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Original Research

Transcatheter Aortic Valve Replacement for Left Ventricular Assist Device–Related Aortic Regurgitation: The Michigan Medicine Experience

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ABSTRACT

Background: Aortic regurgitation (AR) is common and detrimental in patients with left ventricular assist devices (LVADs). Off-label use of transcatheter aortic valve replacement (TAVR) has emerged as a potential treatment option. Further data are required regarding the feasibility and outcomes of TAVR to treat AR in LVAD recipients.

Methods: A retrospective review of all patients with LVADs who underwent TAVR for the treatment of AR at a single center was performed. All echocardiograms were independently reviewed to ensure accuracy.

Results: Eleven patients with continuous-flow LVADs underwent TAVR for AR. All patients had moderate or severe AR with New York Heart Association (NYHA) class III and IV symptoms. Implantation of more than 1 valve was required in 4 (36.3%) patients; 1 patient died during the procedure because of valve migration into the left ventricle and 1 patient died in-hospital after TAVR. Of 9 (81.8%) patients discharged alive, 8 (72.7%) were alive at 12 months and all survivors had improvement in AR severity, natriuretic peptide levels, left ventricle end-diastolic diameter, and NYHA class. Five (62.5%) survivors had a large improvement (>20 points) in the Kansas City Cardiomyopathy Questionnaire score at 1 year. One survivor experienced heart failure, requiring hospitalization, within 1 year.

Conclusions: In this single-center series, TAVR for the treatment of AR in patients with LVADs is technically challenging but feasible in select patients and may produce durable improvements in AR severity, functional status, and quality of life.

Introduction

Native valve aortic regurgitation (AR) is common in patients with continuous-flow (CF) left ventricular assist devices (LVAD), with moderate or severe AR occurring in 30% to 40% of CF-LVAD recipients within 3 years.[1-6] Symptomatic AR is initially medically managed with diuretics, vasodilators, and reduction in LVAD pump speed.[1-3,6,7] Unfortunately, AR commonly progresses to biventricular failure, with high rates of hospitalization and mortality.[6] Therapeutic options for AR refractory to medical management include surgical replacement or heart transplantation (HT). However, patients with LVADs are often at a high risk of complications with redo surgery, and not all patients are appropriate transplant candidates.[8,9] Aortic valve (AV) closure with the Amplatzer (Abbott) septal occluder device has been investigated but has high rates of AR recurrence.[10,11] In addition, AV occlusion makes the patient entirely dependent on LVAD function for systemic perfusion, and LVAD dysfunction is rapidly fatal.[10,11] The role of AR in heart failure (HF) progression in patients with LVADs necessitates the investigation of novel therapeutic options, particularly minimally invasive therapies for patients at a high operative risk who are ineligible for HT.

Transcatheter aortic valve replacement (TAVR) is an established therapy for aortic stenosis across the spectrum of surgical risk.[12,13] TAVR has emerged as a potential off-label treatment for isolated AR with amenable anatomy and prohibitive surgical risk. Unlike patients with aortic stenosis, patients with isolated severe AR often lack significant AV leaflet and perivalvular calcification, which serves as an anchor for

Abbreviations: AR, aortic regurgitation; AV, aortic valve; HT, heart transplantation; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVAD, left ventricular assist device; NYHA, New York Heart Association; TAVR, transcatheter aortic valve replacement; TEE, transesophageal echocardiogram; THV, transcatheter heart valve; TTE, transthoracic echocardiogram.

Keywords: aortic regurgitation; HeartMate 3; left ventricular assist device; transcatheter aortic valve replacement.

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transcatheter heart valves (THVs).[1,2,6,7] Additionally, patients with LVADs often have a dilated AV annulus that also increases the risk of THV instability and possible migration.[1-4] Registry data have demonstrated technical feasibility for the off-label use of TAVR for AR in high-risk, inoperable patients with amenable anatomy and not on LVAD support,[14,15]; however, reports on patients on LVAD support are limited.[16-18] Further data are required regarding safety, durability, and efficacy in the LVAD population. We report a single-center experience of patients with LVADs undergoing TAVR for AR.

