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Bioprosthetic reoperative aortic valve replacement in patients under 50

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ABSTRACT A clinical decision report using:

Chan V, Lam BK, Rubens FD, et al. Long-term evaluation of biological versus mechanical prosthesis use at reoperative aortic valve replacement. *J Thorac Cardiovasc Surg.* 2012;144(1):146-151. <https://doi.org/10.1016/j.jtcvs.2011.08.041>

for a patient considering reoperative aortic valve replacement.

Keywords: *reoperative, aortic valve replacement, bioprosthetic, mechanical*

Clinical-Social Context

Mr. Adam Weiss (pseudonym) is a 47-year-old man with a past medical history of thoracic aortic dissection secondary to TGFBR1 gene mutation with a mechanical aortic valve replacement.¹ He had recently been admitted to a satellite hospital for evaluation of gastrointestinal bleeding and was discharged with the intention of outpatient follow-up. He presented to the Emergency Department with chest pain which was determined to be non-ischemic and on further examination was found to have a hemoglobin drop. He endorsed recent episodes of melena and was given a unit of packed red blood cells and admitted to general practice unit. Once admitted, he was evaluated by the gastroenterology team who performed an endoscopy and found several arteriovenous malformations but could not locate the specific source of bleeding. Mr. Weiss' anticoagulation was held for several days during his hospitalization placing him at risk of thrombus formation. During his admission, Mr. Weiss, his primary team, and the cardiothoracic surgery team discussed his long-term options for managing his anticoagulation needs.

At the age of 29, Mr. Weiss was found to have a genetic mutation that predisposed him to thoracic aortic aneurysm and required aortic valve replacement. Because he was relatively young at the time of operation, he was given a mechanical valve which requires lifelong anticoagulation but is lower risk and requires less reoperation than a bioprosthetic valve. Mr. Weiss experiences Heyde's syndrome, a recognized sequela of mechanical valves, which leads to arteriovenous malformation and gastrointestinal bleeding.² Mr. Weiss' comorbidities require anticoagulation while he is at chronic risk of hemorrhage due to arteriovenous malformations in his gastrointestinal tract.

Mr. Weiss experiences depression because of his medical condition and receives pharmacological treatment from his primary care provider. At this time, he had not sought out cognitive behavioral therapy or other treatments for depression because of personal choice although his primary care provider had encouraged him to do so. His health is a source of anxiety for him, and he also worries about the inheritability of the TGFBR1 gene mutation and its impact on the health of his children.¹ He has the social support of his wife and two children and they do not

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experience food insecurity or lack access to primary health care. He lives several hours from the main hospital which can make follow-up with his cardiothoracic surgeon time-consuming but has good follow-up with his cardiologist in his hometown.

Mr. Weiss and his family were concerned about his quality of life should he decline reoperation with a bioprosthetic valve and continue to experience gastrointestinal hemorrhaging and other side effects because of Heyde syndrome secondary to his mechanical valve.

Clinical Question

Do the risks of hemorrhage caused by Heyde's Syndrome justify the use of a bioprosthetic valve in a patient under 50 years old?

Research Article

Chan V, Lam BK, Rubens FD, et al. Long-term evaluation of biological versus mechanical prosthesis use at reoperative aortic valve replacement. *J Thorac Cardiovasc Surg.* 2012;144(1):146-151. <https://doi.org/10.1016/j.jtcvs.2011.08.041>³

Description of Related Literature

A query on PubMed using the search terms "aortic valve replacement," "reoperation," "mechanical," "biological or bioprosthetic," and "younger" returned 33 results. An additional query on PubMed using the search terms "aortic valve replacement," "reoperation," "mechanical," "bio* or bioprosthetic," and "Middle Aged" [MeSH] yielded 61 results. Studies that evaluated patients older than 18 and younger than 50 years old were prioritized. Studies that were observing patients with additional pathologies (e.g., chronic kidney disease, rheumatoid arthritis) were eliminated from consideration. Studies that evaluated only aortic valve replacement were considered over studies evaluating both aortic and mitral valve replacement. Furthermore, studies that compared mechanical valves to bioprosthetic valves were prioritized over articles that researched outcomes for one type of valve or the other. This article was selected because of its emphasis on *reoperative* aortic valve replacement which most accurately matches the circumstances of the patient. A search of "related articles" in Google Scholar was reviewed to ensure that relevant studies were not overlooked returned no studies. In addition, retrospective studies were evaluated because randomized data was not readily available for this study type.

