

The utility of INR to predict ischemia in patients on warfarin

Cathy Cao, PharmD; Ashley Martinelli, PharmD; Brian Spoelhof, PharmD, BCPS; Rafael Llinas, MD; Elisabeth Marsh, MD

Objectives: Stroke can occur in patients on warfarin despite anticoagulation. A therapeutic INR is typically defined as 2-3. Patients with low INRs should theoretically be at greater risk of an ischemic event, and those therapeutic at lower risk; however, data is scarce regarding the utility of INR to predict ischemia over ischemic stroke mimics in patients on warfarin presenting with acute neurologic symptoms. This study was designed to evaluate the association between INR and likelihood of ischemic stroke in patients presenting to the Emergency Department with acute neurologic symptoms who were on warfarin prior to admission. We further evaluated the predictive value of INR in determining the likelihood of ischemic stroke.

Methods: Patients were identified using the acute stroke registry at a Primary Stroke Center from January 2013 to December 2014. All adult patients undergoing evaluation for acute stroke with prior documented use of warfarin and an INR level at presentation were included. Data were collected regarding patient demographics, medical co-morbidities, stroke severity, reason for anticoagulation, and laboratory studies including INR. Student's t-tests and chi square analysis were used to evaluate factors associated with increased likelihood of ischemia (stroke or transient ischemic attack) versus mimic. Significant results were entered into a multivariable regression analysis. Sensitivity and specificity analyses were conducted to determine the negative predictive value of INR for ischemic stroke risk.

Results: 116 patients were included; 46 were diagnosed with ischemia, 70 were diagnosed as mimics. 75% of patients were on warfarin for atrial fibrillation versus 25% for venous thrombosis. There was a significant difference in mean INR for ischemic patients versus mimic patients [1.7 (subtherapeutic) versus 2.8 (therapeutic); $p < 0.001$]. In multivariable analysis, subtherapeutic INR ($p < 0.001$) and atrial fibrillation as an indication for anticoagulation ($p = 0.014$) were statistically significant predictors of ischemia. In patients with an INR ≥ 2 the chances of not having ischemia was 79%. No ischemic events were observed at INR values of ≥ 3.6 . The area under the curve for predicting ischemia using INR and indication for anticoagulation was high at 0.77.

Conclusions: Initial subtherapeutic INR and atrial fibrillation as an indication for warfarin are strongly associated with ischemic events in patients on warfarin presenting with acute neurologic symptoms. We conclude that ischemia is uncommon in patients on warfarin when the INR is therapeutic and highly unlikely with an INR greater than 3.6.