Platelet-to-White Blood Cell Ratio: A Prognostic Predictor for 90-Day Outcomes in Ischemic Stroke Patients with Intravenous Thrombolysis

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Background: This study is aimed to investigate the relationship between platelet-to-white blood cell ratio (PWR) and 90-day outcomes in acute stroke patients with intravenous thrombolysis (IVT). *Materials and Methods:* A retrospective analysis was performed on 168 patients receiving IVT for acute ischemic stroke. Complete blood count evaluation was conducted at admission before IVT. A modified Rankin Scale (mRS) score of 3-6 at 90 days was considered an unfavorable outcome. *Results:* A total of 168 patients were included from 2013 to 2015. The mean age of the sample was 64.6 (±12.3) years, and 23.2% were women. The median baseline National Institutes of Health Stroke Scale score was 7.5 (interquartile range [IQR] 8.0) and the 90-day mRS score was 2 (IQR 2). In our multivariate logistic regression model, a PWR greater than 23.52 (odds ratio .454, 95% confidence interval: .212-.973, $P < .050$) was a predictor of 90-day outcomes. In addition, there was a significant difference in the PWR values of patients between favorable outcome and unfavorable outcome in the large-artery atherosclerosis subtype (28.241 ± 11.581 and 21.899 ± 9.107, respectively; $P = .005$). *Conclusions:* The PWR at admission predicts 90-day outcomes in ischemic stroke patients with IVT. With the easy and routine use of hemogram analysis, the PWR should be investigated in further prospective randomized controlled trials of acute stroke. **Key Words:** Outcomes—ischemic stroke—intravenous thrombolysis—platelet-to-white blood cell ratio.

Introduction

Stroke is the leading cause of mortality and morbidity worldwide which contributes to the rising costs of medical treatment and cure.[1] Prompt treatment with recombinant tissue plasminogen activator (rt-PA) by intravenous thrombolysis (IVT) has been demonstrated as the only existing early therapy to restore blood flow before irreversible damage to brain cells has occurred and to improve clinical recovery after acute ischemic stroke (AIS) in some people.[2,3] Therapeutic effects indicated by functional outcomes differ among AIS patients who underwent treatment with IVT with rt-PA.

Thromboembolism, the most common mechanism of cerebrovascular occlusion, has been considered as a complication of blood vessel injury and systemic inflammatory

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disorders.[4] Platelets play a pivotal role in the process of thrombosis after they are activated under various conditions, including atherosclerosis, inflammation, and hemorheology changes.[5,6] Activated platelets aggregate at sites of damaged endothelial cells and participate in the development of atherosclerotic lesions, which ultimately leads to intracranial bloodstream interruption by arterial thrombosis arising from plaque rupture.[7-9] Many investigators have elucidated that higher mean platelet volumes (MPVs) imply severer stroke and worse prognosis,[10-12] whereas lower platelet counts (PLTs) are presented in AIS patients, and platelets are largely expended with the formation and development of thrombosis.[13,14]

White blood cells (WBCs) are also implicated in the pathophysiology of ischemic vascular disease.[15] Leukocytes are also recruited with increased tissue damage in the ischemia area and neutrophils release various inflammatory mediators, such as proteases and reactive oxygen species, which result in endothelium damage and tissue necrosis.[16,17] Elevated peripheral total leukocyte and neutrophil counts are also associated with stroke severity on admission,[18] a higher recurrence of ischemic stroke,[19] and even poorer functional outcome.[20]

Recent studies have also elaborated on the interactions between platelets with leukocytes in ischemic stroke[21] and acute coronary syndrome.[22] This interplay has been elucidated to be correlated with ischemia–reperfusion injury.[23,24] Early prediction for prognosis of stroke patients with IVT is benefit to attracting the attention of clinicians at the time of admission, which may influence the decision of treatment to improve functional recovery. We for the first time analyzed peripheral platelet-to-white blood cell ratio (PWR) and aimed to investigate whether this ratio on admission was associated with functional outcome for AIS with intravenous (IV) rt-PA and might be an independent risk factor for stroke with the other conventional risk factors. We also investigated the association between the initial severity of acute stroke and this parameter in systematically documented patients.

Materials and Methods

Study Population

We conducted a single-center analysis reviewing the medical records of consecutive AIS patients admitted to the Department of Neurology, The First Affiliated Hospital of Wenzhou Medical University, recruited from March 2013 to December 2015, and received IVT after informed consent. The diagnosis of AIS was confirmed by computer tomography perfusion imaging or diffusion-weighted magnetic resonance imaging; Intravenous rt-PA (0.9 mg/kg up to a maximum of 90 mg) was used with 10% of the total dosage as a bolus and the rest over 1 h. No patient received antithrombotic agents within 24 hours after rt-PA infusion.

Exclusion criteria were according to the protocol of the Safe Implementation of Thrombolysis in Stroke-Monitoring Study,[25] except for the 80-year-old age limit, history of stroke, and concomitant diabetes. Patients with an onset-to-treatment time (OTT) of 3-6 hours after symptom onset were also not excluded.[26] Exclusion criteria also included patients with hematologic disorders, immunosuppressant drug users, those with an infection history within 2 weeks before onset of stroke, a stroke history within 6 months, patients with a history of malignancy, incomplete follow-up, and a baseline modified Rankin Scale (mRS) score higher than 2. One hundred sixty-eight patients were included and 22 patients excluded: five were beyond the therapeutic window, nine had incomplete follow-up, and eight had insufficient medical records.

Patients were treated following the guidelines of the Study Group for Neurologic Diseases of the Chinese Medical Association. Physical therapy and standardized rehabilitation were applied when the status of the patients were stable. The subtypes of stroke were classified as large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel disease (SVD), other determined etiology, and undetermined etiology.[27] Neuroimaging evaluation and neurofunctional assessments were taken by trained investigators who were blinded to patient distribution.

Clinical Characteristics and Functional Outcomes of the Patients

Clinical characteristics of the patients included demographic findings; medical history such as history of previous stroke or transient ischemic attack (TIA), atrial fibrillation, coronary artery disease (CAD), hypertension, diabetes mellitus, dyslipidemia, and atherosclerosis; smoking and drinking; medication before admission, which included therapy with statins, antiplatelets, and anticoagulants; thrombolysis-related information including OTT, NIHSS score on admission, and incidence of symptomatic intracranial hemorrhage; baseline information including blood pressure (BP) before treatments, baseline blood glucose, creatinine, baseline blood PLT, and WBC count; lipid profile measured within 48 hours after admission, including total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C); etiology of stroke; mRS score at 3 months; and dosage and type of statin administrated for at least 3 weeks after the stroke onset. Statin dosages in the present study were categorized into 2 levels according to the attainable reduction of LDL-C described in head-to-head comparisons, because the efficiency of various types of statin differs substantially.[28] Atorvastatin 20 mg and rosuvastatin 10 mg were determined as low dose level; atorvastatin 40 and 60 mg or rosuvastatin 20 mg were determined as high dose level. All patients had a computed tomography at admission and at 24 hours after