Mechanical Valves

The HealthTrust Physician Advisor Network provided insight on the use of Mechanical Valves and market trends.

Overview

Prosthetic heart valves are used to replace diseased or damage native or prosthetic valves.[1,2] They are classified into three categories (mechanical heart valves, bioprosthetic valves and homografts) and placed via an open surgical procedure or transcatheter aortic valve replacement (TAVR). The goal for implanting a prosthetic valve is to have it function like the native valve it has replaced, while reducing risk for complications to the patient. Mechanical valves consists of a ring and two pyrolytic carbon leaflets and include a fabric sewing ring. Mechanical valves are often the valve of choice in younger patients without contraindications to blood thinners because of its durability. The metal surface on these valves increases risk for blood clots which necessitates lifetime anticoagulant therapy. This is typically achieved through the use of a vitamin K antagonist (VKA), such as warfarin, with routine blood draws to maintain a target international normalized ratio (INR) and lifestyle modifications.[1,2]

The potential for abnormal flow in the vicinity of heart valves may create a favorable environment for thrombus formation through imposing forces on cell elements causing cell destruction and changes in the frequency of contact (increased contact time between blood elements) leading to hemolysis and platelet activation.[3,4] Adjustments have been made to the structure of mechanical valves to reduce thrombus formation, including the creation of a bileaflet valve to reduce shear and leakage and the use of pyrolytic carbon to reduce platelet adhesion. Thrombus development on blood contacting medical devices are composed of fibrin and platelet aggregates, making antiplatelet agents and/or anticoagulants the primary mode of prevention in this space.[3,4]

Clinical Evidence

As early as 2010, a randomized trial investigated the use of low intensity oral anticoagulant therapy in bileaflet mechanical aortic valve preplacement (LOWERING-IT).[5] A proposed target INR of 1.5-2.5 was found to be safe and feasible when compared to the standard target of 2.0-3.0 in low-risk patients receiving bileaflet aortic mechanical valve replacement. This study did not utilize one specific brand of valve.[5]

A meta-analysis evaluating 6 randomized controlled trials representing 5,497 patients with bileaflet mechanical valve placement found lower INR targets were associated with significantly less bleeding, 22% vs 40% (p=0.03), with no difference in thromboembolism (p=0.20) or mortality (p=0.047).[6] Several factors negatively impacted confidence in the results: the number and size of studies available were limited, and the studies reviewed had variable definitions of low-intensity anticoagulation and bleeding, introducing a risk of bias and imprecision.[6]

One industry sponsored, prospective, randomized, multi-center trial (PROACT) investigated the safety and effectiveness of managing a mechanical valve with a lower INR target (1.5-2.0) after an initial three months of standard VKA therapy.[7] The test group experienced significantly lower major bleeding rates (1.57% vs 3.87%pt-yrs; p=0.007) with similar incidence of stroke, transient ischemic attack, total neurologic events and all-cause mortality. This study was used to achieve FDA approval for INR of 1.5-2.0 with low dose aspirin after 3 months of standard anticoagulation for the studied mechanical valve only.[7]

The RE-ALIGN (Randomized, Phase II Study to Evaluate the Safety and Pharmacokinetics of Oral Dabigatran Etexilate in Patients after Heart Valve Replacement) study was terminated prematurely due to excessive thromboembolic events and bleeding in the dabigatran arm.[8] The study was attempting to determine safety and efficacy of a direct thrombin inhibitor versus the standard dose of VKA.[8]

The PROACT Xa trial is a randomized, phase II, industry sponsored trial with 1,000 participants enrolled.[9] This study is seeking to demonstrate safety and efficacy of the use of apixaban (dosage 2.5 mg and 5 mg) in patients with placement of one specific valve against a VKA control group. Primary completion of the study is anticipated in November, 2022, with estimated completion date of July, 2024.[9]

Clinical Practice Guidelines

The 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease recommends targeting an INR to a lower goal of 1.5-2.0 along with low dose aspirin (81 mg) after 3 months of standard warfarin dosing with low dose aspirin in patients without risk factors who receive a mechanical On-X aortic heart valve.[10] The AHA/ACC guidelines declare insufficient evidence to support the use of novel oral anticoagulant (NOAC) therapy in patients with mechanical heart valves until the results of the RE-ALIGN study can be explained.[10]

A historical review and analysis of anticoagulation therapy in mechanical valve replacement published in the December 2019 issue of *Circulation* pointed to the lack of high quality evidence and the differences between current guideline recommendations as contributing factors in the uncertainty surrounding optimal anticoagulation intensity.[11] Difficulty in managing patients on VKAs due to pharmacodynamics, pharmacokinetic interactions, patient adherence and limited use in certain populations (intolerance, pregnancy) are all challenges to this treatment regimen. In considering the use of warfarin at a lower target, it is important to evaluate the patient's ability to adhere to the treatment regimen and perform home monitoring of INR as use of a lower target does not leave much latitude for falling below the therapeutic level.[11]

Physician Advisor Insight: January-February, 2021

A panel of Cardiovascular/Thoracic Surgeons within our HealthTrust Physician Advisor Network offered the following insight with regard to mechanical valves.[12]

- Valves are individualized to the patient according to age, physiologic condition, need for anticoagulation, location, preference and other factors.
- Mechanical valve preferences:
    - Most commonly used in the aortic or mitral position
    - Typically used in younger patients less than 60-65 years of age
    - May be preferred in patients who are already on anticoagulant for another reason
    - Preferred in patients with a very small aortic annulus
    - **Not** used in patients who have a contraindication to anticoagulation
- Physician selection may be based on valve performance, lowest possible hemodynamic obstruction (valve gradient), training, comfort level with current device, or supplier support
- The Abbott/St. Jude valve is "tried and true" and is most widely implanted due to:
    - Low profile device
    - Physician comfort level with the device and training
- The On-X valve is associated with low gradient and lower target ranges for INR
    - Target INR is a possible driver for increased utilization in the market
    - Some physician advisors felt the On-X was more difficult to insert due to size and design and did not see the lower target INR as a significant advantage
    - A market shift is anticipated depending on the results of the current trial evaluating direct oral anticoagulant (DOAC) use over warfarin in this mechanical valve
- TAVR
    - Responsible for the decline in aortic mechanical valve usage
    - TAVR has exceeded surgical aortic valve replacement (SAVR) since 2019, with growth anticipated to continue as technology advances
- During a conversion, understanding supplier relationships may be important.

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