



Peer-Reviewed Case report

Reversal of fixed pulmonary hypertension with transcatheter valve replacement for aortic insufficiency on ventricular assist device support

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"Reversal of fixed pulmonary hypertension with transcatheter valve replacement for aortic insufficiency on ventricular assist device support"

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Abstract

We present a 43-year-old woman with a nonischemic cardiomyopathy implanted with a ventricular assist device (VAD) as bridge to transplant due to severe, "fixed" pulmonary hypertension (PH). Within three months of VAD implant, her "fixed" PH had resolved entirely. Nearly two years later, still supported with a VAD because of severe HLA allosensitization, she developed dyspnea and "moderate" aortic insufficiency (AI) by standard criteria. Invasive hemodynamics revealed recurrence of severe PH in the setting of elevated left-sided filling pressures. We concluded the AI was indeed severe and the cause of her symptoms and recurrent PH. Despite her noncalcified aortic valve and small body habitus, after a thorough assessment, including meticulous annular measurements and appropriate valve



sizing, she underwent a transcatheter aortic valve replacement (TAVR) with complete resolution of both her AI and recurrent, severe PH. This case highlights, in a single patient, reversal of “fixed” PH with adequate left ventricular unloading, that “moderate” AI by standard criteria is often “severe” and must be considered in a VAD patient with recurrent PH, and the need for meticulous pre-procedural planning for TAVR in patients with VADs, including accurate measurements of the aortic annulus to ensure adequate oversizing of the valve.

Keywords: HVAD, LVAD, TAVR, mechanical circulatory support, pulmonary hypertension, aortic insufficiency

Currently, more than 40% of patients undergo bridging with a durable ventricular assist device (VAD) prior to heart transplantation for various reasons, including for the presence of severe, “fixed” pulmonary hypertension.¹ However, a bridging strategy with a VAD has potential limitations. In the perioperative phase of the VAD implant, the need for blood product transfusions may result in human leukocyte antigen (HLA) antibody sensitization, thus potentially limiting the recipient donor pool.² Moreover, VAD-related complications may ensue while on VAD support,³ which may impact transplant candidacy or create new obstacles to overcome to achieve a successful transplant outcome. Herein, we report on a challenging case that highlights each of these obstacles and the strategies employed to overcome them, all of which occurred in the same patient.

A 43-year-old woman (body surface area of 1.6 m²; body mass index of 24.3 kg/m²) with a dilated cardiomyopathy underwent Heartware[®] ventricular assist device (HVAD; Heartware International, Inc., Framingham, MA) implant for end-stage heart failure as a bridge to heart transplantation. A bridge strategy was employed because, in addition to having New York Heart Association Class IV heart failure symptoms, we diagnosed severe pulmonary hypertension (PH) and found her to be highly sensitized, which would likely require a long wait time on the transplant list. With respect to her allosensitization status, she was highly sensitized with major histocompatibility complex (MHC) Class I=100% and Class II=100%. Regarding her severe PH, right heart catheterization (RHC) prior to VAD implant revealed a pulmonary artery pressure (PAP) of 67/33/47 mm Hg, a pulmonary capillary wedge pressure (PCWP) of 26 mm Hg, a cardiac output (CO) by thermodilution of 2.12 L/min, and a pulmonary vascular resistance (PVR) of 9.9 Wood units, which did not significantly improve during acute vasodilator testing with intravenous nitroprusside. Pre-operative echocardiography revealed a normal sized aortic root with no aortic insufficiency (AI). She underwent a successful HVAD implant and her pre-discharge echocardiogram revealed an adequately unloaded left ventricle with a closed aortic valve throughout the cardiac cycle.

