Defying Dogma
Recovery After Left Ventricular Assist Device Implantation and Aortic Valve Replacement for Bicuspid Aortic Valve
Brett W. Sperry, MD; Miriam S. Jacob, MD; Venu Menon, MD; Edward G. Soltesz, MD; E. Rene Rodriguez, MD; Zoran B. Popović, MD, PhD

Aortic valve stenosis leads to compensatory myocyte hypertrophy that initially restores wall stress to normal levels. When left untreated, myocardial fibrosis and decreased systolic function ensue with development of a cardiomyopathy of pressure overload. Clinically, this may present as a low-gradient, low ejection fraction (EF) aortic stenosis, and management of this clinical entity is well defined. Subjects with contractile reserve in the setting of dobutamine stimulation have been shown to benefit from aortic valve replacement (AVR). In contrast, the lack of contractile reserve after dobutamine is a high-risk finding. AVR in this setting is related to high-operative mortality, and therefore, many patients are denied valve replacement. We present an extreme case of a patient with severe aortic stenosis and Stage D heart failure that recovered left ventricular (LV) function after left ventricular assist device (LVAD) implantation allowing for LVAD disconnection despite absent contractile reserve and pathological evidence of significant myocardial fibrosis. This case highlights the challenges of the conventional treatment paradigm and provides us unique insights into myocardial contractile recovery.

Case Report
The patient was a 53-year-old man who initially presented to a community hospital with 3 months of progressive dyspnea, orthopnea, edema, and decreased exercise tolerance. He had a past medical history of hypertension, hyperlipidemia, type 2 diabetes mellitus, and a murmur first noted in adolescence. He denied a history of alcohol, drug, or stimulant use and had no family history of cardiovascular disease. Results of a complete metabolic panel, blood count, thyroid stimulating hormone, and iron studies were unremarkable. Echocardiography demonstrated a bicuspid aortic valve with severe low EF low-gradient aortic stenosis and a dilated and hypertrophied left ventricle. He was transferred to our institution for further care. On physical examination, there was elevated jugular venous pressure, auscultatory findings of severe aortic stenosis, rales, and pedal edema. ECG showed sinus tachycardia with left atrial enlargement, left ventricular hypertrophy, and an intraventricular conduction delay with QRS duration of 116 ms. The initial echocardiogram demonstrated moderate left ventricular hypertrophy with an EF of 13% (Figure 1). There was low-gradient aortic stenosis with an aortic valve area of 0.85 cm², peak gradient 44 mm Hg, mean gradient 24 mm Hg, and dimensionless index 0.17. Left ventricular end-diastolic diameter was 6.6 cm, volume 288 mL, and global longitudinal strain (GLS) −1.15. N-terminal pro-brain natriuretic peptide was 5423 pg/mL. Dobutamine stress echocardiography showed no contractile reserve and no change in gradients across the aortic valve (Figure 2; Movie 1 in the Data Supplement). Coronary angiography did not reveal obstructive coronary artery disease.

The patient decompensated further with worsening dyspnea at rest and signs of end organ malperfusion. Right heart catheterization was performed showing a right atrial pressure of 17 mm Hg, right ventricular pressure 58/19 mm Hg, pulmonary artery pressure 58/30 mm Hg (mean, 39 mm Hg), and pulmonary capillary wedge pressure 31 mm Hg. Cardiac output was 3.19 L/min and cardiac index 1.42 L/min per m² by the Fick method. Pulmonary artery catheter–guided intravenous diuresis and vasodilation with sodium nitroprusside was initiated. An intra-aortic balloon pump was later inserted because of hypotension and continued cardiogenic shock. The cardiac index improved to 1.8 L/min per m².

Because of the severely depressed EF, left ventricular strain, and lack of contractile reserve, the patient underwent a bioprosthetic AVR along with primary HeartWare LVAD implantation as a bridge to transplantation. The postoperative course was uncomplicated. Histology of the apical core showed myocyte hypertrophy and moderate interstitial fibrosis (Figure 3). After hospital discharge, the patient was able to tolerate a significant amount of neurohormonal blockade. Medications were uptitrated to carvedilol 50 mg twice daily, lisinopril 20 mg twice daily, hydralazine 100 mg 3× daily, spironolactone 37.5 mg daily, and amlodipine 10 mg daily to target a mean arterial pressure below 90 mm Hg. He was free of heart
failure symptoms while his EF and GLS gradually improved. (Figure 4) Echocardiography performed 1 year later showed a recovered EF of 60%. His left ventricular end-diastolic volume decreased to 177 mL and GLS improved to −11. After a successful LVAD outflow graft balloon occlusion study in the operating room, the device was disconnected by outflow graft ligation through a right anterior thoracotomy incision. The driveline was cut at the level of the skin and the device was left in situ. Five months after disconnection, the patient was free from heart failure symptoms with an EF of 60%, left ventricular end-diastolic volume 123 mL, and GLS −10.5 at 2-month screening (Movie 2 in the Data Supplement).

