**Retrospective Analysis of Warfarin Induced Calcification in Patients with Aortic Stenosis Requiring Anticoagulation for Atrial Fibrillation or Atrial Flutter**

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**Background:**

Calcific aortic valve stenosis (AS) is the most prevalent valvular heart disease in high-income countries. About 30% of AS patients require oral anticoagulation for concomitant conditions such as atrial fibrillation, however, there is limited evidence regarding the effect of anticoagulation on the progression of AS.1 The 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) atrial fibrillation guidelines recommend direct oral anticoagulants (DOACs) over vitamin K antagonists (VKA) such as warfarin, however some patients may remain on warfarin for a variety of reasons (primarily due to cost).2 Retrospective evidence has associated the use of warfarin with increased aortic valve calcification in humans3, due to the inhibition of vitamin-K dependent osteocalcin and matrix Gla protein, an inhibitor of vascular calcification. To date, only one small study has been published that evaluated rivaroxaban versus warfarin use in this patient population.

**Objective**:

This study aims to further elucidate the effects of warfarin on progression aortic valve calcification in patients with mild to moderate AS requiring anticoagulation for atrial fibrillation (AF) or atrial flutter (Aflutter), and will include patients receiving any DOAC (apixaban, rivaroxaban, dabigatran, edoxaban) compared to warfarin.

**Methods**:

This is a retrospective cohort study that will evaluate patients at UNC REX Hospital with mild to moderate AS requiring anticoagulation for AF or Aflutter from July 1, 2015 to August 1, 2021. Patients will be included if they are at least 18 years old with mild to moderate AS, have an ECHO and/or multidetector CT (MDCT) repeated at least 6 months after diagnosis, and taking warfarin or a DOAC for AF or Aflutter for at least 1 year. The primary outcome is hemodynamic progression of aortic stenosis measured by progression of peak aortic jet velocity (Vpeak) on Doppler echocardiography. Secondary outcomes include anatomic progression of aortic stenosis measured by progression of aortic valve area (AVA) on MDCT, and hemodynamic obstruction measured by mean pressure gradient. Differences in the independent variables were estimated using t-tests, chi-square tests, or Fisher exact tests according to the metric and distribution across variables. Linear regression models for the bivariate and multivariate effects of treatment of the primary and secondary outcomes were performed, controlling for demographics and for independent variables related to treatment. All significant tests were two-tailed at p<0.05.

**Results**:

150 patients were reviewed, 75 taking warfarin and 75 taking a DOAC. For the primary outcome, warfarin was associated with a 7.05% increase in Vpeak (p=0.19). For the secondary outcomes, warfarin was associated with 2.92% increase in mean gradient (p=0.02) and 0.13% decrease in AVA (p=0.34).

**Conclusion**:

This study suggests that use of warfarin appears to worsen the progression of AS. The use of warfarn was associated with a statistically significant difference in AVA compared DOACs. Due to study limitations including small sample size, retrospective review, lack of stratification based on time on anticoagulation or time between ECHOs, and not controlling for all potential confounders, definitive conclusions cannot be made. This study is, however, hypothesis generating in which anticoagulant may be best for patients with AS.