Methods

We conducted a retrospective review of all patients with LVADs who underwent TAVR for an indication of AR at the University of Michigan from 2014 to 2019 (Appendix). Each case was independently reviewed by 3 members of the study team (K.T.G., M.C.T., and D.S.). When there were discrepancies with specific data points during abstraction, the 3 study team members met and arrived at a consensus. All echocardiograms, including baseline studies, were independently reviewed by a level 3 echocardiography-trained advanced HF cardiologist (M.C.T.). All data were deidentified and accessible only to the investigators. This study was approved by the institutional review board at the University of Michigan.

Outcome measures

We collected data on demographic and clinical characteristics, diagnostic testing, procedural details, and outcomes. Outcome measures included the length of stay, survival to discharge, echocardiographic parameters, hospitalizations, and mortality up to at least 12 months after TAVR. We assessed functional status and the quality of life with the New York Heart Association (NYHA) functional class and the Kansas City Cardiomyopathy Questionnaire (KCCQ), respectively. KCCQ is a 23-item self-administered questionnaire that assesses specific health domains pertaining to HF symptoms and is combined into an overall summary score (KCCQ-OS) from 0 to 100, with higher scores indicating a better quality of life.[19,20] Echocardiographic data, natriuretic peptide levels, NYHA functional class, and KCCQ scores were compared between baseline levels (within 30 days prior to TAVR) and those at 1 year (between 12 and 14 months after TAVR), when available.

TAVR evaluation

All patients with LVADs are observed by a multidisciplinary LVAD team. Routine transthoracic echocardiograms (TTEs) are obtained for patients to evaluate LVAD and cardiac structure and function. At our institution, our advanced HF cardiologists and cardiac surgeons often refer patients with LVADs to the multidisciplinary Heart Team for consideration of valve replacement if they are found to have at least moderate AR that, after ruling out or treating other causes, is believed to be a principal driver of the patient's clinical decline or decompensation. The purpose of pursuing TAVR is to minimize AR and adverse left ventricle (LV) remodeling while on LVAD support, not necessarily to promote forward flow through the prosthesis. Patients are evaluated by at least 1 interventional cardiologist and 1 cardiac surgeon to determine candidacy for TAVR. These patients are then discussed at our weekly multidisciplinary comprehensive Heart Team meeting to determine if TAVR is technically feasible and the best management option for each patient. We reach a consensus determination only after excluding other causes of acute decompensation or worsening cardiomyopathy. Given the limitations of standard echocardiographic criteria for grading AR on LVAD support, patients with moderate AR are sometimes referred for consideration of valve replacement if no other conditions reasonably explain the patient's clinical decline and conservative interventions have failed to improve the patient's clinical status. Of note, patients with LVAD-associated AR may be determined to not be suitable TAVR candidates for multiple reasons, including alleviation with conservative or medical management, eligibility for surgical intervention, eligibility for HT, anatomic unsuitability for TAVR, or patient preference for conservative or palliative management.

For all patients evaluated for TAVR, a TTE was obtained as part of routine evaluation of worsening HF symptoms. AR severity was graded as minimal, mild, moderate, or severe in accordance with American Society of Echocardiography guideline recommendations.[21] TTE assessment with a turndown in LVAD support was performed to assess AV opening and to obtain the most representative measure of the aortic annulus and left ventricular outflow tract. During this study, LVAD speed was incrementally reduced until maximal AV opening was visualized to assess the maximal aortic annular diameter during systole. If the AV did not open, we used the maximal measurements that were attainable until symptoms or hemodynamics precluded further turndown. We used the LVAD speed that demonstrated maximal valve opening and thus annular dimensions on a turndown TTE during multidetector computed tomography (MDCT) angiography to obtain the largest possible measurements of the aortic root, annulus, and left ventricular outflow tract to inform optimal THV selection.

