

An Early Coagulation Factor Dominant Hypercoagulability is Followed by a Prolonged Platelet-Dominant Hypercoagulability in Patients Requiring Hip Fracture Surgery

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INTRODUCTION: The risk for venous thromboembolism (VTE) after hip fracture surgery (HFS) remains high. A sub-analysis of the FAITH and HEALTH trials demonstrated a 2.5% VTE rate, with 45.3% of VTE events occurring more than six weeks post-fracture, beyond currently recommended thromboprophylaxis. Thrombelastography (TEG) is a whole-blood assay which provides a comprehensive analysis of hemostasis from clot initiation to fibrinolysis. This study used serial TEG analysis to determine the different phases of coagulation responsible for hypercoagulability after HFS.

METHODS: This is a single centre prospective cohort study of consecutive patients requiring HFS. Following institutional research ethics board approval, eligible participants who provided informed or surrogate consent underwent serial TEG analysis until 12-week follow-up. Hypercoagulability was defined by TEG parameter values beyond the reference range for clot initiation [Activated Clotting Time (ACT), Reaction-time (R-time)] and clot propagation [Kinetic-time (K-time) and Alpha-angle (α -angle)]. A hypercoagulable threshold of 65mm or greater was used for Maximal Amplitude (MA), a measure of platelet contribution to maximal clot strength. Paired sample t-tests were used to compare admission values to timepoints when TEG parameters were beyond reference ranges. One-sample t-tests were used to compare MA values and the hypercoagulability threshold at each timepoint.

RESULTS: In total, 251 patients were included with a median age of 79 (IQR 71-87) and with 66% being female. There were six symptomatic VTE events (2.4%), where significantly elevated MA occurred on POD5 (mean MA=70.7, SD=1.5; $p<0.001$) and at 2-weeks (mean MA=76.1, SD=4.2; $p<0.001$; Figure 1). In the overall cohort, ACT and R-time demonstrated shorter time to clot initiation until 2-week follow-up [(ACT mean difference =6.7sec, 95% CI=3.79-9.66; $p<0.0001$) and (R-time mean difference=0.07min, 95% CI=0.04-0.1; $p<0.0001$)], signifying early increased coagulation factor-dominant hypercoagulability. MA values (clot strength) peaked at two weeks (mean MA difference=8.87, 95% CI=7.90-9.84; $p<0.0001$), as well as α -angle (rate of clot formation; mean difference=5.75, 95% CI=5.15-6.35; $p<0.0001$). A total of 86% of patients had persistently elevated MA at four weeks (mean=67.5, SD=3.5; $p<0.0001$) and 72% remained hypercoagulable at six weeks (mean= 65.7, SD=4.6; $p=0.021$), supporting prolonged platelet-predominant hypercoagulability.

DISCUSSION: Serial TEG analysis demonstrated early hypercoagulability after HFS related to increased procoagulant factor activity, supporting early thromboprophylaxis with anticoagulants that target procoagulant factors (oral anticoagulants or LMWH). Prolonged platelet-dominant hypercoagulability (72% remained hypercoagulable at six weeks post-operatively) extended beyond currently recommended thromboprophylaxis (up to 35 days), suggesting that extended antiplatelet thromboprophylaxis may be beneficial.

SIGNIFICANCE/CLINICAL RELEVANCE: This large prospective cohort of patients requiring HFS who underwent serial TEG analysis supports the need for further investigation into optimal thromboprophylaxis regimens for this elderly patient population, who are high risk for VTE. This novel data supports that future studies targeting procoagulant factors and platelet hyperactivity may help prevent VTE after HFS.

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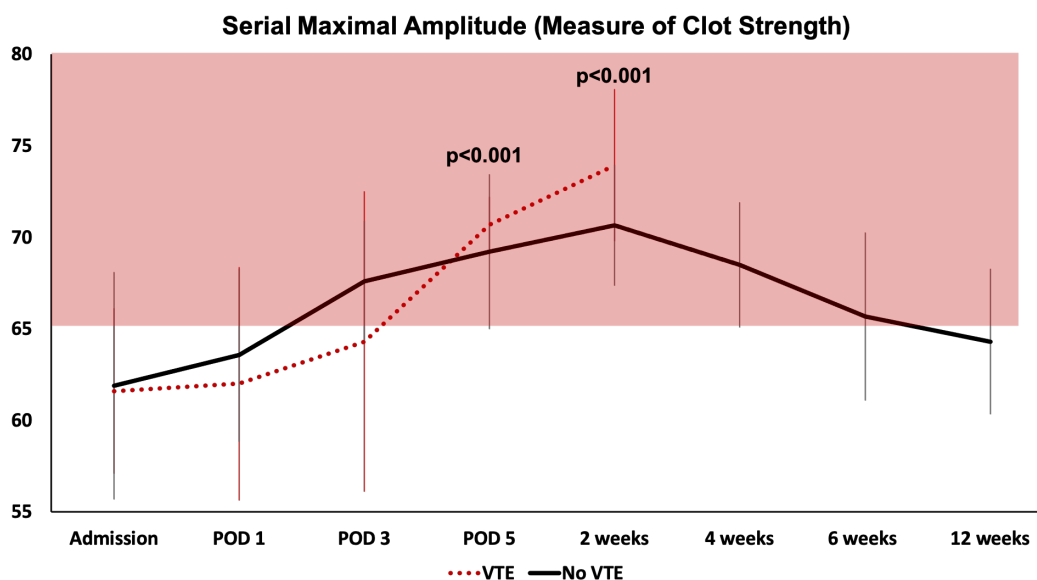


Figure 1: Maximal amplitude (MA) in patients requiring hip fracture surgery, demonstrating elevated MA in those who suffered symptomatic VTE above the hypercoagulability threshold of ≥ 65 mm (indicated by p-values) and prolonged platelet-mediated hypercoagulability until at least 6-weeks post-operatively (indicated by red shaded area). All VTE events occurred within two weeks post-operatively in this cohort.