Approximately one year after HVAD implant, despite what has previously been coined “fixed” PH defined as the presence of a PVR > 5 Woods units, a transpulmonary gradient > 15 mm Hg, and non-reversible hemodynamics with vasodilator administration,⁴ her PH had nearly resolved entirely. Specifically, her remeasured hemodynamics during a subsequent RHC demonstrated a PAP of 34/11/20 mm Hg and a PCWP of 11 mm Hg. As the patient was not treated with any PH-targeted medical therapies during this time span, the reversibility of her



severe PH, which some may have been inclined to consider to be “fixed” or irreversible, could be attributed to the impact of excellent left ventricular unloading of sufficient duration. Despite efforts at desensitization with plasmapheresis, IVIG, and bortezomib she remained with MHC Class I and Class II antigens of 100%. However, many of her titers reduced sufficiently with the desensitization treatments to allow us to continue to consider her for heart transplantation, which she strongly desired.

Two years after VAD implantation, while continuing to wait for an acceptable HLA matched donor, she began to experience a gradual increase in dyspnea. Repeat RHC revealed a recurrence of her severe PH but also now with evidence of inadequate left ventricular unloading. Specifically, she had a PAP of 60/30/43 mm Hg, a PCWP of 19 mm Hg, CO by thermodilution of 3.07 L/min and a PVR of 7.8 Wood units. There was no evidence for VAD thrombosis, her blood pressure was well controlled, and increases in her VAD speed did not lower her PCWP (or PAPs) further as would normally be expected to occur. Echocardiography revealed the presence of new, at least “moderate” aortic insufficiency (AI) by standard grading criteria (Figure 1)⁵ in the setting of a normal sized aortic root and no overt aortic leaflet pathology. However, we were convinced that the continuous nature of the “moderate” AI in this clinical context was sufficient to explain her heart failure symptoms, elevated left sided filling pressures and recurrence of her severe PH,⁶ which rendered her ineligible yet again for proceeding with transplantation.

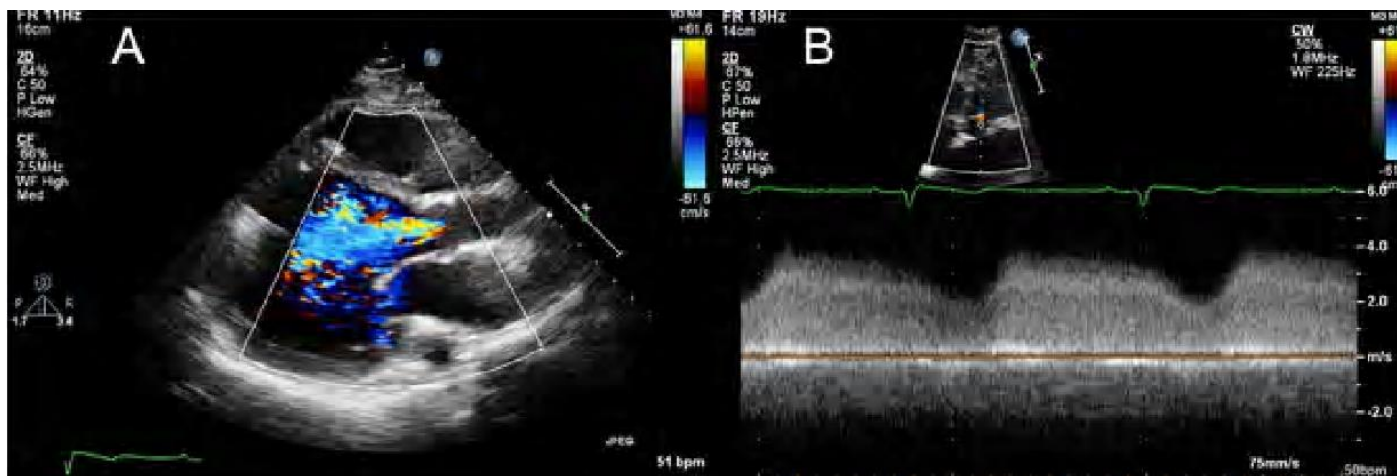


Figure 1. Evaluation of aortic insufficiency by echocardiogram. Panel A shows at least moderate aortic insufficiency by color Doppler in the parasternal long axis view. Panel B illustrates the continuous flow nature of the aortic insufficiency by interrogation with continuous wave Doppler.