Finally, THVs were oversized by at least 15% beyond the maximal annular diameter to ensure appropriate sizing. THV oversizing was calculated using the device annular sizing ratio,[22]: device annular sizing ratio = ([THV perimeter − annulus perimeter] ÷ annulus perimeter) × 100. Patients 1 to 4 did not have a turndown study performed because they underwent TAVR before routine implementation of the LVAD turndown protocol in 2016. Additionally, patient 3 did not have an MDCT angiogram because of severe renal dysfunction and instead had a transesophageal echocardiogram (TEE) and noncontrasted computed tomography scan of the aorta for preprocedural planning.

TAVR procedural protocol

Our site preferentially uses the self-expanding Medtronic THV during these procedures owing to the ability to recapture the device if there is device malpositioning or instability during deployment. We employ several techniques to ensure THV stability during deployment in the absence of a calcified AV annulus and leaflets. We use a stiff guide wire, either the Amplatz Super Stiff (Boston Scientific), Safari 2 (Boston Scientific), or Lunderquist (Cook Medical) guide wire, to increase our ability to properly position the device during each phase of deployment. After positioning the THV across the AV, we turn down the LVAD speed to the lowest hemodynamically tolerated setting to decrease aortic load and prevent THV migration. Next, we initiate rapid pacing at 120 to 160 beats per minute to decrease LV pulsatility and ectopy, allowing for more precise valve positioning. We deploy the THV to the 80% position, after which we stop pacing and confirm THV positioning via transesophageal echocardiography and angiography. At the 80% position, the valve on the THV is fully functional, but the device may be recaptured, if necessary. We monitor the THV valve at the 80% position for 5 to 10 minutes as we slowly increase LVAD flows, release tension on the guide wire, and center the nosecone of the THV. If the valve migrates during this time, we are still able to recapture the device and determine whether we should attempt reimplantation or abort the procedure. Moreover, by waiting at the 80% position, the nitinol frame is given time to expand and attain a secure position within the annulus. After 5 to 10 minutes, the remaining 20% of the THV is deployed slowly while pacing at 100 to 130 beats per minute and with LVAD speed turned down. After release, hemodynamics and positioning are reevaluated, and the guide wire is removed. LVAD flow is slowly returned to preprocedure speeds, and the THV prosthesis is observed

by transesophageal echocardiography and fluoroscopy to ensure stability. Patients with LVADs are indefinitely maintained on antiplatelet therapy, generally aspirin, and anticoagulation with warfarin with a goal international normalized ratio of 2.0 to 3.0.

Results

Baseline clinical and anatomic characteristics

Eleven patients with CF-LVADs (6 with HeartWare [Medtronic] ventricular assist device, 3 with HeartMate 3 [Abbott], and 2 with HeartMate II [Abbott]) at a large academic center underwent TAVR for AR (Tables 1 and 2). The majority were men (63.6%) and White (90.9%), with a median age of 60 years (range, 37-79 years) at the time of TAVR. Six (54.5%) patients had LVAD implanted as a bridge to transplant (BTT), whereas 5 (45.5%) patients had LVAD implanted as destination therapy (DT). No patient had greater than mild AR before LVAD implantation or AV intervention at the time of their LVAD implantation. All patients had significant functional impairment with NYHA functional class III or IV symptoms and a mean pre-TAVR KCCQ-OS of 32 (n = 8). All patients were on maximally-optimized medical therapy and deemed to be at a high or extremely high risk for cardiac surgery (Supplemental Tables S1 and S2). Six (54.5%) patients were urgently evaluated for TAVR in the inpatient setting owing to AR-related decompensated HF and cardiogenic shock. All patients had moderate to severe, continuous native valve AR upon echocardiography (Table 2). Eight (72.7%) patients had no AV calcium, and one patient had a calcium score of 1 Agatston unit.

