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Transplant & Mechanical Support: Short Report

The Challenges of Aortic Valve Management After Left Ventricular Assist Device Implantation

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ABSTRACT

BACKGROUND Continuous retrograde flow across the aortic valve from left ventricular assist device (LVAD) therapy can result in cusp damage and progressive aortic regurgitation, potentially triggering recurrent heart and multiorgan failure. The management of aortic regurgitation after LVAD implantation has not been well defined.

METHODS This study retrospectively reviewed the investigators' experience with the management of de novo aortic regurgitation requiring intervention in patients with continuous-flow LVAD.

RESULTS Six patients who had undergone LVAD implantation and who required intervention were identified. Two patients underwent redo sternotomy with bioprosthetic aortic valve replacement, and 4 patients underwent percutaneous management, including Amplatzer device (Abbott) placement and transcatheter aortic valve replacement. All patients had resolution of aortic regurgitation with improved hemodynamics and relief from heart failure. One early and 2 late deaths occurred. Valve function was intact, with all valves opening intermittently without greater than trivial aortic regurgitation.

CONCLUSIONS Multiple treatment modalities exist for LVAD-induced aortic valve regurgitation, including open surgical and percutaneous strategies. With a tailored risk-adjusted approach, acceptable results may be achieved.

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The aortic valve's sophisticated structure and function, consisting of side-specific cellular and biochemical components, a specific gravity equal to that of blood, and innervation that subtends an ability to open before the delivery of the stroke volume, results in an energy-conserving capacity far beyond that of any artificially constructed valve.[1] This sophistication underlies the valve's capacity for rapid presystolic opening, laminar flow in the ascending aorta, and prevention of aortic

IN SHORT

- AR is a common complication of continuous-flow LVADs.
- Treatment options include open surgery and percutaneous approaches, but the multiple comorbidities associated with these patients may complicate management.
- Treatment selection on the basis of patient risk profile maximizes hemodynamic improvement and survival rate.

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regurgitation (AR). In the setting of profound heart failure (HF) requiring left ventricular assist device (LVAD) therapy, the aortic valve is required only to be competent, assuming the left ventricle contributes minimally to cardiac output.

The development of significant AR can be a catastrophic event for the LVAD recipient by reducing the effective cardiac output, overloading the ventricle, and potentially triggering significant pulmonary edema and multiorgan failure. Several preventive and treatment strategies have been advocated for the management of AR after LVAD implantation. These are challenging patients because of their comorbid burden and treatment strategies that must anticipate their future needs, including postoperative anticoagulation and possible heart transplantation. Here we describe our experience with the management of AR after LVAD implantation, including percutaneous and surgical therapies and their roles.

PATIENTS AND METHODS

We retrospectively reviewed all aortic valve interventions in patients with a preexisting continuous-flow LVAD at The University of Pennsylvania Health System (Philadelphia, PA). Six patients were identified, and their records were analyzed. Given the retrospective design of the study, individual patient consent was waived on condition that no identifying data were included.

Data on preoperative characteristics, perioperative details, and postoperative short-term outcomes were extracted from the chart in a deidentified form. Standard clinical follow-up consisted of 30-day postoperative visits and monthly to 4-monthly HF clinic follow-up visits. In this series, follow-up was 100% complete.

TABLE 1 Preoperative Patient Characteristics

Characteristics	Open	Percutaneous	Total Group
Number of patients	2	4	6
Age, y	25, 63	19, 58, 59, 60	35.6 ± 23.8
Sex, % female	50	50	50
Height, m	1.75 ± 0.2	1.70 ± 0.14	1.72 ± 0.15
Weight, kg	130 ± 96	76.5 ± 29	94.3 ± 55
Diabetes mellitus, %	0	25	16
Liver failure, %	…	25	16
Renal failure, %	0	25	16

Values are n, %, or mean ± SD.

STATISTICAL ANALYSIS. Continuous variables are presented as mean ± SD. Noncontinuous variables are presented as a percentage of the group. The Wilcoxon matched *t* test on the basis of a non-normally distributed population was performed to assess echocardiographic differences.

RESULTS

PATIENT COHORT. Patient characteristics are described in Table 1. The cohort consisted of 3 men and 3 women aged between 19 and 63 years at the time of aortic intervention. HF causes were familial cardiomyopathy, ischemic cardiomyopathy, chemotherapy-induced cardiomyopathy, noncompaction cardiomyopathy, and dilated cardiomyopathy (in 2 patients). All patients had continuous-flow LVADs: 3 HeartMate II devices (Abbott) and 3 HeartWare devices (Medtronic). The median interval between LVAD implantation and aortic valve replacement (AVR) was 2.15 ± 1.69 years. The intended use of the LVAD was destination therapy in 3 patients, a bridge to decision in 1 patient, and a bridge to heart transplantation in 2 patients. No patient has undergone heart transplantation. One patient had a mildly thickened aortic valve with trace aortic insufficiency, and 1 patient with a previous bioprosthetic valve had a mild to moderate paravalvular leak at the time of the index LVAD operation.

