Can the Neutrophil-to-Lymphocyte Ratio Appropriately Predict Carotid Artery Stenosis in Patients with Ischemic Stroke?—A Retrospective Study

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Background: Carotid stenosis is a risk factor in ischemic stroke. Although C-reactive protein, interleukin-6, and tumor necrosis factor-alpha are known to predict carotid atherosclerosis, they are difficult to obtain in clinical practice. By studying the association between neutrophil-to-lymphocyte ratio (NLR) and carotid artery intima–media thickening (IMT) in patients with ischemic stroke, we determined that the NLR can predict carotid stenosis. *Methods:* We selected 252 patients with acute to subacute ischemic stroke who underwent carotid ultrasonography and complete and differential blood cell count tests. We collected data on sex, age, body mass index (BMI), alcohol consumption, smoking, hypertension, diabetes mellitus, dyslipidemia, and heart disease. Male and female patients were analyzed separately. We divided the subjects into 2 groups according to carotid IMT, and compared baseline characteristics and NLR between the 2 groups. The regression analysis was adjusted for confounding factors such as age, BMI, NLR, smoking, alcohol consumption, and a medical history of hypertension, diabetes mellitus, dyslipidemia, or heart disease. *Results:* Carotid IMT tended to significantly increase with NLR and age in men and with age in women. In men, multiple linear regression analyses adjusted for confounding factors showed that NLR ($P < 0.001$) and age ($P = 0.001$) had a significant positive association with carotid IMT (adjusted $R^2 = 0.185$, root mean squared error [MSE] = 0.152). However, no parameters showed significant positive associations in women. *Conclusion:* NLR can be a clinically significant predictor of the degree of carotid stenosis in male patients with ischemic stroke. However, additional studies are required to obtain more concrete results. **Key Words:** Neutrophil-to-lymphocyte ratio—Carotid artery stenosis—Atherosclerosis—Ischemic stroke—Atherosclerosis predictor.
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Introduction

Carotid stenosis is accompanied by the narrowing or constriction of the lumen of the carotid artery. It is usually caused by atherosclerosis and is known to be a risk factor for ischemic stroke. Asymptomatic carotid stenosis is present in 50%-99% of ischemic stroke cases, and the annual incidence of stroke is approximately 1%-3.4%.[1] As carotid stenosis is considered a causal factor of ischemic stroke, it is actively studied worldwide. At present, carotid artery endarterectomy and percutaneous angioplasty of the carotid artery are considered as secondary prevention for high-risk patients with ischemic stroke.[2-5]

It has been shown recently that circulating biomarkers related to the systemic immune system, including C-reactive protein, interleukin (IL)-6, and tumor necrosis factor-alpha (TNF-α), reliably predict atherosclerosis in carotid intima–media thickening (IMT).[6] This shows that atherosclerosis is the focal expression of a systemic disease affecting medium- and large-sized arteries. In this manner, immune factors play a key role in the progression of atherosclerosis. However, immune-related biomarkers such as IL-6 and TNF-α are difficult to obtain in common clinical practice. Therefore, simpler and more convenient markers are needed.

We considered that the neutrophil-to-lymphocyte ratio (NLR) can serve as an alternative marker for predicting carotid stenosis. NLR has already been used to predict subclinical inflammation in patients with cancer[7,8] or vascular disease (including coronary artery disease and stroke).[9-13] Thus, NLR has been known as a prognostic predictor of acute stroke,[10-13] coronary artery disease,[9] and cancer.[7,8] However, to the best of our knowledge, no study has investigated the potential of NLR to predict carotid stenosis in patients with stroke.

In the present study, we determined that the NLR can serve as a predictive index for carotid stenosis by studying the association between NLR and carotid artery IMT in Korean patients with ischemic stroke.

Methods

Subjects and Data Collection

In the present study, we collected patient information for the period from August 2008 to December 2014 at Kyung Hee University Hospital and Kyung Hee University Korean Medicine Hospital. We selected 252 subjects (133 men and 119 women) who met the following inclusion criteria: (1) patients with acute to subacute ischemic stroke, (2) patients who underwent carotid ultrasonography within 1 month of stroke onset, and (3) patients who received a complete blood count (CBC) and differential blood count test at admission. Subjects with missing data were excluded.

We retrospectively collected data from subjects' medical records including sex, age, and body mass index (BMI). We also investigated the prevalence of hypertension, diabetes mellitus, dyslipidemia, and heart disease (including coronary heart disease, cardiac valve disease, heart failure, and arrhythmias) based on medical records. We obtained the maximum IMT of both internal carotid arteries from the carotid ultrasonography results and calculated the NLR based on the CBC results.

We evaluated alcohol consumption by asking patients their consumption amount per drinking event and weekly frequency of drinking during the previous 1-year period. Subjects were asked on smoking status, including how many packs of cigarettes they consume per day and how long they have been smoking (pack-year).

Physical Measurements

BMI was calculated by dividing the body weight (kg) by the height squared (m²).

CBC Measurements

CBC and differential counts were measured using an ADVIA 2120i (Siemens, Munich, Germany). The NLR was calculated by the following equation:

$$NLR = Neutrophil\ counts/Lymphocyte\ counts$$

Internal Carotid Artery IMT Measurements

The IMT of both internal carotid arteries was measured. We measured the minimum and maximum IMT in each internal carotid artery. Among the 4 IMT values (minimum and maximum in each artery), we selected the thickest as the maximum IMT of the carotid artery.

Statistical Analysis

Data were analyzed by sex. We divided the subjects into 2 groups according to the maximum IMT values: the low IMT group (maximum IMT ≤ 1 mm) and the high IMT group (maximum IMT > 1 mm). Baseline characteristics (age, BMI, NLR, alcohol consumption, prevalence of risk factors) were compared between men and women. Paired *t*-tests were performed for continuous values and chi-square tests were performed for categorical values. In the regression analysis, the dependent variable was IMT. The analysis was adjusted for the following confounding factors: age, BMI, NLR, smoking history, alcohol consumption, and a medical history of hypertension, diabetes mellitus, dyslipidemia, or heart disease.

All statistical analyses were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL), and significance was defined as a *P* value less than 0.05. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Results

Baseline Characteristics

The mean ages of the subjects were 65.91 ± 11.00 (mean ± standard deviation) and 70.45 ± 10.23 years for men and women, respectively. The mean BMI was 23.98 ± 2.93 kg/m² for men and 22.95 ± 3.20 kg/m² for women. The mean maximum IMT was 1.12 ± .43 mm for men and 1.14 ± .52 mm for women. The mean NLR was 3.27 ± 2.02 for men and 3.52 ± 3.60 for women. The mean smoking amount was 24.73 ± 25.34 pack-years for men and 1.25 ± 5.86 pack-years for women. The mean alcohol consumption was 2.57 ± 3.95 for men and 0.13 ± 0.62 for women. The prevalences of hypertension, dyslipidemia,