**Discussion**

This case highlights several novel points about aortic stenosis and the reversibility of left ventricular dysfunction. The patient had severe bicuspid aortic stenosis which progressed to profound systolic dysfunction before he became aware of his condition. By all noninvasive findings, the left ventricular dysfunction would have been considered irreversible. The systolic function and GLS were extremely compromised, and dobutamine stress echocardiography showed lack of contractile reserve. This was confirmed postoperatively, as histology demonstrated moderate interstitial fibrosis. These factors have all been shown to portend a worse prognosis at the time of AVR. However, it is important to note that even patients without contractile reserve tend to increase their EF if they survive surgery. This perioperative survival was aided in our patient by LVAD implantation.

Recovery of left ventricular function is promoted by a higher EF at baseline, shorter time with heart failure, higher systolic blood pressure, shorter QRS duration, and a smaller LV diastolic diameter. The patient’s age, relatively short duration of heart failure symptoms, elevated blood pressure, and ventricular synchrony likely contributed to his improvement. This improvement was facilitated by LVAD implantation because the mechanical unloading of the left ventricle has been shown to decrease left ventricular size and mass. However, <2% of patients have significant recovery allowing for device disconnection at 1 year.

In summary, we present a case of severe bicuspid aortic stenosis having progressed to Stage D heart failure and cardiomyopathy which reverse remodeling and recovered function after LVAD implantation allowing for LVAD disconnection. This was despite an EF of 13%, absent contractile reserve and the histological presence of significant myocardial fibrosis. It defies the dogma that these factors suggest an inability of the myocardium to significantly recover.

Replacement of the aortic valve is routinely performed in subjects undergoing LVAD when significant aortic regurgitation is present. Our data suggest that a similar strategy in subjects with cardiomyopathy secondary to severe aortic stenosis should be considered to enhance the possibility of ventricular recovery. In addition, mechanical support devices may help promote recovery in patients being evaluated for AVR but who would otherwise be considered too high risk for AVR alone. Replacement of the aortic valve, neurohormonal blockade and LVAD unloading may give the ventricle the time and environment needed to recover function.

**Disclosures**

None.

**References**


**Key Words:** aortic valve stenosis ■ fibrosis ■ heart assist devices ■ heart failure ■ transplantation
Figure 1. Transthoracic echocardiogram in an apical 4 chamber view at the time of presentation showing a mildly dilated left ventricle and biatrial enlargement. The ejection fraction was 13%, aortic valve area 0.85 cm², mean gradient 24 mmHg, and dimensionless index 0.17. bpm indicates beats per minute.

Figure 2. Dobutamine stress echocardiography showing pulsed wave Doppler across the left ventricular outflow tract (A) and continuous wave Doppler across the aortic valve (B) with measurements taken at rest. After 20 μg/kg per min of dobutamine stimulation, there was a <20% increase in left ventricular outflow tract velocity time integral (LVOT VTI), which (C) suggests a lack of contractile reserve. Aortic valve gradients and VTI did not significantly increase (D). bpm indicates beats per minute; HR, heart rate; and PG, pressure gradient.
Figure 3. Light micrograph with hematoxylin and eosin stain (A) showing moderate myocyte hypertrophy. Movat pentachrome stain (B) showing yellow strands of collagen deposition in the interstitial space.

Figure 4. Graphs (A) of left ventricular end diastolic volume (EDV) and end systolic volume (ESV) and (B) left ventricular ejection fraction (EF) and global longitudinal strain (GLS) over time. The dotted line represents left ventricular assist device (LVAD) implantation and the solid line represents LVAD disconnection. LVEF indicates left ventricular ejection fraction.
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Supplemental Material

Video Legends

Video 1. Dobutamine stress echocardiography showing apical four chamber view of the left ventricular contractility at rest (A) and after dobutamine infusion at 5mcg/kg/min (B), 10mcg/kg/min (C) and 20mcg/kg/min (D). Left ventricular contractility does not significantly increase.

Video 2. Transthoracic echocardiography in a modified apical four chamber view showing recovered LV function after LVAD disconnection. LVAD cannula is seen in the left ventricle (*).