The indication for AVR was severe AR causing HF in all patients. Preoperatively, all valves opened at least intermittently, and in 1 patient the aortic valve opened with every beat.

CHOICE OF INTERVENTION. All patients were considered for open AVR initially. Contraindications to open surgery included a heavily calcified aorta in 1 patient, age, right ventricular (RV) failure and comorbidities (for n = 2 patients), and cirrhosis in 1 patient. In 2 patients, Amplatzer (Abbott) devices were chosen because of comorbidities in 1 of the patients and an extremely calcified aorta in the other. One of these patients was in extremis with multiple complications, including prolonged intubation and sepsis on multiple pressors, after LVAD implantation 109 days before the aortic intervention.

PROCEDURAL OUTCOMES AND COMPLICATIONS. The valve prostheses used and other details are included in Table 2.

Operative times for the 2 open procedures were 131 and 137 minutes of cardiopulmonary bypass,

TABLE 2 Operative Outcomes

Outcomes	Open	Percutaneous	Total Group
Prosthesis	23-mm MagnaEase (Edwards Lifesciences) pericardial valve or25-mm Mosaic (Medtronic) pericardial valve	1 Amplatzer (Abbott), 2 transfemoral Evolut CoreValve (Medtronic) TAVRs (26 mm, 29 mm), 1 transaxillary Evolut CoreValve 29 mm	N/A
Hospital mortality, %	0	25	16
PRBC transfusions/patient	1, 1	0, 7, 20, 0	…
Intubation time, h	9, 5	4, 14, 240, 0	…
ICU LOS, d	5.5 ± 0.7	34.5 ± 57	24.6 ± 46.7
Hospital LOS, d	10.5 ± 3.5	43.5 ± 53.5	32.5 ± 44.5
New renal failure, %	0	25	16

Values are %, n, or mean ± SD. ICU, intensive care unit; LOS, length of stay; N/A, not applicable; PRBC, packed red blood cell; TAVRs, transcatheter aortic valve replacements.

with 60 and 37 minutes of cross-clamp time, respectively. These times are not substantially different from those expected for redo sternotomy for AVR.

Several challenges were encountered during the percutaneous procedures. The Amplatzer device used to cover the aortic valve in 1 patient embolized into the left ventricle. During percutaneous retrieval of this device, a limited iatrogenic type B aortic dissection was noticed. This patient subsequently underwent transaxillary transcatheter AVR (TAVR) as a result of heavy aortic calcification. In another patient, during TAVR, aortic migration occurred during final prosthesis deployment and required redeployment with larger-sized prosthesis.

EFFECT OF AORTIC REGURGITATION ELIMINATION ON RIGHT- AND LEFT-SIDED HEART FUNCTION. All 6 patients left the operating room with mild aortic insufficiency or less, as shown in the echocardiograms in Figures 1 and 2 ($P < .05$). Although there was a tendency for AVR to reduce left ventricular (LV) dimensions and the degree of mitral valve regurgitation, these results were not statistically significant. There was no change in LV ejection fraction. Right-sided heart size and function were stable, with a tendency toward reduced tricuspid regurgitation after AVR.

SURVIVAL. There was 1 early death, on day 16 after Amplatzer device implantation. This was a 59-year-old man with a history of nonischemic cardiomyopathy, bioprosthetic AVR, and mitral annuloplasty 17 years before LVAD implantation. He was transferred from an outside hospital on inotropic support and had acutely decompensated cardiogenic shock. He underwent redo sternotomy and HeartWare LVAD implantation with tricuspid annuloplasty. There was a moderate paravalvular leak preoperatively on the bioprosthetic valve, which was stable postoperatively. The patient subsequently had a protracted course in the intensive care unit as a result of moderate RV dysfunction requiring inotropic support, and he also had severe sepsis, new-onset renal failure requiring continuous renal replacement therapy, and progressive liver failure. Serial echocardiograms showed improved RV size and function but development of severe AR and moderate to severe mitral regurgitation. Given his critical illness and heavy aortic calcification, an Amplatzer device was implanted 109 days after LVAD implantation without complications, with resolution of AR to mild. Unfortunately, the patient remained pressor dependent and elected withdrawal to comfort measures.

There were 2 late deaths, 1 at 503 days after AVR from suicide and another at 630 days after AVR from spontaneous intracerebral hemorrhage.

