Thrombelastography Suggests Hypercoagulability in Patients with Renal Dysfunction and Intracerebral Hemorrhage

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Background: The objective of this study was to quantify coagulopathy using thrombelastography (TEG) in patients with renal dysfunction and intracerebral hemorrhage (ICH). *Methods:* We reviewed patients admitted with spontaneous ICH between November 2009 and May 2015. TEG was performed at the time of admission. Creatinine clearance (CCr) was calculated using the Cockroft–Gault equation. Patients were divided into 2 groups based on normal (CCr ≥ 90) or reduced renal function (CCr < 90). Multivariable regression models were conducted to compare the differences of TEG components. *Results:* A total of 120 patients were included in the analysis. The normal CCr group was younger (56.1 versus 62.3 years, $P < .01$), was more often male (73.6% versus 53.7%, $P = .03$), and had higher mean admission hemoglobin (14.2 versus 13.2 mEq/L, $P < .01$) than the reduced renal function group. The 2 groups were similar with respect to antiplatelet or anticoagulant use, coagulation studies, and baseline ICH volume. Following multivariate analysis, the reduced renal function group was found to have shorter K (1.5 versus 2.2 min, $P = 004$), increased angle (66 versus 62.2 degrees, $P = .04$), increased MA (67.3 versus 62.3, $P = .02$), and increased G (11.3 versus 9.9 dynes/cm^2, $P = .04$) compared with the normal group. Mortality, poor functional outcome (modified Rankin Scale score 4-6), hematoma enlargement, hospital length of stay, and surgical interventions were not different between the 2 groups. *Conclusions:* Patients with ICH and reduced CCr display faster clotting rate and increased clot strength, suggesting that patients with renal dysfunction present with a relatively hypercoagulable state based on TEG parameters thought to reflect platelet activity.

Key Words: Thombelastography—intracerebral hemorrhage—stroke—coagulation—acute kidney injury—kidney disease—uremia.

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Introduction

Intracerebral hemorrhage (ICH) accounts for up to 30% of stroke admissions, with significant morbidity in up to 50%.[1] In the United States, there are about 17 cases per 100,000 persons per year.[2] Mortality at 1 year can vary from 51% to 65%, depending on location.[1] Major risk factors include age and hypertension.[2] Larger hematoma size, poor neurological status on presentation, hematoma expansion, intraventricular extension, the use of blood thinning medications, and brainstem location all predict worse outcomes.[2]

Renal dysfunction has been associated with both thrombotic and hemorrhagic complications.[3,4] Patients presenting with ICH and concomitant kidney dysfunction present with larger hematoma volumes[5] and increased risk of hematoma expansion.[6] Severity of renal dysfunction also correlates with worsened neurological outcome and increased mortality, especially among those with the most severe dysfunction.[7-9] Patients with end-stage renal disease (ESRD) have been reported to have 2- to 4-fold higher mortality rates from ICH compared with the general population.[10-12]

Historically, the most established test of coagulability in renal dysfunction has been skin bleeding time.[13,14] Thrombelastography (TEG) has been increasingly utilized to graphically show overall coagulation status.[15] The purpose of our study was to quantify the coagulopathy of patients presenting with ICH and renal dysfunction using TEG. As renal dysfunction impairs hemostasis via platelet interactions, identification of a quantifiable coagulopathy using TEG may have treatment implications in these patients.

Methods

Patient Selection

Patients admitted to Memorial Hermann Hospital with a diagnosis of spontaneous ICH were prospectively enrolled between November 2009 and May 2015. TEG was performed in all patients at the time of admission. Patients were excluded if ICH was secondary to other underlying etiologies, such as vascular malformation or aneurysm, vasculopathy, tumor, or trauma. Patients with a known disorder of coagulation or thrombocytopenia were also excluded. The present study was approved by the University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects.

TEG Analysis

Upon patient arrival to Memorial Hermann Hospital, a citrated vial containing whole blood (4.5 mL) was collected by nursing staff. This sample was kept at room temperature and processed within 2 hours of collection. One milliter of whole blood was pipetted (polyethylene) into a kaolin vial and gently mixed by inverting 5 times. Three hundred forty microliters was then transferred from the kaolin vial into a disposable cup within the TEG machine well. The citrate was then reversed with 20 µL of 0.2 M calcium chloride and gently mixed in the disposable cup by pipette. TEG analysis was then immediately initiated using a computerized coagulation analyzer (Model 5000; Haemonetics Corporation, Braintree, MA). The following measurements were recorded at the completion of TEG: *R* (minutes), *K* (minutes), delta (*R* – SP, minutes), α angle (degrees), maximal amplitude (MA, mm), *G* (dyne/cm^2), and LY30 (percentage). SP represents the time that elapsed from the start of the sample until fibrin is first detected. *R* is the time to clot formation, measured from the start of the sample until the amplitude reaches 2 mm. Delta indicates the time to reach top speed to initial clot formation and is the difference between *R* and SP. *K* is the time that elapsed from *R* until the clot stiffness reaches an amplitude of 20 mm. Angle (angle) is the angle between the horizontal axis and the slope of the line starting at *R* running tangent to the TEG tracing. Angle measures the rate of clot strengthening. Maximum amplitude (MA) is the maximum width of the tracing and represents maximum clot strength. MA is thought to be the parameter most representative of platelet function (thromboelastography). *G* (dyne/cm^2) is derived from MA $\{G = (5000 \times MA)(100 - MA)\}$ and is another measure of clot strength. All personnel performing TEG processing were trained to carry out the procedure. Quality assurance of the TEG machine was maintained through daily quality control procedures using normal and abnormal controls.

Study Design

Creatinine clearance (CCr) was calculated using the Cockroft–Gault equation, and patients were divided into 2 groups based on normal renal function (CCr ≥ 90) or reduced renal function (CCr < 90). Normal renal function was defined according to the National Kidney Foundation guideline value of glomerular filtration rate of 90 or higher. Patients with ESRD on hemodialysis were automatically included in the reduced renal function group. Baseline demographics, pre-hospital medications, and other laboratory data were also obtained. Those with normal renal function were compared with those with reduced renal dysfunction to distinguish differences in TEG parameters, as well as multiple outcome parameters. Poor functional outcome was defined as a modified Rankin Scale score of 4-6 at discharge.

Statistical Analysis

Continuous variables with normal distributions were summarized by mean (standard deviation), and variables with skewed distributions were summarized by median and interquartile range. Categorical variables were summarized by percentages. The differences among dif-