We decided to pursue transcatheter aortic valve replacement (TAVR) as the least invasive means by which to treat her AI while limiting her risk of surgical complications including the possibility of requiring additional blood products.



However, TAVR for AI, especially in a patient with a VAD and a non-ischemic cardiomyopathy, can be fraught with procedural complications, such as valve migration in the setting of a non-calcified aortic valve. Among the strategies to consider includes slightly oversizing the aortic valve which is critical to ensure sufficient anchoring to reduce the risk of migration while also optimizing valve function and hemodynamics.⁷ In this patient, careful pre-procedural planning to ensure safe valve placement included the temporary addition of intravenous dobutamine 5 μ /kg/min and the transient lowering of the patient's VAD speed from 2800 RPM to 2300 RPM, both of which were required to induce aortic valve opening in an effort to precisely measure her aortic annulus. Ultimately, a TAVR was performed via a right transfemoral approach with a Medtronic (Medtronic, Dublin, Ireland) Evolut™ Pro 26 mm valve. There were no procedural complications and the final aortogram revealed a well seated valve with no AI (Figure 2).

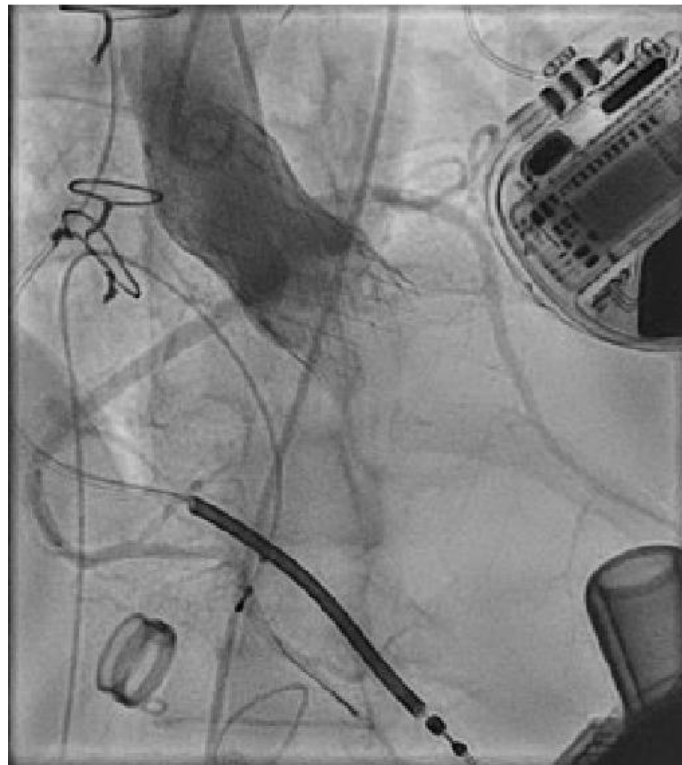


Figure 2. Aortography after transcatheter aortic valve replacement. In the Left Anterior Oblique 30 degrees and Cranial 15 degrees view, aortography shows a well-seated, bioprosthetic aortic valve without evidence of aortic insufficiency and without compression of the left or right coronary arteries.

At six weeks following her TAVR, her symptoms had resolved entirely. Repeat RHC revealed a normalization of her PAPs with a PAP of 31/10/18 mm Hg, a PCWP of 6 mm Hg, and a CO of 3.7 L/min. (Table 1 and Figure 3). Repeat echocardiography confirmed a well-seated valve and complete absence of AI. Her eligibility for transplant was subsequently re-opened.



