

# Association between PDW and Long Term Major Adverse Cardiac Events in Patients with Acute Coronary Syndrome



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## Background

The aim of the present study was to perform a preliminary evaluation of the potential association between platelet distribution width (PDW) and frequency of major adverse cardiovascular events (MACEs) development in an observational study of acute coronary syndrome (ACS) patients.

## Methods

A total of 679 consecutive patients with ACS (498 (73.3%) males; mean age was  $63.31 \pm 11.2$  years; study population composed of 320 patients with acute myocardial infarction and 359 patients with unstable angina pectoris) subjected to primary percutaneous coronary intervention with transradial approach (TRA) were retrospectively enrolled to the study. Tertiles were formed based on PDW levels. The associations between PDW and in-hospital and long-term MACEs were analysed.

## Results

The frequencies of in-hospital in-stent thrombosis ( $P=0.05$ ), long-term in-stent restenosis ( $P=0.005$ ) and long-term total MACEs ( $P=0.008$ ) were higher in tertiles having a high PDW value. In multivariate analyses, PDW was an independent predictor of in-hospital and long-term MACEs (odds ratio 1.081, 95% confidence interval 1.003-1.165;  $p=0.042$ ). The projected Kaplan-Meier incidence of a MACEs in the PDW tertiles groups were 12.8%, 12.1%, and 21.6% at 40 months (respectively,  $p=0.003$ ).

## Conclusions

The pre-procedural PDW may be an independent predictor of both in-hospital and long-term adverse outcomes in patients with ACS.

## Keywords

Platelet distribution width • Acute coronary syndrome • Transradial • Primary percutaneous coronary intervention • Major adverse cardiac events

## Introduction

Acute coronary syndrome (ACS) is a multi-factorial disease where multiple endogenous and exogenous risk factors are held responsible [1]. However, in the majority of the ACS cases, only some of such risk factors can be identified [1]. Thus, studies are being carried out to establish new risk factors to help predict both the diagnosis and the prognosis in ACS patients.

Platelets have an important role in the pathogenesis of ACS [2]. Plaque rupture is followed by platelet activation and thrombus formation which cause coronary artery occlusion [2]. Anti-platelet agents have a significant role in the treatment of ACS. As acetylsalicylic acid, thienopyridine and glycoprotein 2b/3a inhibitors prevent the functions of platelets, they are used in the treatment of ACS [2,3].

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Volume and activities of platelets vary [4]. Platelet size has been shown to increase once the platelet activation starts [5]. This activation increase is measured by mean platelet volume and platelet distribution width (PDW) [5]. Therefore, PDW is a marker of platelet activation [5,6]. Larger platelets are more adhesive and more prone to aggression [5–7]. An increase in platelet volume facilitates coronary thrombus formation in cases having ACS [5]. However, there are no sufficient data on the effects of PDW on the prognosis of ACS and on the frequency of major in-hospital and long-term adverse outcomes.

The aim of the present study was to evaluate the association between PDW and frequency of major adverse cardiovascular events (MACEs) development in patients with ACS.

## Method

We retrospectively evaluated the data of a total of consecutive 816 ACS patients applying to the hospital between June 2009 and January 2013. Those admitted to the hospital with symptoms starting within the previous 24 hours of admission were included in the study. Those undergoing femoral intervention or fibrinolytic treatment, having active infections, systemic inflammatory disease or end-stage liver and kidney failure, having symptoms starting before the last 24 hours, having no laboratory findings and being lost to follow-up, namely a total of 137 patients, were excluded from the study. The final study group consisted of 679 patients.

A typical chest pain lasting more than 30 min and 1 mm ST elevation in two consecutive leads at electrocardiography or newly developed left branch block was defined as acute myocardial infarction [8]. Additionally, ST-T alteration at electrocardiography and typical chest pain without any increase at cardiac enzymes was defined as unstable angina pectoris [8]. All the patients underwent a 12-electrode electrocardiography (ECG), and ischaemic ECG alterations were interpreted by senior cardiologists.

300 mg acetylsalicylic acid, 70U/Kg intravenous heparin and 300 mg loading dose of clopidogrel was administered after the initial diagnosis of ACS. All the patients underwent coronary angiography by transradial approach. Medical treatment, balloon angiography and stent, coronary artery bypass graft operation were performed based on the outcome of coronary angiography. Stent type was chosen by the operator during the operation. Maintenance therapies were performed in all patients according to the most up-to-date guidelines [9,10].

Blood samples for laboratory analysis were taken from all patients on admission. The blood samples obtained were drawn into standard test tubes containing dipotassium edetic acid (EDTA). All samples were analysed on Sysmex K-X-21N auto-analyser. Along with platelet count, mean platelet volume (MPV) showing that indicator of the platelet volume, PDW, platelet large cell ratio (PLCR) were checked too.

Follow-up data was obtained from the hospital archive, the patients and relatives of the patients. In-stent stenosis or stent

thrombosis, non-fatal myocardial infarction and cardiac related death were defined as MACEs.

## Statistical Analysis

Normal distribution of data was evaluated using the Kolmogorov Smirnov test. For stratification analysis, the study population was divided into three tertiles according to PDW (1<sup>st</sup> tertile: <12, 2<sup>nd</sup> tertile: 12-13.7 and 3<sup>rd</sup> tertile: >13.7). Continuous data was reported as mean and standard deviation while the data that are not normally distributed were reported as median; and the groups were compared using the Student's t-test or a Mann-Whitney U test. The measurements in PDW tertiles were compared with the one-way ANOVA. Categorical variables were summarised as percentages and compared using the Chi-square test. Post hoc analysis was performed by Tukey test. The association of different variables with in-hospital and long-term MACEs were calculated in the univariate analysis. The cumulative survival curve for one-year CV mortality was constructed using the Kaplan-Meier method and compared using the log-rank test. The variables having an unadjusted p value less than 0.10 were considered as potential risk factors. Then, these were included in the multivariate model. Backward elimination multivariate logistic regression analyses were utilised. A p value <0.05 was considered significant. All the statistical analyses were performed using SPSS version 15.0 (SPSS, Inc., Chicago, IL).

## Results

The study population consisted of 679 consecutive ACS patients (498 (73.3%) males, mean age = 63.31 ± 11.2 years). The baseline characteristics of the patients according to PDW tertiles are presented in Table 1. In terms of coronary risk factors, there were statistically significant differences regarding high density lipoprotein, serum glucose level and previous coronary artery disease (p for trend, p<0.048, p<0.022, p<0.035 respectively). Coronary risk factors, including current smoking, diabetes mellitus, hypertension, low density lipoprotein, did not differ among tertiles. The ratio of patients to undergo percutaneous coronary intervention (PCI) and coronary artery bypass as a result of coronary angiography was statistically similar in each tertile. However, the ratio of patients to receive medical treatment only was statistically significantly higher in tertile 1 when compared to the other groups (P=0.001).

When it comes to angiographic characteristics, there were statistically significant differences in terms of one, two, three-vessel diseases and coronary slow flow among the PDW tertiles (p for trend, p<0.003, p<0.003, p<0.0003 and p<0.004 respectively). Incidence of left main coronary artery (LMCA) disease did not show any difference among the tertiles (p=0.0643) (Table 2).

The Pearson correlation analysis revealed a statistically significant positive correlation between PDW values and three-vessel disease (r:0,321; p<0,001).

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