A recent systematic review in 2017 by Head raised the question of whether a mechanical or prosthetic valve should be used for valve replacement and evaluated the risks, benefits, and outcomes of bioprosthetic compared to mechanical valves. Head et al. outlined the indications for both mechanical and bioprosthetic valves and identify the use of life-long anticoagulation in mechanical valve and the risk of valve deterioration requiring reoperation in bioprosthetic valve as the major hazards associated with each valve. Head et al. go on to delineate European and American guidelines which both recommend mechanical valves in patients younger than 60 and the use of bioprosthetic valves in patients older than 65 in European guidelines and older than 70 in American guidelines. Overall, the review found that despite European and American guidelines that recommend the use of mechanical valves in younger patients and insufficient evidence to support use of bioprosthetic valves in younger patients, the use of bioprosthetic valves has increased significantly despite awareness that deterioration of bioprosthetic valves is accelerated in younger patients and increased life expectancy in younger patients will likely require reoperation. While reoperation rates were higher in bioprosthetic valves, the risk of stroke, endocarditis and valve thrombosis was similar between mechanical valve and bioprosthetic valve.⁴ Although this study evaluates the risks and benefits of mechanical and bioprosthetic valves, it does not focus specifically on younger patients like Mr. Weiss.

In a 2017 retrospective analysis, Schnittman et al. propensity score matching yielded 1175 patient pairs between 18 to 50 years old and assessed mortality as the primary outcome and stroke, bleeding, and reoperation as secondary outcomes. The authors note that recent guideline changes have included patient preference to avoid lifelong anticoagulation in clinical decision making and may have aided the increase in bioprosthetic valves in younger patients. Like Head et al., Schnittman et al. note that this shift has happened despite the lack of clear evidence demonstrating the equality or superiority of bioprosthetic valves over mechanical valves. They found that there was no survival difference between bioprosthetic valves compared to mechanical valves in the propensity matched



cohort (79.0% vs 81.5%) in a 15-year follow-up period. In addition, rates of stroke and bleeding were lower with a bioprosthetic valve, however reoperation rates were also higher in this group. Notably, over 15 years, the risk of major bleeding in the group with bioprosthetic valves was 4.2% vs. 8.4% in the mechanical valve group ($p < .001$). Moreover, at 15 years, the incidence of reoperation was significantly higher in recipients of bioprosthetic valves compared to mechanical valves (24.5% vs. 9.3%) with a steep increase after 7 years. Their study also argues that younger patients have been underrepresented in clinical trials evaluating valve choice during replacement making the distinction between mechanical over bioprosthetic valve replacement less clearly defined in this group and necessitating more rigorous study.⁵ While this paper also evaluates risks and benefits based on valve type, it does not look at patients undergoing aortic valve reoperation.

In a single-center comparative study, Hirji et al. assessed aortic valve replacement in patients under age 50 and included coronary artery bypass grafting and mitral valve procedures. They propensity score-matched patients resulting in 170 patient pairs; the primary study end points were operative mortality and long-term survival with secondary end points being stroke, major bleeding, and re-operative aortic valve replacement. Like the other studies discussed, the authors found similar rates of operative mortality and stroke with increased risk of reoperation in the bioprosthetic aortic valve cohort (13.6% vs. 1.6%, $p < 0.001$) and increased major bleeding with the mechanical aortic valve cohort (8.5% vs. 2.2%, $p = 0.006$). Of note, the authors identified a 3.8-fold increased risk in major bleeding events with mechanical aortic valve replacement and a near eightfold increased risk of reoperative aortic valve replacement with bio-prosthesis at 10 years. Overall, their study noted the neither the risk of reoperation after bioprosthetic valve nor major bleeding incidents after mechanical valve replacement were reflected in midterm or long-term survival differences between patient groups.⁶ While this paper finds similar outcomes to previous studies, it also does not at the specific subgroup of patients undergoing reoperative aortic valve replacement as Mr. Weiss would be pursuing.

Greco et al. characterized the outcomes of patients undergoing reoperative aortic valve replacement and complex aortic valve procedures in a retrospective analysis. Their study was focused on patients' indications for re-do surgery as well as the morbidity and mortality of these surgeries. They found that 61% of patients were younger than 60 and 37.5% chose a mechanical valve over a bioprosthetic valve. They also found that many patients had contraindications for transcatheter aortic valve replacement (TAVR) including aortic regurgitation, infective endocarditis, paravalvular leak, patient-prosthesis mismatch and proximal aortic disease. While the authors did focus on reoperative aortic valve replacement, their study was more focused on the immediate post-operative period and lacked characterization of long-term outcomes (e.g. hemorrhage, reoperation) comparable to the other studies cited.⁷

Chan et al. focused their study on *reoperative* aortic valve replacement and evaluated survival and adverse outcomes with bioprosthetic vs mechanical aortic valve replacement. The authors note that there is less literature about this subgroup of aortic valve replacement patients. They found there no was decreased survival with the use of bioprosthetic aortic valve at reoperation however there was demonstration of risk of major hemorrhage in patients receiving mechanical valves like what is shown by previous studies on initial valve replacement. Like first-time valve replacement, use of a bioprosthetic valve increases risk of reoperative aortic valve replacement which in this subgroup represents third-time aortic valve replacement. Overall, the authors found that while there is increased risk of third-time aortic valve replacement with use of a bioprosthetic valve, perioperative mortality risk was similar and long-term survival was equivalent.³ As there are no randomized control trials for studies of this type, this study was determined to be 2C based on SORT criteria.⁸

Critical Appraisal

Chan et al. conducted an ambispective follow-up study to determine the outcomes of reoperative aortic valve replacement between mechanical and bioprosthetic valves with the objective of providing more information for younger patients making this decision. As the authors note, younger patients may determine that the lifestyle benefits of bioprosthetic valves, namely freedom from oral anticoagulation may outweigh the disadvantage of reoperation. In addition, failed bioprosthetic aortic valve can now be repaired with valve-in-valve transcatheter aortic valve implantation.