TAVR procedure

We present an example of a preprocedural and postprocedural echocardiogram and representative fluoroscopic images during TAVR for one of the patients (patient 8; Central Illustration). Procedural details are presented in Table 3. Patients underwent TAVR at a median of 18 months (range, 3-65 months) after LVAD implantation. Four (36.4%) patients required multiple THV prostheses. Two of these patients required additional THV owing to the presence of significant paravalvular regurgitation with the initial THV implantation. The first patient (patient 2) had severe AR after deployment of a 31-mm CV at a depth of 12 mm. This THV was snared back, and a second 31-mm CV was successfully deployed 9 mm higher. Notably, patient 2 did not have a preprocedural turndown TTE study because they underwent TAVR before the creation of the turndown transthoracic echocardiography protocol. The second patient (patient 5) had severe AR after a CV was deployed at a depth of 10 mm. This THV was snared and pulled up, and a second 31-mm CV was deployed. These 2 patients had complete resolution of AR with no further procedural complications. One patient (patient 6) underwent postimplantation balloon valvuloplasty to ensure complete THV expansion.

Two patients required multiple THV prostheses owing to THV migration into the LV cavity. The first patient (patient 11) had a 34-mm Evolut (Medtronic) positioned at the intended level; however, the THV migrated toward the LV immediately after release from the guide wire. This THV was snared and held in place, and a second 34-mm CV was deployed 10 mm higher while the LVAD speed was reduced to <400 revolutions per minute. Persistent AR after the second THV necessitated deployment of a third THV, a 29-mm SAPIEN 3 (Edwards Lifesciences). LVAD speed was increased to 5500 revolutions per minute with appropriate THV stability. A TEE revealed trace postdeployment AR, and the patient had no further complication. The second patient (patient 3) with THV migration did not have a preprocedural turndown TTE study because they received TAVR before creation of the turndown transthoracic echocardiography protocol. They additionally did not have a MDCT angiogram because of severe renal dysfunction. Thus, THV oversizing was based on annular measurements on a TEE, which may have contributed to undersizing and valve migration. A 29-mm CV was deployed at the 4-mm position and immediately migrated toward the LV. This THV was snared out of the annulus and positioned in the descending aorta. A second 31-mm CV was deployed in the same fashion but again immediately migrated into the LV. The patient developed ventricular fibrillation and died despite attempted snaring and cardiopulmonary resuscitation.

Table 3 shows echocardiographic AR grade after successful THV deployment. Immediately after TAVR and return of LVAD speed to baseline, all 10 procedural survivors had absent or minimal AR.

Postprocedural complications

Ten (90.9%) patients survived the TAVR procedure. Table 4 and Supplemental Table S3 demonstrates patient complications. After the procedure, 1 patient (patient 8) developed a rectus sheath hematoma, requiring embolization of the right inferior epigastric and medial femoral circumflex arteries. Two patients (patients 2 and 4) developed femoral artery hematomas, requiring blood transfusions. One patient (patient 7) developed a parietal subarachnoid hemorrhage without neurologic deficits 3 days after TAVR. This patient was readmitted 1 month after TAVR because of LVAD pump thrombosis and died from right ventricular failure after pump exchange. One patient (patient 8) developed inotrope-dependent right ventricular failure for 1 month after TAVR and was discharged in stable condition. One patient (patient

Table 1. Baseline patient characteristics at the time of transcatheter aortic valve replacement.

