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Thromboelastography Indices for Predicting Outcomes after Aneurysmal Subarachnoid Hemorrhage: A Prospective Study

Hussein A. Zeineddine, MD¹, Wen Li, PhD², Peeyush Thankamani Pandit, PhD¹, Devin McBride, PhD¹, Ari Dienel, PhD¹, Glenda Torres, BS¹, James Grotta, MD³, Jude Savarraj, PhD¹, Tiffany Chang, MD¹, Huimahn A. Choi, MD¹, Pramod Dash, PhD⁴, Spiros Blackburn, MD^{1,†}

¹Department of Neurosurgery, University of Texas McGovern Medical School, Houston, Texas

²Department of Internal Medicine, University of Texas McGovern Medical School, Houston, Texas

³Clinical Innovation and Research Institute, Memorial Hermann Hospital, Houston, Texas

⁴Department of Neurobiology and Anatomy, University of Texas McGovern Medical School, Houston, Texas

Keywords

Subarachnoid hemorrhage; delayed cerebral ischemia; thromboelastography

Aneurysmal subarachnoid hemorrhage (aSAH) and the resulting delayed cerebral ischemia (DCI) carry significant morbidity and mortality. Hypercoagulability and microthrombosis are main mediators of DCI.^{1–3} Since classical laboratory tests do not provide a sensitive assessment of the coagulation status, we sought to examine the coagulation profile of aSAH patients using Thromboelastography (TEG). Published data suggests that TEG indices correlate with aSAH outcomes.^{1,2} The objective of this prospective study is to determine whether TEG predicts DCI and clinical outcomes after aSAH.

METHODS

The manuscript adheres to the AHA Journals' implementation of the Transparency and Openness Promotion (TOP) Guidelines and data is available upon reasonable request.

This was a prospective observational study. TEG indices included R, K, MA, G, and alpha angle. These were correlated to DCI and 3-month modified-Rankin Scale(mRS). Samples were collected at predetermined time points: <24 hours(T₁), 24–48 hours(T₂), 3–5 days(T₃), 6–9 days(T₄), and 10 days(T₅). A univariable analysis was conducted to determine variables associated with poor outcomes and DCI. These were validated in a multivariable

[†]**Corresponding author:** Spiros Blackburn, Department of Neurosurgery, University of Texas at Houston, spiros.blackburn@uth.tmc.edu.

Supplemental Material:
Expanded Materials and Methods and Results
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analysis which included age, Hunt-Hess grade, Fisher scale, and co-morbidities. Receiver operating characteristics (ROC) were performed to determine predictive potential. For expanded methods, see Supplementary Material.

RESULTS

201 patients were enrolled. On univariate analysis, increased Hunt-Hess grade, Fisher scale and age correlated with poor 3-month mRS (3–6). Method of aneurysm treatment (endovascular versus surgical) was neither associated with outcome nor DCI. Of 201 patients, 70 developed DCI. Univariate analysis showed significant association between various TEG parameters and DCI. Findings were lost in multivariate analysis except for R, K and angle at T4 ($p=0.03$, 0.042 and 0.023 respectively).

Of 144 patients with 3-month follow-up, 63 had poor mRS(3–6). Several indices were significantly associated with poor outcome on univariate analysis. This was lost in multivariate analysis except for higher MA values at T₁ and T₅ ($p=0.019$ and 0.043 respectively) and G at T₅ ($p=0.017$).

Using ROC analysis, TEG indices were not predictive of DCI or poor outcomes (Figure 1). 41 patients received antiplatelets (aspirin /Plavix) prior to/during the hospitalization and this did not affect mRS or DCI. Analysis excluding those patients showed that increased MA and G at T₅ predicted poor 3-month mRS with an area under the curve (AUC) of 0.75 for each. For detailed results, see Supplementary Material.

DISCUSSION

Evidence for hypercoagulability and microthrombosis after aSAH continues to accumulate. There is increased interest for evaluating platelet function and the coagulation cascade in association with outcomes and DCI. Prior studies have revealed associations between TEG indices and outcomes^{1,2} and proposed TEG as a predictive biomarker.³ These results were a promising development since TEG is a rapidly available test and widely used in ICU management. Our study reports the largest prospective cohort of aSAH undergoing serial TEG measurements in relation to mRS and DCI, and we hoped to confirm prior findings.

