and who had AMI, severe heart valve disease and heart failure were not included in the study. Moreover, 7 patients who had impaired renal function (an increase in serum creatinine greater than 0.3 mg/dL) in the postoperative period were excluded from the study because this could affect troponin levels.

This study was approved by the ethics committee of our hospital. Then, the patients were included in the study in accordance with the stated principles in the Guidelines for Good Clinical Practice and Good Laboratory Practice in the Declaration of Helsinki. Permission was obtained after the patients were informed.

Data collection and definitions

Demographic characteristics and comorbidities of all the patients were recorded. High-sensitivity troponin cardiac troponin T (hs-cTnT) levels were measured 3 times in the postoperative period, including immediately after surgery and the morning of the first and third day. In addition, ECG changes and ischemic symptoms were recorded.

Hypertension (HT) was defined as the use of antihypertensive drugs or blood pressure greater than 140/90 mmHg. Diabetes mellitus (DM) was defined as fasting blood glucose level > 126 mg/dL or HbA1c level ≥ 6.5% together with use of oral antidiabetic drug and insulin. Body mass index (BMI) values were calculated from weight and height. Kidney functions were assessed by the CKD-EPI (the Chronic Kidney Disease Epidemiology Collaboration equation) method. The presence of CAD was assessed through medical reports of the patients. Hyperlipidemia (HL) was defined as total cholesterol level greater than 240 mg/dL and triglyceride level greater than 200 mg/dL. Being a smoker was defined as smoking at least one cigarette every day for 1 year before evaluation.

Laboratory analyzes

Blood collection was performed after a 12 hour fasting (within 24 hours preoperatively). All biochemical analyzes were performed within the first two hours after blood collection. Glucose, creatinine, total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride and C-reactive protein (CRP) levels were measured. Blood count analysis was performed using an automated cell counter (Sysmex XE-2100, Kobe, Japan). The NLR was obtained by dividing the absolute neutrophil count by the absolute lymphocyte count. In addition to routine analyzes, hs-cTnT levels were measured 3 times in the postoperative period, including immediately after surgery and the morning of the first and third day, by immunoassay method (Elecsys 2010 Troponin T hs STAT, Roche Diagnostics). For statistical analysis, the threshold value for hs-cTnT was accepted as 14 ng/L (99th percentile URL).[13]

Statistical analysis

Statistical analyzes were performed using the Statistical Package for the Social Sciences version 17.0 (SPSS, Chicago, Illinois). The continuous variables were given as mean ± standard deviation (if normal distribution) and median (interquartile range) (if not normal distribution). The categorical variables were given as percentage. The Chi-square (χ^2) test was used to compare the categorical variables between the groups. The Kolmogorov-Smirnov test was used to assess whether the variables were normally distributed. The Student-t or Mann-Whitney U test was used to compare the continuous variables between the groups acccording to whether it was normally distributed or not. In order to determine the independent predictors for MINS, the variables, which were found to be associated with it at $p < 0.1$ level as a result of univariate analysis, were included in the multivariate logistic regression analysis in which the Backward LR method is used. In order to determine the optimal cutoff value for NLR in terms of development of MINS, ROC (receiver operating characteristic) curve analysis was used. The results were evaluated within a 95% confidence interval and at a significance level of $p < 0.05$.

Results

262 patients were initially included in the study. However, 255 patients were analyzed because 7 patients with elevated creatinine level postoperatively were excluded from the study. The mean age of the patients was 61.8 ± 6.2, and 135 (52.9%) of them were male. When the distribution of non-cardiac surgeries was examined, 60 (23.5%) were orthopedic surgery, 123 (48.2%) were general surgery, 21 (8.2%) were urological and genitourinary surgery, 14 (5.5%) were neurological surgery, 14 (5.5%) were plastic surgery, and 23 (9.0%) were ear-nose-throat surgery (Table 1). Of the surgical procedures, 213 (83.5%) were performed under general anesthesia and 42 (16.5%) were performed under spinal anesthesia.

When the threshold value for hs-cTnT was based on 14 ng/L, MINS was detected in 30 (11.8%) patients. The mean age of the group with MINS was 64.03 ± 7.9, and 13 (43.3%) of them were female. There was no significant difference between the groups with and without MINS in terms of the incidence of HT, CAD and HL. The incidence of DM was higher in the group with MINS (28 (12.5%) vs. 8 (26.7%), $p = 0.037$). There was no significant difference between the groups with and without MINS in terms of gender and BMI. However, the mean age of the group with MINS was higher (64.03 ± 7.9 vs. 61.50 ± 5.9 years, $p = 0.037$) (Table 2). In the group with MINS, ECG changes were detected in 11 (36.7%) patients, including 9 (30%) T-wave change and 2 (6.7%) ST depression. Moreover, ischemic symptoms occurred in 4 (13.3%) patients in the group with MINS.

When the group with MINS was compared with the group without MINS, the neutrophil count was higher (6498 ± 819 vs. 5978 ± 998 mm^{-3}, $p = 0.007$), CRP level was higher (3.0 (1.9) vs. 2.5 (1.6) mg/L, $p = 0.020$) and NLR was higher (3.79 ± 0.7 vs. 2.69 ± 0.6, $p < 0.000$), but lymphocyte count (1857 ± 331 vs. 2038 ± 391 mm^{-3}, $p = 0.016$) was lower (Figures 1 and 2). Peak hs-cTnT level was higher in the group with MINS compared to the group without MINS (126.6 (36) vs. 7.5 (3), $p < 0.000$) (Table 3).

Table 1
Types of surgery

Orthopedic (n,%)	60 (23.5%)	
General surgery (n,%)	123 (48.2%)	
	Breast (n,%)	17 (6.6%)
	Endocrine (n,%)	25 (9.8%)
	Gastroenterologic surgery (n,%)	50 (19.6%)
	Hepatobiliary surgery (n,%)	31 (12.2%)
Urological and genitourinary surgery (n,%)	21 (8.2%)	
Neurological surgery (n,%)	14 (5.5%)	
Plastic surgery (n,%)	14 (5.5%)	
Ear-nose-throat surgery (n,%)	23 (9%)	