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ORIGINAL ARTICLE

Platelet Distribution Width and Mean Platelet Volume in Idiopathic Pulmonary Arterial Hypertension

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Background Previous studies have demonstrated that platelet activation occurs in patients with pulmonary arterial hypertension (PAH). Mean platelet volume (MPV) and platelet distribution width (PDW) are two markers of platelet activation, and have recently been recognised as risk predictors of cardiovascular diseases. This study aimed to investigate whether MPV and PDW would be useful to reflect disease severity and predict prognosis in idiopathic PAH (IPAH).

Methods MPV and PDW levels were measured in 82 IPAH patients without antiplatelet or anticoagulant treatment on admission and 82 healthy controls. Concurrent collected data included clinical, haemodynamic and biochemical variables. All patients were followed-up from the date of blood testing. The endpoint was all-cause mortality.

Results MPV and PDW were significantly higher in patients with IPAH than in age and sex-matched control subjects (11.4 ± 0.9fl vs. 10.3 ± 0.9fL and $14.3 \pm 2.9\%$ vs. $11.9 \pm 1.9\%$, respectively; $p = 0.000$). Pearson's correlation analysis revealed that MPV and PDW correlated positively with right ventricular systolic pressure, mean pulmonary arterial pressure and pulmonary vascular resistance. After a mean follow-up of 14 ± 8 months, 12 patients died of right heart failure. Receiver operating characteristic analysis showed that MPV and PDW could not predict all-cause mortality. Multivariate Cox regression analysis suggested that right/left ventricular end-diastolic diameter ratio and NT-proBNP were independent predictive parameters of all-cause mortality.

Conclusions Our results suggest that MPV and PDW were elevated in patients with IPAH. They could partly reflect disease severity, but did not predict prognosis.

Keywords Pulmonary arterial hypertension • Idiopathic pulmonary arterial hypertension • Platelet Distribution Width • Mean Platelet Volume • Prognosis

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Introduction

Pulmonary arterial hypertension (PAH) is a devastating disease characterised by increasing pulmonary vascular resistance due to vasoconstriction, pulmonary vascular remodelling, and thrombosis in situ [1]. Recent studies have suggested that platelet activation leading to the formation of thrombosis in situ may contribute to the progressive pulmonary vascular changes in patients with sickle disease and haemolysis-associated pulmonary hypertension [2,3]. Mean platelet volume (MPV) and platelet distribution width (PDW) reflect the platelet size and the variability in platelet size, and are two markers of platelet activation. Increased MPV and PDW reflect either increased platelet activation or increased numbers of large, hyper-aggregable platelets and is accepted as an independent risk factor for coronary and peripheral artery disease [4,5]. For example, high MPV is associated with higher mortality following myocardial infarction [6].

Recently, Can et al. [7,8] found that MPV was significantly higher in adult patients with idiopathic pulmonary arterial hypertension (IPAH) than in healthy control patients, suggesting that platelet activation may directly impact pathogenesis of PAH. Kaya et al.'s [9] study also suggested that MPV was significantly higher in patients with atrial septal defect and correlated with systolic pulmonary artery pressure and right ventricular diameter. However, limited by the small number of patients as well as the cross-section design, clinical implications of the increase of MPV and PDW in PAH have not been well demonstrated, especially the prognostic value of MPV and PDW in IPAH. Therefore, this study was aimed at determining whether MPV and PDW would be useful to reflect disease severity and predict prognosis in IPAH.

Materials and Methods

Study Population

Eighty-two patients with idiopathic pulmonary arterial hypertension (IPAH) were enrolled in Fuwai hospital from January 2011 to May 2013. The diagnosis of IPAH was established according to the guidelines by Galie et al. (2009) [10]. Patients with one or more of the following conditions were excluded: (1) other types of pulmonary hypertension; (2) significant left ventricular diseases, such as coronary artery disease; (3) acute heart failure; (4) chronic respiratory disorders; (5) connective tissue diseases; (6) diabetes mellitus; (7) prior targeted therapy; (8) other diseases, including chronic inflammatory processes or renal or hepatic failure. None of the participants were on anticoagulant and antiplatelet drug therapy including aspirin on admission.

Eighty-two control subjects were selected from a cohort of healthy volunteers. The mean age of control subjects was 30.8±8.7 years, and the ratio of women was 65/82 (79.3%). Informed consent was obtained from all the study participants. This study complied with the Declaration of Helsinki and was approved by the Institutional Review Board of Fuwai Hospital.

Clinical Assessment

Right heart catheterisation was performed according to standard procedures without sedation. Baseline mean pulmonary artery pressure (mPAP), mean right atrial pressure (mRAP), pulmonary vascular resistance (PVR), cardiac index (CI) and pulmonary capillary wedge pressure (PCWP) were measured. Other data collected included basic demographics, echocardiographic parameters, laboratory tests, medications and exercise tolerance as assessed by the 6-minute walk distance (6MWD) and World Health Organization functional classification (WHO-FC). All patients were followed-up by outpatient clinic interview or telephone contact from the date of blood sampling. The primary endpoint was all-cause mortality. Data were collected until the latest follow-up on June 31, 2013.

Biochemical Measurements

Blood samples were obtained in the non-fasting state. Routine biochemistry was analysed on fresh samples in the clinical laboratory of Fuwai hospital. Plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) and big endothelin-1 (Big ET-1) concentrations were determined by a commercially available assay (Biomedica, GmbH, Germany). Mean platelet volume and platelet distribution width were measured in a blood sample collected in dipotassium EDTA tubes. An automatic blood counter (XT-1800i; Sysmex Corporation, Japan) was used for whole blood. In order to prevent EDTA-induced swelling [11], the blood samples were sent to the testing laboratories and tested within 30 minutes. A technician who was blinded to patients' data performed the blood test. The reference values for MPV ranged between 9.3 and 12.5 fL. The reference values for PDW ranged between 9.0 and 17.0%.

Statistical Analysis

The data were described using mean (SD) for continuous variables and number (%) for categorical variables. Statistical differences between the two groups were analysed using an independent Student t test and the χ^2 or Fisher test for normally distributed variables. Pearson's correlation test was performed to assess correlations between variables of interest. Receiver operating characteristic (ROC) curve was generated to identify the optimal cutoff value of MPV and PDW for predicting mortality. Survival curves were derived using the Kaplan-Meier method. A univariate Cox proportional hazard regression model was used to select potential predictors of mortality. Multivariate Cox proportional hazard regression with backward elimination was used to identify independent predictors of mortality. Statistical analysis was performed by SPSS 16.0 (SPSS, Chicago, USA). $P < 0.05$ was considered statistically significant.

Results

MPV and PDW in IPAH Patients and Controls

Eighty-two patients with IPAH and 82 age and sex-matched controls were enrolled in the study. Baseline demographic,