FOLLOW-UP. Follow-up is 100% complete. Median follow-up was 28.92 ± 15.23 months, with a range of 16 to 2737 days.

No new AR was documented during follow-up. All valve prostheses at least intermittently opened at latest follow-up, a finding suggesting that these prostheses can function late after surgery and do not necessarily thrombose. There were no HF-related admissions during follow-up.

COMMENT

We describe our experience with management of AR after implantation of continuous-flow LVADs. We show that there are both open and percutaneous options available for resolving AR, including redo sternotomy with surgical bioprosthetic implantation, transcatheter implantation, and use of the Amplatzer device. These

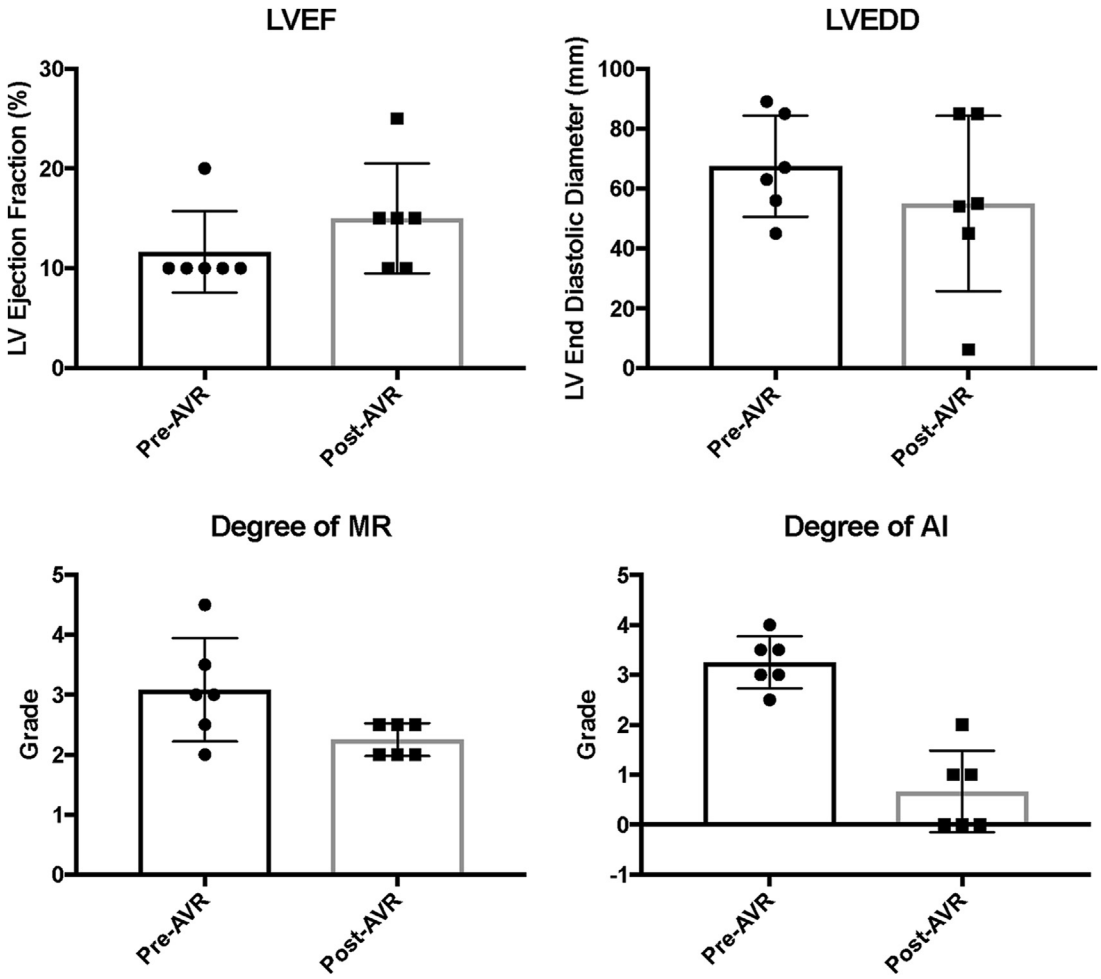

FIGURE 1 Echocardiographic impact of aortic valve replacement (AVR) on left-sided heart structure and function. (AI, aortic insufficiency; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation.)

options were associated with acceptable outcomes in this modest series. Although all patients in this series were considered for open surgery, this report demonstrates a growing role for percutaneous therapies in this cohort. Resolution of AR is associated with improved hemodynamics and relief of HF. All these options are durable within the limits of the follow-up of this study. Importantly, all valves appeared to function at least intermittently in later follow-up.