Table 1. Serial invasive hemodynamic measurements with right heart catheterization at critical time points in the patient’s clinical course

Right Heart Catheterization	Prior to LVAD implant	One year after LVAD implant	Two years after LVAD implant with “moderate” AI	Six weeks after TAVR
Pulmonary artery pressure (mean), mm Hg	67/33 (47)	34/11 (20)	60/30 (43)	31/10 (18)
Pulmonary capillary wedge pressure, mm Hg	26	11	19	6
Transpulmonary pressure gradient, mm Hg	21	9	24	12
Cardiac output by thermodilution, L/min	2.1	3.4	3.1	3.7
Pulmonary vascular resistance, Woods units	9.9	2.6	7.8	3.5

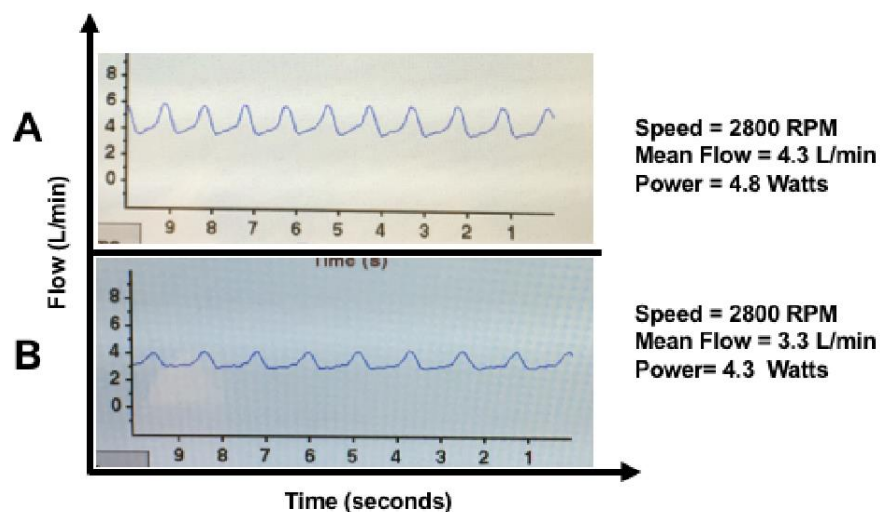


Figure 3. HVAD waveforms before and after transcatheter valve replacement. Immediately prior to transcatheter aortic valve replacement (Panel A), a modest but higher mean flow was present owed to the regurgitant aortic insufficiency volume which dropped immediately after transcatheter aortic valve replacement (Panel B) due to the elimination of the regurgitant flow through the pump.



This case illustrates several key teaching points. First, PH in left heart failure is nearly always due to persistent elevations in left sided filling pressures yet is also nearly always reversible once the filling pressures are lowered, even in the presence of a severely elevated, “fixed” PVR.⁴ Indeed, our patient’s severe PH was due to her left heart failure and reversed shortly following her VAD implant. When a recurrence of her severe PH occurred, particularly in the setting of elevated left sided pressures, a limited and finite list of culprit possibilities exist in a VAD patient, one of which is AI. By eliminating the AI via TAVR and consequently re-normalizing her left-sided filling pressures, her severe PH again resolved. Second, diagnosing de novo AI and its management in patients with continuous flow VADs deserves special attention. Clinically important AI in VAD supported patients may not meet standard severe AI grading criteria, thus requiring a high index of suspicion when present such as in our patient whose pre-TAVR imaging consistently suggested her AI to be “moderate” and not “severe”. The inability to unload the LV despite increases in VAD speed and the presence of novel, echocardiographic parameters⁸ may be two potential indicators of its true severity. Third, the absence of aortic valve opening at time of discharge after LVAD implant has been associated with increased risk of the development of AI and may have contributed in this case.⁹ However, the vast majority of patients with an LVAD will not develop clinically significant AI even in the absence of intermittent aortic valve opening. This patient required a sufficient VAD speed to maximally unload the LV to induce reversibility of her PH; moreover, occasional attempts to lower her VAD speed resulted in a recurrence of heart failure symptoms, making the decision to maintain a higher VAD speed appropriate. Lastly, TAVR evaluation in the setting of a VAD requires careful pre-procedure planning regarding the valve type, valve size, and intra-procedure monitoring for valve migration. In particular, meticulous efforts aimed at precisely measuring aortic annulus dimensions and a slight oversizing of the aortic valve may be critical in VAD patients undergoing TAVR.

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