The study followed 437 patients who underwent reoperative aortic valve replacement over a mean of 7.6 +/- 6.8 years and extending up to 31.8 years. The authors used the Kaplan-Meier method to compare survival and freedom from valve-related complications; risk factors for third-time aortic valve replacement were determined by multivariable Cox proportional hazards models. Patients receiving reoperative bioprosthetic valve were older (62.9 +/- 13.8 yrs vs 56.7 +/- 14.0 years, $p < .001$), more likely

to have New York Heart Association Stage III or IV heart failure preoperatively ($p = 0.3$) and more likely to undergo coronary artery bypass grafting at reoperative aortic valve replacement ($p = .003$). Bioprosthetic valve was not associated with increased survival compared to mechanical valve (hazard ratio, 0.8; bioprostheses vs mechanical 95% confidence interval, 0.3-2.1; $p = 0.6$) after adjusting for factors including older age of bioprostheses recipients, concomitant coronary artery bypass graft and preoperative left ventricular function. In follow-up there were 161 deaths, most commonly because of congestive heart failure, noncardiac causes, cancer and unknown causes. Hemorrhage and thromboembolism were considered collectively, with events observed in 28 of 135 patients, of which 7 had received a bioprosthetic valve and 20 had received a mechanical valve at reoperation. Lifetime incidence for hemorrhage or thromboembolism was 7.1% for bioprostheses and 18.3% for mechanical valve.

The authors note that there is no survival benefit associated with one valve type over the other. However, there is increased risk of third-time aortic valve replacement with reoperative bioprosthetic aortic valve replacement which should be considered against the risks of mechanical valve which include increased cumulative risk of hemorrhage and thromboembolism. In addition, patients with mechanical aortic valve replacement experience lower quality of life and greater disease perception which is pertinent to Mr. Weiss' perceived poor quality of life and associated depression.

Although this study attempted to control for patient difference, it is limited because the decision between mechanical and bioprosthetic valve is not randomized and there is the possibility of unknown bias or other confounding factors. In addition, the study was limited by relatively small size and follow-up.³

Clinical Application

At 47 years old, Mr. Weiss is a relatively young man who experiences long-term psychological and physical sequelae because of mechanical aortic valve replacement surgery. The literature demonstrates that the decision to pursue reoperative aortic valve replacement with a bioprosthetic valve is one that could reduce Mr. Weiss' disease burden and greatly improve his quality of life by eliminating the need for anticoagulation.

New Knowledge Related to Clinical Decision Science

In making his decision, Mr. Weiss weighed the risk of reoperation with the risk that the replacement with a bioprosthetic valve would likely result in a third-time aortic valve replacement. He suffers from recurrent gastrointestinal bleeding, in part because of the anticoagulation necessary to prevent thrombosis formation as well as Heyde syndrome which results in arteriovenous malformation in his gastrointestinal tract leading to hemorrhage. Although his symptoms are theoretically manageable with close observation, they impact his quality of life and Mr. Weiss also has depression secondary to his valve replacement. While the literature demonstrates that there is no decreased survival with second or third-time reoperation with bioprosthetic valve replacement, repeated surgery does carry inherent risk.

The 2020 guidelines from the American College of Cardiology and the American Heart Association strongly recommend "a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for and risks of anticoagulant therapy and the potential need for and risks associated with valve reintervention."² In discussion with Mr. Weiss' cardiologist, he thought a reoperative aortic valve replacement was an extreme option and recommended lowering his target INR to 1.5-2 as a more appropriate intervention to decrease his chance of hemorrhage and ideally increase his overall quality of life. In addition, we emphasized the need for close follow-up with his primary care doctor, anticoagulation clinic and cardiothoracic surgeon should he decide to reevaluate surgery later. Another critical intervention to consider would be more proactive management of his depression with either medical management or psychotherapy.

In accordance with the ACC/AHA guidelines, Mr. Weiss and his cardiologist weighed the risk of valve reintervention and concluded that a more conservative approach made more sense at this stage in his life. Mr. Weiss' situation is a unique one given his original indication for valve replacement and the side effects that he has suffered since his aortic valve replacement. It would be reasonable for another patient with a similar profile to Mr. Weiss' to proceed with the change to a bioprosthetic valve given the ACC/AHA guidelines and their emphasis on shared decision-making which considers the patient's preference, the risks of anticoagulant therapy and the need for valve reintervention.



Conflict Of Interest Statement

The author declares no conflicts of interest.

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