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ORIGINAL ARTICLE

Association of Neutrophil-to-lymphocyte Ratio with Contrast-induced Nephropathy in Patients with Non-ST-elevation Acute Coronary Syndrome Treated with Percutaneous Coronary Intervention

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Background A higher neutrophil-to-lymphocyte ratio (NLR) is associated with poor clinical outcomes in various cardiovascular diseases, including acute coronary syndromes. However, the relationship between NLR and contrast-induced nephropathy (CIN) in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) undergoing percutaneous coronary intervention (PCI) has not been known. Hence, we investigated whether admission NLR is associated with CIN after PCI in patients with NSTE-ACS.

Methods A total of 478 patients (mean age 62.8±12.6 years, and 64.2% men), who were admitted to our hospital for NSTEACS and underwent PCI with stent, were recruited. Neutrophil-to-lymphocyte ratio was calculated via dividing neutrophil count by lymphocyte count. The patients were divided into two groups: CIN (+) and CIN (-). Contrast-induced nephropathy was defined as a ≥0.5 mg/dL and/or a ≥25% increase in serum creatinine within 48-72 hours post-PCI.

Results Admission NLR was significantly higher in patients with CIN than in patients without CIN (median 5.43, interquartile range 3.23-7.73 vs. median 2.59, interquartile range 1.83-3.88, P<0.001). On multivariate analysis, NLR ≥ 3.46 value (OR=2.631, 95%CI 1.146-6.060, P=0.022), estimated glomerular filtration rate (OR=0.963, P=0.004), high sensitivity C-reactive protein (OR=1.028, P=0.016) were independent factors of CIN.

Conclusion Increased NLR is independently associated with risk of CIN in NSTE-ACS patients treated by PCI.

Keywords Neutrophil-to-lymphocyte ratio • Contrast-induced nephropathy • Non-ST-elevation acute coronary syndrome • Percutaneous coronary intervention

Introduction

Contrast-induced nephropathy (CIN) is one of the most serious complications after invasive cardiovascular procedures including percutaneous coronary intervention (PCI), and is correlated with higher in-hospital stay, increased cost, and increased short- and long- term morbidity and mortality [1–3]. The occurrence of CIN in patients who have undergone unplanned PCI because of acute coronary syndrome (ACS) is known to be higher than that in patients who received PCI

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under elective conditions [4,5]. The pathogenesis of CIN is not completely understood. But, several studies demonstrated a close relationship between the systemic inflammatory biomarkers and the occurrence of CIN, and patients with increased inflammatory marker levels being at high risk for acute renal insufficiency after contrast media (CM) exposure in stable coronary artery disease and ACS [6–11]. In addition to increased inflammatory response, previous studies have shown that reduced renal blood current, increased oxidative stress, renal parenchymal hypoxia, and direct tubular toxic effect of CM may also be responsible for the development of CIN [12–14].

The neutrophil-to-lymphocyte ratio (NLR) is a useful and reliable inflammatory prognostic marker for predicting adverse outcomes in various cardiovascular diseases. An increased NLR at the time of admission was found to be an independent predictor of short- and long- term mortality and morbidity in both non-ST-elevation-ACS (NSTE-ACS) and ST-elevation myocardial infarction (STEMI) patients [15–18]. Although the relation of the NLR to development of CIN after PCI has been well-known in patients with STEMI [9], the predictive value of the NLR for the development of CIN in NSTE-ACS is unknown.

Given the role of inflammation in damage and pathogenesis of CIN, this study aimed to evaluate the association of the NLR with development of CIN in NSTE-ACS patients who underwent PCI.

Methods

Patients

Between February 2013 and February 2015, a total of 520 patients with NSTE-ACS undergoing urgent PCI were enrolled consecutively in the study. All patients were prospectively registered. The inclusion criteria included the diagnosis of unstable angina pectoris (UA) or non-ST-elevation myocardial infarction (NSTEMI). Unstable angina pectoris and NSTEMI were described as NSTE-ACS. Patients with active infection (n=2) or previously proven systemic inflammatory disease (n=5), known malignancy (n=8), haematologic disorders (n=4), advanced stage liver (alanine aminotransferase >50 IU/L, n=4) or renal (serum creatinine >3 mg/dl, n=16) disorders and patients who died during index PCI (n=1) or within the first 72 hours of hospitalisation following PCI (n=2) were excluded from the study. After an evaluation according to exclusion criteria, the remaining 478 patients were enrolled in the study.

Patients were diagnosed as NSTE-ACS if there were appropriate clinical manifestations including chest pain or angina-equivalent suggesting UA with or without positive biomarkers of cardiac necrosis in the absence of electrocardiographic ST-segment elevation. Unstable angina pectoris was defined as angina pectoris with at least one of three features: 1) chest pain occurring at rest and usually lasting >20 min; 2) chest pain being severe and usually described as frank pain; or 3) chest pain occurring with a crescendo pattern. We differentiated between NSTEMI and UA based on cardiac troponin I with at least one value above the 99th percentile of the upper reference level [19]. Hypertension was defined as repeated systemic blood pressure measurements exceeding 140/90 mm Hg or treatment with any antihypertensive drugs for a known diagnosis of hypertension. Diabetes mellitus was diagnosed by fasting plasma glucose level >125 mg/dl, a random plasma glucose level of >200 mg/dl, or a history of diabetes mellitus, including those treated with diet, oral anti-diabetic drugs, or insulin. Hypercholesterolaemia was defined as a baseline cholesterol level of >200 mg/dl and/or a low-density lipoprotein cholesterol level of >130 mg/dl or previously diagnosed and treated hypercholesterolaemia. Current smokers were those with regular smoking in the previous six months. Family history of coronary artery disease was defined as a coronary event occurring prior to 55 and 65 years, for first-degree male and female relatives respectively.

The study protocol was approved by the hospital local Ethics Committee, and written informed consent was obtained from all patients.

Echocardiographic Examination

Transthoracic echocardiography was performed in all patients on admission by using Vivid 3 Dimension® (GE Medical System, Horten, Norway) echocardiography machine. Left ventricular ejection fraction (LVEF) of each patient was calculated by using biplane Simpson's method.

Laboratory Data and Neutrophil-to-lymphocyte Ratio

Blood samples were taken from each patient upon their admission. The serum creatinine level was measured in all patients upon hospital admission (prior to coronary angiography), daily for the three days after PCI, upon discharge from the coronary care unit and upon hospital discharge. White blood cell (WBC) and differential counts were measured at the time of admission before the patients were transferred to the catheter laboratory. The total numbers of neutrophils and lymphocytes were determined using an automated blood cell counter (XE-2100, Sysmex Inc., Kobe, Japan), and NLR were automatically calculated by loading all the data to the statistical program used. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease formula [20] and utilising the baseline creatinine level. Hs-CRP levels were also measured once the patient had been admitted to the coronary intensive care unit.

Percutaneous Coronary Intervention and Medications

Coronary angiographies were performed within the 1-72 hours after admission. All procedures were carried out using standard femoral approach (Siemens Axiom Artis zee 2011; Siemens Healthcare, Erlangen, Germany). Coronary lesions were treated with standard PCI techniques by