Prevalence of Risk Factors and Low Response to Antiplatelet Medications in the Prospective Randomized On-X Anticoagulation Clinical Trial (PROACT)

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Objective - PROACT was conducted in North America (NA) to test safety and efficacy of alternative anticoagulation in aortic valve replacement (AVR) patients with the On-X valve. The study segregated patients by clinical and hematologic risk factors for thromboembolism (TE) and by antiplatelet response. Prevalence of these factors in this population is heretofore unreported.

Methods - AVR patients were recruited and separated into a high risk and low risk group by clinical risk factors for TE and hypercoagulability and by antiplatelet response. Clinical factors included atrial fibrillation, enlarged left atrium (>50mm), low ejection fraction (<30%), spontaneous echo contrasts, ventricular aneurysm, women on estrogen therapy, clinical history of neurological events or peripheral/carotid vascular pathology. Factor V Leiden mutation, prothrombin mutation, antithrombin III activity, proteins C and S, factor VIII activity and elevated low density lipoproteins (LDL) were tested for hypercoagulability. Antiplatelet response was measured by Accumetrics P2Y12 for clopidogrel (≥35% inhibition), and urine thromboxane (≤298 pg/µl) for aspirin after at least 1 week on 75mg/day clopidogrel and 81mg/day aspirin. The rates of occurrence of these conditions in the AVR high risk group are reported.

Results - The study enrolled 425 high risk patients of which 375 were randomized to either test (185 at INR target of 1.5-2.0) or control (190 at INR target of 2.0-3.0). Atrial fibrillation was uncommon (4.5% - 19). The most common clinical factor was history of vascular pathology (14.1% - 60) which is similar to the occurrence of LDL (18.5% - 44/237) and indicative of the prevalence of obesity in NA. Reduced antithrombin III activity was the most common hypercoagulability factor (22.5% - 55/244). The degree to which there was a poor response to antiplatelet medication, clopidogrel (47.1% - 106/225) and aspirin (80.4% - 164/204), was astonishing.

Conclusion - The number of patients randomized to the high risk AVR arm of the trial because of poor antiplatelet therapy response alone was surprising. Antiplatelet drug response is important to consider for safe alternate drug therapy in a mechanical valve patient population because of the prevalence of poor responders.