Prediction of Long-Term Mortality Based on Neutrophil-Lymphocyte Ratio After Percutaneous Coronary Intervention

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ABSTRACT

Background: The preprocedural neutrophil-lymphocyte ratio (NLR) is related to adverse outcomes in patients with coronary artery disease. We hypothesized that high NLR is a predictor of cardiac death after percutaneous coronary intervention (PCI). The objective of this investigation was to assess the associations of NLR, high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro-B type natriuretic peptide (NT-proBNP) with the occurrence of cardiac death after PCI.

Materials and Methods: The NLR, hs-cTnT and NT-proBNP were analyzed in 372 patients who underwent PCI. The primary end point was cardiac death.

Results: The median NLR was 2.3 (interquartile range: 1.5–4.1). There were 21 cardiac death events during a mean follow-up duration of 25.8 months. With the NLR cutoff level set to 3.3 using the receiver-operating characteristic curve, the sensitivity and specificity for differentiating between the group with cardiac death and the group without cardiac death were 85.7% and 59.3%, respectively. Kaplan-Meier analysis revealed that the higher NLR group ($\geq$3.3) had a significantly higher cardiac death rate than the lower NLR group ($<$3.3) (11.1% versus 1.4%, log-rank: $P < 0.0001$). This value was more useful in patients with heart failure (NT-proBNP $\geq$ 300 ng/L) or myocardial injury (hs-cTnT $\geq$ 100 ng/L).

Conclusions: The outcomes of the current study demonstrate that high NLR is a predictor of cardiac death after PCI, especially in patients with heart failure or myocardial injury.

Key Indexing Terms: Neutrophil-lymphocyte ratio; Troponin T; NT-proBNP; Percutaneous coronary intervention; Cardiac death. **[Am J Med Sci 2016;351(5):467–472.]**

INTRODUCTION

Inflammation is known to play an important role in the initiation and development of atherosclerosis.[1] White blood cell count and its components are typical markers of inflammation in cardiovascular disease.[2] In recent times, neutrophil-lymphocyte ratio (NLR) has been known to be a powerful systemic inflammatory indicator that is associated with death and adverse cardiac outcomes in many cardiovascular disorders.[3-11] Specifically, it has been investigated as a prognostic predictor in patients who undergo percutaneous coronary intervention (PCI).[8] This study aimed to determine the associations of NLR, high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro-B type natriuretic peptide (NT-proBNP) with the occurrence of cardiac death after PCI.

MATERIALS AND METHODS

Subjects

The current study was a retrospective investigation of 372 consecutive patients who underwent assessment of pre-PCI NLR, peak hs-cTnT and NT-proBNP before undergoing PCI because of stable angina pectoris refractory to maximal medical therapy and acute coronary syndrome between January 2010 and April 2011 at Chosun University Hospital. The protocol was approved by the Chosun University Hospital Research Ethics Committee (CHOSUN 2015-01-013). Occurrence of the main end point was analyzed after PCI to evaluate the predictive value of NLR, peak hs-cTnT and NT-proBNP in the prediction of cardiac death. The present study protocol was approved by the Chosun University Hospital Research Ethics Committee (approval CHOSUN 2015-01-013).

Measurements

NLR was calculated as the ratio of neutrophil and lymphocyte counts obtained at the time of admission. Peak hs-cTnT values (the peak levels throughout hospitalization) were determined using the Cobas 6000 (Roche Diagnostics, Penzberg, Germany) with a lower detection limit of 0.003 ng/mL. The baseline serum

NT-proBNP levels were assessed using a BN II Nephelometer Analyzer (Siemens Healthcare Diagnostics, Tarrytown, NY) within 5 hours of sample collection.

Clinical Follow-Up

The primary end point was cardiac death. Cardiac death was defined as death resulting from an evident cardiac cause, including myocardial infarction, heart failure (HF) or sudden cardiac death. Mortality data were obtained by reviewing outpatient documentation or by telephone interviews, and timing of cardiac death was confirmed by review of the electronic medical records.