Patient	Age (y)	Sex	eGFR	CMP	NYHA functional class (I-IV)	LVAD (BTT/DT)	BNP (pg/mL)	KCCQ-OS	Indications for TAVR
1	75	F	33	NICM	III	HM II (DT)	620	49	Worsening HF
2	79	M	42	ICM	IV	HVAD (DT)	552	40	Worsening HF
3	48	M	32	ICM	III	HM II (DT)	229	N/A	Cardiogenic shock (IP)
4	73	F	32	ICM	III	HVAD (DT)	976	38	Cardiogenic shock (IP)
5	66	M	59	ICM	IV	HM3 (BTT)	1053	N/A	Cardiogenic shock (IP)
6	67	F	58	NICM	III	HVAD (BTT)	696	25	Worsening HF
7	37	M	54	NICM	IV	HVAD (DT)	870	39	Worsening HF
8	57	F	46	NICM	IV	HVAD (BTT)	974	22	Cardiogenic shock (IP)
9	58	M	26	ICM	IV	HVAD (BTT)	1045	38	Cardiogenic shock (IP)
10	55	M	44	ICM	IV	HM3 (BTT)	942	0	Cardiogenic shock (IP)
11	62	M	52	ICM	IV	HM3 (BTT)	571	N/A	Worsening HF

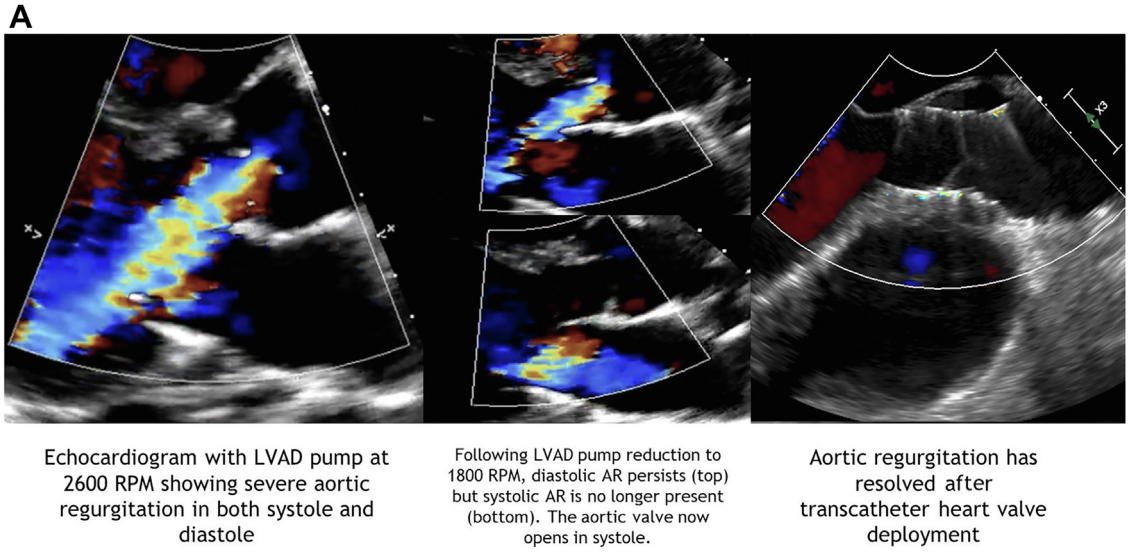
Aortic regurgitation was graded from 0 to 4: 0 = none, 1 = trace/minimal, 2 = mild, 3 = moderate, and 4 = severe.
BNP, B-type natriuretic peptide; BTT, bridge to transplantation; CMP, cardiomyopathy; DT, destination therapy; eGFR, estimated glomerular filtration rate; F, female; HF, heart failure; HM3, HeartMate 3; HM II, HeartMate II; HVAD, HeartWare ventricular assist device; ICM, ischemic cardiomyopathy; IP, inpatient evaluation; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall score; LVAD, left ventricular assist device; M, male; N/A, not applicable; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association; TAVR, transcatheter aortic valve replacement.

Table 2. Technical characteristics before transcatheter aortic valve replacement.

