

CASE REPORT

Aortic Valve Replacement and Factor V Leiden: A Difficult Clinical Decision

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ABSTRACT

Factor V Leiden is a common inherited mutation leading to activated protein C resistance and a hypercoagulable state. We discuss a 72-year-old male heterozygous for the factor V Leiden mutation who presented with significant aortic stenosis, requiring an aortic valve replacement. There is controversy regarding the choice between mechanical and bioprosthetic substitute valves in patients with a hypercoagulable state, given that many patients are already on life-long anticoagulation for deep venous thrombosis prophylaxis. Benefits and risks regarding the choice of valve should be carefully considered because of significant impacts on peri-operative and post-operative management.

INTRODUCTION

Factor V Leiden (FVL) is an inherited mutation found in 5% of the Caucasian population, and is the most common inherited thrombophilic clotting disorder.¹ FVL is associated with an increased risk of several thrombotic complications, such as recurrent venous thrombosis, cerebral sinus thrombosis, and renal transplant rejection.¹ In FVL patients requiring aortic valve replacement (AVR), the choice of mechanical over bioprosthetic valves remains controversial. The primary advantage of a bioprosthetic valve over a mechanical valve is freedom from life-long anticoagulation, and current guidelines by the American Heart Association, American College of Cardiology and the American College of Chest Physicians recommend early anticoagulation with heparin, followed by warfarin therapy for 3 months post-operatively.² Bleeding and thromboembolism account for about 80% of complications associated with mechanical prostheses.³ Regarding the choice of valve replacements, current guidelines recommend a mechanical valve for patients aged less than 65 years, who are expected to live longer and experience a lower incidence of complications associated with warfarin, as contrasted with patients older than 75 years, for whom bioprosthetics are more suitable.³

CASE PRESENTATION

A 72-year-old man was evaluated for the possibility of an AVR and coronary artery bypass grafting. He was generally asymptomatic because his peripheral vascular disease limited

his activity level considerably, although he admitted to progressively worsening shortness of breath over the past eight years. His symptoms were aggravated by heat and humidity. He denied any syncope, presyncope, paroxysmal nocturnal dyspnea, orthopnea or ankle edema.

His cardiac risk factors included a 50-pack-year history of smoking, diabetes mellitus for 11 years, treated with insulin, and hypertension for 15 years. Past medical history was notable for chronic atrial fibrillation. There was also a history of chronic venous insufficiency and deep vein thrombosis complicated by compartment syndrome in the right lower extremity, which had required the placement of an inferior vena cava filter and fasciotomies. He was placed on warfarin for these conditions. A coagulation profile revealed that he was heterozygous for a Factor V Leiden mutation, which was also present in other male members of his family, including his son.

On physical examination, his blood pressure was 100/55, with a heart rate of 88 bpm which was irregularly irregular. Head and neck examination revealed no carotid bruits. Cardiac auscultation revealed a variable intensity second heart sound and a harsh Grade II-III/VI systolic ejection murmur heard over much of the precordium. A murmur of aortic insufficiency was not appreciated. The femoral and popliteal pulses were significantly diminished, and the pedal pulses in the right lower extremity were not appreciated. Varicose veins were also noted on the left lower extremity.

The patient had been followed by serial echocardiography. His latest echocardiography (performed one month earlier)

showed atrial fibrillation with a normal sized right ventricular chamber with mild left ventricular hypertrophy. There was also a mild global systolic impairment overall (Grade II LV). The echocardiogram also showed progression of aortic valve stenosis (AS) from the echo taken 16 months previously. It showed severe calcific aortic stenosis with mild to moderate aortic insufficiency, and an aortic valve area of 0.7cm². The peak gradient across the valve was 124 mmHg, with a mean gradient of 68 mmHg. Moderate bi-atrial enlargement was also identified, consistent with chronic atrial fibrillation. His right coronary artery had mild irregularities, and there was a 50-60% stenosis in the mid-left anterior descending artery.

Individuals with normal aortic valves have a valve area between 3.0 to 4.0 cm². The severity of AS would be considered moderate if the valve area was between 1.0 and 1.5 cm², severe if between 0.75 and 1.0 cm², and critical if it were less than 0.75 cm². Based on the hemodynamic measurements from an echocardiogram, a mean gradient greater than 60 mmHg and an aortic jet velocity greater than 5.0 m/sec would be classified as extremely severe AS.⁴ However, the decision to proceed with an AVR should not be based solely on valve area calculations and gradient measurements.

Currently, the AHA/ACC recommends AVR in patients with symptomatic AS, in patients with moderate AS who require another cardiac surgery, and those with an ejection fraction less than 50%.⁴ With this patient, we decided to proceed with aortic valve replacement due to his progressively worsening dyspnea along with his significant echocardiographic findings." instead of "In this patient, a decision was reached to proceed with an AVR due to his progressively worsening dyspnea along with his significant echocardiograph findings.

PHYSIOLOGY OF FACTOR V LEIDEN

Factor V is an inactive cofactor that circulates in the plasma, which is then activated by thrombin to form Factor Va. Factor Va in turn acts as a cofactor in the conversion of prothrombin to thrombin. A sequence of enzymatic events must occur in order to inactivate Factor Va, with activated protein C cleavage of Arg506, then at Arg306 and Arg679.⁵ A transitional mutation in individuals with Factor V Leiden replaces arginine at position 506 with glutamine.⁵ The resulting Factor V Leiden gene product is not susceptible to inactivate Factor Va: activated protein C cleaves Arg506, so its inactivation is impaired.⁵ The physiological consequence of this mutation is the development of a hypercoagulable state due to poor susceptibility to cleavage by APC, as well as impaired APC cofactor activity.⁶

DISCUSSION

Factor V Leiden mutations are found in 5% of the general population, and are the most common inherited thrombophilic

clotting disorder.¹ The major clinical manifestation of FVL is deep vein thrombosis (DVT), with or without pulmonary embolism. Relative risk of DVT is increased seven-fold in FVL heterozygote patients, and eighty-fold in homozygotes.⁷

Few candidates for aortic valve replacement have been diagnosed with FVL prior to surgery. This leads to a debate regarding the choice of a mechanical or bioprosthetic valve in patients with FVL. The major drawback of the mechanical valve is the requirement for life-long warfarin therapy as a prophylaxis, and the adverse events accompanying this therapy. The patient described in this case had already started life-long warfarin therapy due to his chronic atrial fibrillation and history of deep vein thrombosis. The main benefit of a mechanical valve is its greater durability compared to the bioprosthetic valve, and the much lower likelihood of a re-operation. After careful consideration and consultation with the thrombosis service, the more prudent course was taken and a bioprosthetic valve was implanted. The procedure was completed without complications, and the patient recovered well. He was instructed to continue his warfarin therapy due to his history of DVTs and atrial fibrillation. Reasons for this choice include the patient's relative advanced age, and the risk of thrombosis of bioprosthetic valves with anticoagulation reversal at the time of future non-cardiac surgery.⁸ This choice would have been much more difficult in a considerably younger patient given the increased durability of the mechanical valve. However, mechanical valves carry an increased risk of thrombosis and thromboembolism, therefore, life-long anticoagulation is required. In FVL patients under the age of 65, the choice of a mechanical valve may be reasonable given that many of these patients are already on life-long anticoagulant therapy for prophylaxis of recurrent deep vein thrombosis. Careful consideration of all benefits and risks is required in a multidisciplinary approach because of significant impact on both peri-operative and post-operative management. †

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