Significant AR after LVAD implantation has been described in 3% to 30% of patients.[2] LVADs appear to reduce aortic valve compliance, activate leaflet protein expression, and trigger fibrosis,[3] but whether these effects are causally related to the development of AR is not known. A valve that does not open well and lower LV dimensions are putative risk factors for AR development. Aortic valve opening also appeared to be protective in the series reported by Saeed and colleagues[2] of 34 patients who received the European HeartWare device with an intrinsic low-speed Lavare cycle to promote opening. The mechanism of this protective effect of valve opening is unknown, but it may relate to thrombus formation prevention and cusp fusion,[4] with some investigators suggesting LVAD titration to ensure intermittent aortic valve opening.

The status of the aortic valve at the time of surgery also has a major impact on the risk of AR. In patients with a mechanical aortic valve, most surgeons would either replace it with a bioprosthesis or patch close the LV outflow tract or proximal aorta out of concerns that in the absence of consistent valve opening, the thromboembolic risk is high.[5] Ahn and colleagues[6] showed that

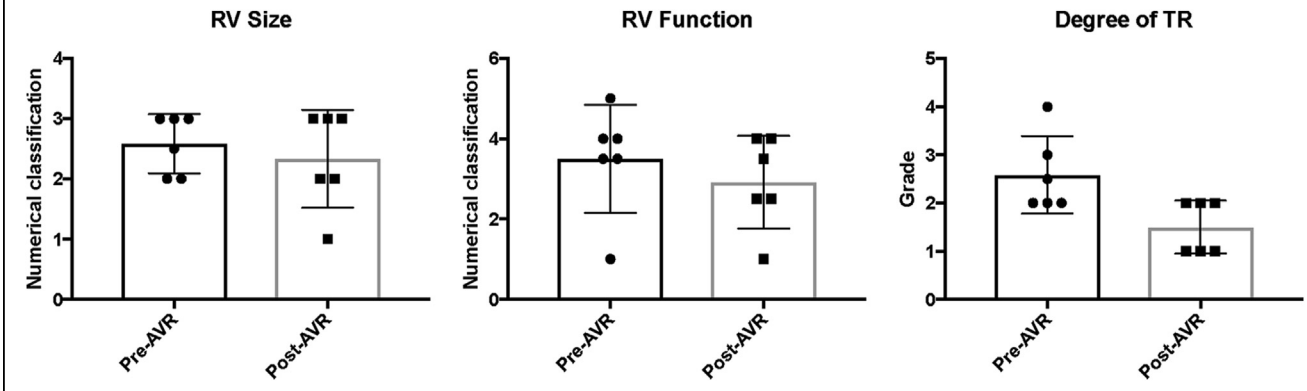

FIGURE 2 Echocardiographic impact of aortic valve replacement (AVR) on right-sided heart structure and function. (RV, right ventricular; TR, tricuspid regurgitation.)

when a mechanical aortic valve is left in situ, there is increased complexity of anticoagulation management, as seen with valvular thrombus formation and an increased risk for hemorrhagic stroke. Such data reinforce the strategy of either patch exclusion of mechanical prosthesis or replacement with a bioprosthesis.

Although some groups promote aortic valve opening as a means of protection from AR in the setting of a bioprosthesis or native valve, others have adopted an aggressive approach to prophylactic aortic valve closure in all patients with greater than mild AR at the time of LVAD implantation.[7] McKeller and colleagues[7] showed that patients who underwent prophylactic aortic closure did not experience significant AR compared who 18% of patients who did not receive prophylactic measures, and prophylactic aortic closure seems to protect from de novo AR in the midterm.[8] However, permanent aortic valve closure must be considered in view of the dangers of the rare event of pump failure because cardiac output is derived entirely from the LVAD.

There are many options for de novo AR, including redo sternotomy with patch closure of the aortic valve or LV ventricular outflow tract, TAVR, or surgical bioprosthesis. Atkins and colleagues[9] described 6 patients with significant AR after LVAD implantation managed with either redo sternotomy and AVR (4 initially) or TAVR (2, with 1 patient requiring open surgery subsequently). These results were similar to ours, with 1 patient death caused by multiorgan failure and sepsis, but overall good relief from AR and HF. Both series show that in the properly selected patient, open surgical bioprosthesis remains an effective and safe strategy. In the present series, we showed a more effective use of TAVR for the management of these patients. One patient in our series required deployment of a second valve because of valve migration, but otherwise all patients who underwent TAVR left the operating room with good echocardiographic and clinical results. Importantly, this strategy avoids repeat sternotomy, a feature that may be of special importance in the patient who is listed for heart transplantation. TAVR and other percutaneous options are likely to increase in importance in the future given the risk profile of many patients with LVADs.

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