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Case Report

Utility of point of care assessment of platelet reactivity (using the PFA-100®) to aid in diagnosis of stroke☆

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ABSTRACT

Background: Rapid and accurate diagnosis of patients presenting with symptoms of stroke is needed to facilitate the timely delivery of proven effective treatment for patients with acute ischemic stroke (AIS). The aim of this study was to determine whether early assessment of platelet reactivity in patients presenting with symptoms of AIS was associated with a diagnosis of AIS, transient ischemic attack (TIA), or stroke mimic.
Methods: This prospective study included patients with symptoms of AIS treated at an inner-city emergency department (ED). Blood samples were obtained and assayed for platelet reactivity (quantified by closure time). Patients were grouped by discharge diagnosis into: AIS, TIA, or stroke mimic. Binary logistic regression model was used to predict the association of closure time with the final diagnosis of 1) either AIS or TIA or, 2) stroke mimic.
Results: Of 114 patients enrolled, 32 were diagnosed with AIS, 33 TIA, and 49 were diagnosed as a stroke mimic. There was no significant difference in closure times among patients with a diagnosis of AIS or TIA versus stroke mimic. A history of migraines and history of seizures were independently associated with lower odds of an AIS or TIA diagnosis (OR 0.31, 95% CI 0.10 to 0.94 and OR 0.08, 95% CI 0.01 to 0.88, respectively).
Conclusion: Closure time was not found to be a clinically reliable differentiator of patients with a diagnosis of AIS, TIA, or stroke mimic in the ED.

1. Introduction

Guidelines for emergency department (ED) stroke care recommend a door to computer tomography scan time ≤ 25 min and a door to drug time ≤ 60 min. Therefore, a prompt diagnosis of acute ischemic stroke (AIS) and the timely delivery of treatments, such as tissue plasminogen activating factor (tPA) or vascular intervention, are critical to promote favorable patient outcomes [1]. Avoidance of these AIS-specific therapies in patients presenting with transient ischemic attacks (TIA) and stroke mimics is central to patient safety as well [2]. Rapid assessment of potential AIS includes patient history, physical examination, the National Institutes of Health Stroke Scale (NIHSS), coagulation studies, and imaging but thorough assessments are time consuming and not always definitive.

To improve early diagnoses, interest has focused on the innovative diagnostic techniques to facilitate the timely triage of patients with suspected ischemic stroke. Despite the involvement of platelet activity in the pathogenesis of AIS and the proven efficacy of antiplatelet therapy in the prevention of new ischemic stroke [3,4], no study to date has evaluated the diagnostic utility of platelet reactivity to differentiate between AIS or stroke mimics. Several studies in cardiovascular research exist which compare the variability of platelet function with patients' clinical outcomes that may be applicable to a model of ischemic stroke [5-7]. Darling et al. evaluated patients with chest pain indicative of acute coronary syndromes using a measure of platelet reactivity ("closure time") and concluded that a long closure time was associated with lack of acute disease [6].

Abbreviations: ED, emergency department; tPA, tissue plasminogen activator; TIA, transient ischemic attack; ACS, acute coronary syndrome; AIS, acute ischemic stroke; PFA100®, platelet function analyzer-100.

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The aim of this study was to determine whether measurement of platelet reactivity, as indicated by an assessment of closure time, can aid in the accurate and rapid diagnosis of patients with AIS, TIA, and stroke mimic in the ED. Specifically, we examined the association of closure time with the final diagnosis.

2. Methods

2.1. Study design

A convenience sample of patients enrolled at an urban hospital (stroke center) was included. Patients, ages 18–83 years with signs and symptoms of AIS or TIA presenting within 12 h of symptom onset were eligible (July 2012 to February 2014). Excluded were those with traumatic injuries or those with a clear alternate diagnosis (such as seizures or hypoglycemia), and prisoners. Written informed consent was obtained and the study was approved by Wayne State University IRB.

2.2. Determination of platelet function

Platelet reactivity was quantified using the Siemens Platelet Function Analyze (PFA-100®) collagen-ADP test cartridge as previously described [6]. The maximum test duration for the PFA-100® is 300 s and if closure was not obtained within this period, the closure time was considered a failure and the patient was excluded from analysis.

