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The impact of admission red cell distribution width on the development of poor myocardial perfusion after primary percutaneous intervention

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ABSTRACT

Background: The purpose of this study was to evaluate the predictive value of red cell distribution width (RDW) on the electrocardiographic no-reflow phenomenon in patients undergoing primary percutaneous coronary intervention (PCI).

Methods: One-hundred consecutive patients (mean age 61.3 ± 12.8 years and male 77%) with ST-elevation myocardial infarction, who were treated with primary PCI, were analyzed prospectively. RDW and high sensitive C reactive protein (hs-CRP) were measured. The sum of ST-segment elevation was obtained immediately before and 60 min after the restoration of coronary flow. The difference between two measurements was accepted as the amount of ST-segment resolution and was expressed as ∑STR. ∑STR < 50% was accepted as electrocardiographic sign of no-reflow phenomenon.

Results: There were 30 patients in the no-reflow group (Group 1) and 70 patients in the normal re-flow group (Group 2). RDW and hs-CRP levels on admission were higher in Group 1. An RDW level ≥14% measured on admission had 70% sensitivity and 64% specificity in predicting no-reflow on ROC curve analysis. Mid-term cardiovascular events were significantly higher in Group 1. In multivariate analyses, RDW (OR 2.93, <95% CI 1.42–6.04; $p = 0.004$), and tirofiban (OR 0.16, <95% CI 0.05–0.48; $p = 0.001$) were independent predictors of no-reflow, and RDW (OR 5.89, <95% CI 1.63–21.24; $p = 0.007$), and creatine kinase-MB (CK-MB) on admission (OR 1.01, <95% CI 1.00–1.02; $p = 0.006$) were independent predictors of mid-term mortality.

Conclusions: A greater baseline RDW value was independently associated with the presence of electrocardiographic no-reflow.

1. Introduction

Early reperfusion of infarct related artery plays a critical role in preventing potential cardiac complication. The beneficial effect of the rapid restoration of epicardial coronary flow on myocardial salvage may be jeopardized by insufficient tissue perfusion, a situation referred to as 'no-reflow phenomenon' [1]. Various techniques have been used to evaluate the level of tissue reperfusion. However, ST-segment resolution, which reflects myocardial flow rather than epicardial flow, is the most frequently used method due to it being readily available and its simplicity. ST-segment resolution is also shown to be closely correlated with myocardial contrast echocardiography [2].

Adequate ST-segment elevation resolution could not be obtained (electrocardiographic no-reflow) in one-third of the patients in whom optimal restoration of epicardial flow was achieved [3], and these patients have been shown to have poor prognoses [1]. Therefore, the goal of the therapy shifted to reflow on the microvascular level in ST-elevation myocardial infarction (STEMI) patients. The underlying mechanisms responsible for no-reflow are not clearly known; however, numerous complex mechanisms are suggested in the pathogenesis of the no-reflow phenomenon, such as increased oxidative stress and inflammation [4–8].

Red cell distribution width (RDW) is a measure of the variability in the size of circulating erythrocytes (anisocytosis), and it has been utilized in the differential diagnosis of anemia [9]. Additionally, elevated RDW levels have a close relationship with inflammation [10–12] and oxidative stress [13] and are associated with poor prognoses in acute and chronic cardiac conditions [14–17].

In humans, predictive factors of no-reflow are still poorly understood. Given that the mechanism of increased RDW and

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pathogenesis of no-reflow might be similar, we hypothesized that increased RDW would be associated with the presence of electrocardiographic no-reflow. We evaluated this hypothesis in STEMI patients who underwent a primary angioplasty.

2. Materials and methods

2.1. Study population

The study population consisted of 135 STEMI patients who underwent cardiac catheterization between September 2010 and December 2010. The patients who fulfilled the following inclusion criteria were enrolled in the study: (1) presenting within 12 h (18 h for cardiogenic shock) of the onset of symptoms (typical chest pain lasting for >30 min), (2) ST-segment elevation ≥1 mm in at least two contiguous electrocardiography (ECG) leads. Seventeen patients were excluded from the study because they had not undergone primary percutaneous coronary intervention (PCI) (treated conservatively or referred to surgery); 2 patients were excluded because of new onset of complete left bundle branch block; 4 patients were excluded due to a left ventricular hypertrophy result on baseline ECG, defined as Sokolowe Lyon voltages >35 mV; 6 patients on whom we were unable to succeed in obtaining mid-term follow-up data were excluded; 4 patients were excluded due to the presence of anemia at admission; 2 patients were excluded due to administration of thrombolytic therapy before primary PCI. Finally, 100 non-anemic patients (77% male and mean age 61.3 ± 12.8) with primary PCI were included in the study. Each patient received and signed an informed consent prior to the procedure, and the study was approved by our hospital ethics committee.