In our analysis, higher MA (hypercoagulable state) was associated with worse 3-month mRS. However, no parameter had a reliable predictive value for outcomes or DCI. Our data does not support the generalized use of TEG as a predictive biomarker in aSAH but suggests an association between poor outcomes and hypercoagulability. In the subset of patients that had not received antiplatelets, MA and G-values at T₅ were predictive of poor outcomes at 3 months with acceptable accuracy. This finding is of unclear significance and necessitates further studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Non-standard Abbreviations and Acronyms:

DCI	Delayed cerebral ischemia
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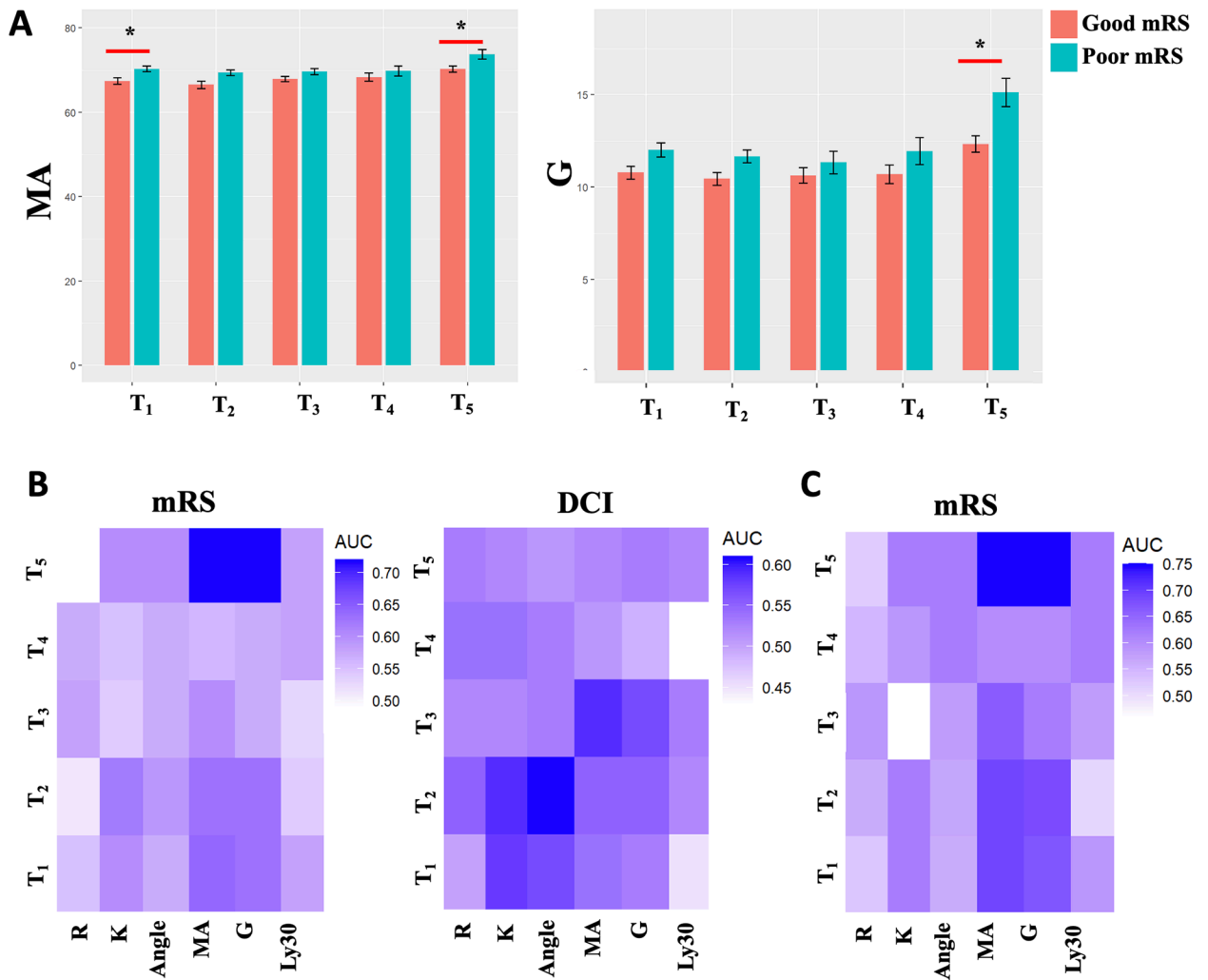


Figure 1. (A) MA values across time in relation to 3-month modified Rankin Scale(mRS). Asterix indicates significant difference on multivariate analysis. (B) Heatmap showing the area under the curve(AUC) for TEG indices across time to predict 3-month mRS(left) or delayed cerebral ischemia(right). (C) Heatmap for patients not on antiplatelets therapy