2.3. Patient identification and enrollment

Emergency department resident and attending physicians responsible for the patient's care were queried, in real time, regarding the preliminary diagnosis (AIS, TIA, or stroke mimic), closure time results were not available to the treating team. A medical interview with the patient was conducted and chart review was performed to obtain study-related information (demographics, medical and social histories, chief complaint, vital signs, physical exam findings, NIHSS, medications, laboratory results, etc.) Patient data was collected through index hospital stay to time of discharge. A follow-up phone call was conducted at 30-days to assess for recurrent TIA, AIS, or any re-hospitalizations.

2.4. Main outcome measure

The primary outcome was the final diagnosis of AIS, TIA, or stroke mimic. The diagnosis was reviewed and confirmed by two independent investigators not having knowledge of the other's diagnosis. The final diagnosis was defined using the index hospital discharge diagnosis, any subsequent hospitalizations, and results of the 30-day follow-up call. When the two reviewers did not agree, a third study physician reviewed the records and finalized the diagnosis.

2.5. Sample size and data analysis

Closure times were stratified by each of the three final diagnosis outcome groups. Sample size calculation was based on the expectation that there would be about 1 AIS or TIA patient for every stroke mimic patient. For sample size calculation, we extrapolated means and standard deviations of closure times obtained from the similar chest pain/acute coronary syndrome study previously published (means and standard deviations not published but are available) [6]. Merino et al. found a rate of AIS and TIA at 28% each and stroke mimic diagnosis at 43% [8]. Since it was likely that closure times would not be normally distributed, sample size calculations were inflated by 15% per group. A sample size of 200 (50, 50, 100) would be adequate to detect potential differences.

Chi-Square and Fisher's exact tests for categorical data and ANOVA or Kruskal-Wallace (continuous data) were used to compare the three groups.

Logistic regression was used to assess the association of closure time with the outcome (binary) of 1) AIS or TIA compared to, 2) stroke mimic. The primary predictor was closure time and other variables considered for inclusion were those theoretically associated with the diagnosis or stroke. All observations were included in this regression with no cases dropping out. Standard model diagnostics were utilized and analyses were performed using SAS ver. 9.4.

3. Results

3.1. Enrollment and exclusions

134 patients were enrolled (Fig. 1), nineteen participants were excluded due to technical issues and one was removed because exclusion criteria were identified after consent was obtained. Enrollment was

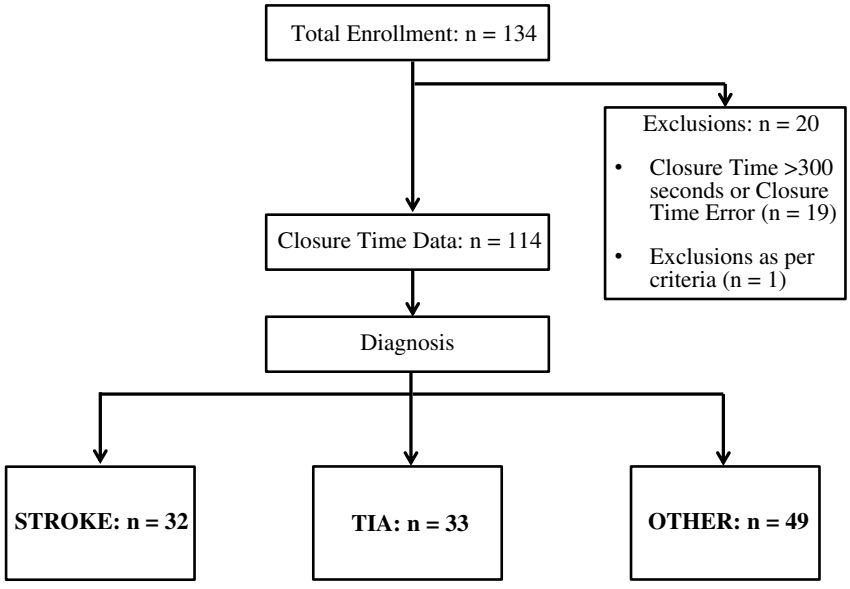

Fig. 1. Flow of Participants through the study.

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