2.2. Definitions

Patients' clinical characteristics, such as age and sex, diabetes mellitus (DM), hypertension, hypercholesterolemia, and smoking status, history of coronary artery disease (CAD), height, and weight were recorded. By dividing weight in kilograms by height in meters squared (kg/m^2) the body mass index (BMI) was calculated. Reperfusion time was defined as the time from onset of chest pain to the first balloon inflation. The diagnosis of DM was based on previous history of diabetes treated with or without drug therapies. Hypercholesterolemia was defined as total cholesterol of ≥200 mg/dl. Anemia on admission was defined as a baseline hemoglobin (Hb) concentration less than 13 mg/dl in men and less than 12 mg/dl in women, in accordance with the World Health Organization criteria. Multi-vessel disease was defined by a stenosis of >50% of two or more major epicardial coronary arteries.

2.3. Coronary angiography and PCI procedure

All primary PCI procedures were performed with standard femoral approach using a 7-French guiding catheter. After administration of 10,000 IU of heparin and 600 mg clopidogrel loading dose conventional wire crossing, direct stenting was implanted whenever possible; in the remaining cases, balloon pre-dilatation was carried out. The use of tirofiban was left to the operator's discretion. In each patient who was treated with tirofiban, tirofiban was administrated at the same time as the primary PCI. Non-ionic low osmolality contrast agent was used in all of the cases.

2.4. Laboratory analysis, electrocardiography and echocardiography

In all patients, antecubital venous blood samples for the laboratory analysis were drawn on admission in the emergency room. Hb, RDW and white blood cell (WBC) count, and other hematological indices were measured, as part of the automated Complete Blood Count (CBC), using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland Inc., Mervue, Galway, Ireland). High sensitive CRP (hs-CRP) was measured by using a BN2 model nephlometer (Dade-Behring).

Measurements were taken from the first ECG, which was obtained immediately before angioplasty, and from the second ECG, which was obtained 60 min after PCI. ST-segment elevation in millimeters was measured 20 ms after the J-point. The sum of ST-segment elevations was measured in leads I, aVL and V1 through V6 for anterior infarctions and in leads II, III, aVF, V5 and V6 for inferior infarctions [18]. The difference between two measurements was accepted as the resolution of the sum of ST-segment elevation and was expressed as $\sum$STR. According to the classification of Schroder [19], patients with $\sum$STR < 50% were accepted as having the electrocardiographic no-reflow phenomenon (Group 1). Patients with $\sum$STR ≥ 50% were accepted as having the electrocardiographic normal-reflow (Group 2).

Transthoracic echocardiography was performed for each patient immediately after primary PCI in intensive cardiac care unit by using a system V (Vingmed; GE, Horten, Norway) with a 2.5 MHz phased-array transducer. Recordings were taken on patients positioned in the left lateral decubitus position. The left ventricular ejection fraction (LVEF) was measured using the modified Simpson's rule [20].

2.5. Clinical endpoints

All of the patients were prospectively followed for 6-months, and the month 6 assessments were conducted either on-site or via telephone. The main endpoints evaluated in this study were the cardiovascular mortality, re infarction (re-MI), and repeat target-vessel revascularization (TVR). Cardiovascular mortality was defined as unexplained sudden death and death as a result of acute MI, heart failure or arrhythmia. Re-MI was defined as an increase in creatine kinase (CK) that was twice the last value associated with CK-MB ≥ 10% of the total CK and ST-segment re-elevations [21]. TVR was defined as the requirement of PCI or coronary surgery because of the restenosis or reocclusion of the infarct related artery (IRA).

2.6. Statistics

Continuous variables are expressed as mean ± SD. Categorical variables are expressed as percentages. To compare parametric continuous variables, the Student's *t* test was used; to compare nonparametric continuous variables, the Mann–Whitney *U* was used; to compare categorical variables, the chi-square test was used. The cumulative survival curves for mid-term cardiovascular mortality were constructed with the use of the Kaplan–Meier method, whereas differences between the re-flow groups and RDW groups were evaluated with log-rank tests. The receiver-operating characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of RDW and its respective optimal cut-off value for predicting poor coronary flow after primary PCI in patients with STEMI. Multivariate logistic regression analysis was used to identify the independent predictors of the presence of electrocardiographic no-reflow and mid-term mortality. All variables showing significance values <0.1 on univariate analysis (age, sex, hypertension, previous CAD, aspirin, b-blocker, RDW, hs-CRP, use of tirofiban, and creatine kinase-MB (CK-MB) on admission) were included in the model. In the logistic regression analysis, we adjusted the RDW level with hemoglobin and all covariates. Association between variables was tested using Spearman or Pearson