UAMS EM Journal Club
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Evaluating the effects of Direct Oral Anticoagulants (DOACs) on TEG and whether TEG can be reliably used to detect patients anticoagulated with DOACs.

Clinical Takeaways:
Overall, after evaluating both of these studies, we need further information. We do not yet have a clear answer if TEG can be reliably used to measure the current effects of the DOAC being experienced by the patient. Overall, the use of this in patients would fit into a narrow population of patients who are currently stable with some bleeding, but at risk of decompensation.

PICO Question:
P: Adult patients on a DOAC
I: Alterations in TEG values (R time and Amplitude) due to DOAC therapy
C: concentration of the drug in blood and Anti Xa levels
O: Prolongation of R time or decreased Amplitude on TEG

Trial 1:
Evaluation of direct oral anticoagulant use on thromboelastography in an emergency department population
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https://pubmed.ncbi.nlm.nih.gov/34952323/

The Basics:
Retrospective, single center cohort study examining DOAC effects of TEG in patients with active bleeding. Both medical bleeding and trauma bleeding were included. Primary end point was if TEG values were affected by the DOAC therapy.

Methods:
This study was only able to include 40 out of 420 screen patients over a 2-year period that met their inclusion criteria. Their inclusion criteria were patients between the ages of 18-89, reported current DOAC use and was documented in the medical record, and had a TEG performed during that encounter. Included patients on rivaroxaban, apixaban, dabigatran, or edoxaban. Patients were included if their last dose was within 12 hours from collection of their TEG assay for once-daily-dosing regimens or within 6 hours from collection of their TEG assay for twice-daily- dosing DOAC regimens. The primary outcome for this study was if DOAC therapy affected TEG measurements. Particular interest was placed on the R time and maximum amplitude. Secondary outcomes were to evaluate for TEG alterations when patients

were known to be within the peak time since taking their last dose (6 hours for BID dosing and 12 hours for daily dosing). Descriptive analysis was performed and TEG values were reported against the standards for their hospital.

Results:
Of the 40 patients included in the study, 20 were trauma patients and 20 were medical patients. These patients were on DOACs for a variety of reasons. Patients in this study were on either Apixaban or Rivaroxaban. For both of these DOACs, their data showed that only 5/40 had a prolonged R time and 1/40 had a decreased maximum amplitude. All other TEG parameters including kinetics, alpha angle, and lysis time were within the normal range for their institution. This data was further separated into 16 of the 40 patients that had an anti Xa level drawn during the same encounter. Of the 16 patients, only 4 had an elevated R time, and all other TEG parameters were within normal limits. Overall, the authors concluded that DOAC use did not show any correlation with TEG values.

Limitations:
Small sample size and the retrospective nature of this study made it difficult to draw many concrete conclusions. Study was also limited by its lack of comparison to a standard which makes it difficult to develop sensitivities, specificities and likelihood rations for this diagnostic test. Further study with larger sample sizes and adequate comparison to a reference standard is needed to further delineate the usefulness of this diagnostic test in patients on a DOAC.

Trial 2

Measurement of Anticoagulation in Patients on Dabigatran, Rivaroxaban, and Apixaban Therapy by Novel Automated Thrombelastography ***TH Open. 2021 Nov 9;5(4):e570-e576. doi: 10.1055/a-1692-1415. PMID: 34984316; PMCID: PMC8718262.***

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/34984316/

The Basics: This article attempted to assess thromboelastography as a means for evaluating DOAC concentration in serum by using the correlation of TEG Reaction time (R-time) and blood DOAC levels noted on previous studies. Additional assessed outcomes were the sensitivity, specificity, and negative predictive value (NPV) of the R-time for measuring clinically useful DOAC concentrations. The article marked DOAC concentration cutoffs of 30ng/mL for urgent invasive procedures, 50ng/mL for antidote administration, and 100ng/mL for thrombolysis in stroke as clinically relevant concentrations to be considered. The study was performed at 5 clinical sites in the United States from the period of August 2016 to September 2017.

Methods: Blood samples from 189 patients were collected at a random time point during either outpatient clinic visit or inpatient presentation in 2 separate groups those on DOACs (165 patients) and those not on DOACs (24 patients). Of those evaluated 50 patients were on Apixaban, 62 patients were on Dabigatran, and 53 patients were on Rivaroxaban. Up to 20mL of blood was obtained from each patient and subsequently evaluated via thromboelastography. R-time and DOAC serum concentration correlation coefficient values were obtained and considered strong if >0.8.

Inclusion Criteria:

-Patient had to be 18 years of age or greater for both DOAC & non-DOAC groups (the only inclusion criteria for the non-DOAC group)

-If in the DOAC group the patient had to be on DOAC doses recommended by the manufacturers for treatment of atrial fibrillation, venous thromboembolism, or thromboembolism prophylaxis for minimum of 7 days uninterrupted.

Exclusion Criteria:
-Patients less than 18 years of age

-DOAC group: genetic bleeding disorders (known or subsequently discovered), DOAC dosage outside of manufacturer's recommended range, heparin or low molecular weight heparin (LMWH) administered within 7 days prior to blood draw, any other FDA approved or experimental anticoagulant, bruising, wounds, or scarring in the area of venipuncture.

-Non-DOAC group: Medical evidence of atrial fibrillation, deep vein thrombosis, or pulmonary embolism. Genetic bleeding disorders (known or subsequently discovered), on any medication containing heparin or LMWH within 7 days, on a DOAC or other anticoagulant, on any medications known to affect coagulation status, strict vegan diet, bruising, wounds, or scarring the area of venipuncture.

Results:

The DOAC group had a mean age of 71 years and 41% female, the non-DOAC group had a mean age of 48 years and was 67% female. R-times and DOAC levels showed correlation coefficients of 0.93 for Dabigatran, 0.92 for Rivaroxaban, and 0.84 for Apixaban. Among the 50 patients on apixaban, one patient had a levels of 29 ng/mL or less, one patient between 30 and 49 ng/mL, and six patients between 50 and 99 ng/mL. Among the 53 patients on rivaroxaban, 4 had a level of 29 ng/mL or less, 7 had between 30 and 49 ng/mL, and 17 had between 50 and 99 ng/mL. Among the 62 patients on dabigatran, 2 had a level of 29 ng/mL or less, 9 had between 30 and 49 ng/mL, and 17 had between 50 and 99 ng/mL. The sensitivity, specificity, positive likelihood

ratio , negative likelihood ratio , and NPVs for the R-time to detect DOAC concentrations of 30, 50, and 100 ng/mL were then determined.

Limitations/Bias: Noted limitations of this study include low sample size which lead to evaluation of one group (Edoxaban) having only 4 patients total and the Apixaban data for levels between 30-40 ng/mL included only 1 patient. Furthermore, the study did not account for time of DOAC intake to the time the sample was collected.