Statistical Analysis

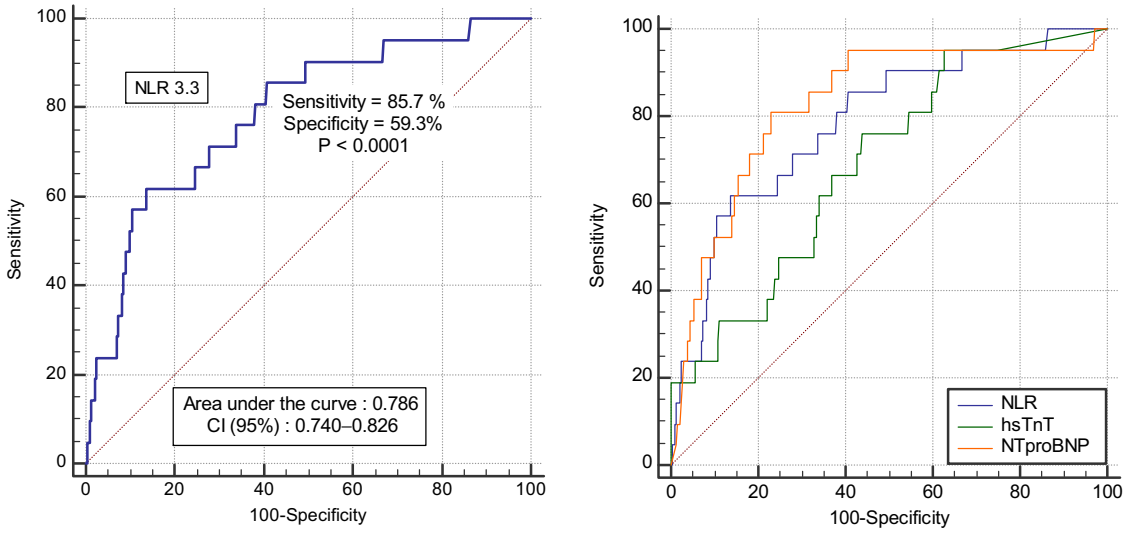
The values are expressed as mean ± standard deviation, median (interquartile range) or as numbers (percentages). The baseline features of the groups were compared using the Mann-Whitney test. Normal distribution of the data was analyzed by means of the Kolmogorov-Smirnov test. Normality was rejected for continuous variables. Categorical variables were summed up as percentages and compared using χ^2 statistics.

Receiver-operating characteristic (ROC) analysis was carried out to establish the sensitivity and specificity with 95% CIs for the cutoff value of NLR. The freedom from cardiac death according to the cutoff value of NLR was estimated using the Kaplan-Meier method, and results were compared using the log-rank test. Independent predictors of cardiac death were calculated by means of Cox proportional hazards regression. Baseline clinical and biochemical factors with a $P < 0.1$ were then entered into a forward stepwise multivariate Cox proportional hazards model. A $P < 0.05$ was regarded as statistically significant. Statistical analyses were conducted using SPSS, version 15 for Windows (SPSS Inc, Chicago, IL) and Medcalc 15.8.

RESULTS

The sensitivity and specificity at the NLR cutoff level of 3.3 using the ROC curve were 85.7% (95% CI: 63.7–97.0) and 59.3% (95% CI: 53.9–64.4), respectively, for differentiating between the group with cardiac death and the group without cardiac death (area-under-the-curve = 0.786; 95% CI: 0.740-0.826; $P < 0.0001$) (Figure 1).

The patients were stratified into 2 groups in accordance with the cutoff value of NLR < 3.3 (210 patients)



Variables	Area	95% confidence interval	P value	Comparison with NLR (Z-statistics/P-value)
NLR	0.786	0.740–0.826	<0.0001	
Peak hs-cTnT	0.662	0.611–0.709	0.0036	2.886/0.0039
NT-proBNP	0.809	0.766–0.848	<0.0001	0.474/0.6354

FIGURE 1. The ROC curve for NLR, peak hs-cTnT and NT-proBNP to predict cardiac death. The area under the ROC was 0.786 and the standard error was 0.0527. The optimal threshold point of NLR was >3.3 with 85.7% sensitivity (95% CI: 63.7–97.0) and 59.3% specificity (95% CI: 53.9–64.4).