Patient	Pre-LVAD AR grade[a]	LVEF	Pre-TAVR AR grade[a]	MR grade[a]	LVEDd (mm)	AV calcification score (AU)	AV annular diameter (mm)	LVAD flow requirement (L/min)
1	1	30	3-4	3	49	0	24	5.3
2	1	15	3	2	67	0	28	3.8
3	2	20	3	2	93	0	26[b]	5.3
4	2	20	3	3-4	47	0	19	3.8
5	2	20	4	2	75	0	26	5.0
6	0	20	4	4	52	0	20	4.4
7	1	10	3-4	1	76	0	25	5.8
8	1	15	3	2	56	0	24	4.0
9	0	15	4	2	58	1	24	4.2
10	0	20	4	3	71	378	25	4.8
11	0	10	4	2	78	37	26	5.3

AR, aortic regurgitation; AU, Agatston unit; AV, aortic valve; LVAD, left ventricular assist device; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; TAVR, transcatheter aortic valve replacement.

[a] MR was graded similar to AR. AR and MR were graded from 0 to 4: 0 = none, 1 = trace/minimal, 2 = mild, 3 = moderate, and 4 = severe. [b] A contrasted multidetector computed tomography angiogram was not obtained for patient 3 because of severe renal dysfunction, and annular diameter was obtained from a transesophageal echocardiogram.



Central Illustration.

(**A**) Preprocedural and postprocedural echocardiograms in parasternal long axis views. (**B**) Fluoroscopic images before the final release and after release of the valve with aortography. Fluoroscopic images during 80% deployment (left) and full deployment and expansion (right) of a transcatheter heart valve prosthesis. AR, aortic regurgitation; LVAD, left ventricular assist device; RPM, revolutions per minute.

Table 3. Procedural details.

Patient	TAVR year	Months from LVAD to TAVR	No. of THVs required	THV type(s), size (no. of THVs required)	THV oversizing[a]	Intraprocedural complication	Postdeployment AR grade[c]	Survived procedure
1	2014	21	1	SE, CV, 31 mm (×1)	21.7%	None	0	Yes
2	2015	40	2	SE, CV, 31 mm (×2)	6.9%[b]	Required multiple THV	1	Yes
3	2015	52	2	SE, EV, 29 mm (×1) SE, CV, 31 mm (×1)	11.5%[b]	THV migration toward LV apex; required multiple THV	4	No
4	2015	3	1	SE, EV, 26 mm (×1)	30.3%	None	1	Yes
5	2016	7	2	SE, CV, 31 mm (×2)	21.0%	Required multiple THV	0	Yes
6	2017	3	1	SE, EV, 26 mm (×1)	25.7%	None	1	Yes
7	2017	65	1	SE, EV, 31 mm (×1)	18.8%	None	0	Yes
8	2018	7	1	SE, EV, 29 mm (×1)	18.3%	None	0	Yes
9	2019	23	1	SE, EV, 29 mm (×1)	23.1%	None	0	Yes
10	2019	4	1	SE, EV, 34 mm (×1)	30.3%	None	0	Yes
11	2019	18	3	SE, EV, 34 mm (×2) BE, S3, 29 mm (×1)	33.5%	THV migration toward LV apex; required multiple THV	0	Yes

AR, aortic regurgitation; BE, balloon expandable; CV, CoreValve (Medtronic); EV, Evolut (Medtronic); PG, peak gradient; LV, left ventricle; LVAD, left ventricular assist device; N/A, not applicable; SE, self-expanding valve; S3, SAPIEN 3 (Edwards Lifesciences); TAVR, transcatheter aortic valve replacement; THV, transcatheter heart valve.
[a] THV oversizing was calculated using the device annular sizing ratio: device annular sizing ratio = ([THV perimeter − annulus perimeter] ÷ annular perimeter) × 100.
[b] Patients 1 to 4 did not have a baseline turndown echocardiogram study performed because they underwent TAVR before implementation of a standardized LVAD turndown protocol. A contrasted multidetector computed tomography angiogram was not obtained for patient 3 because of severe renal dysfunction, and valve oversizing was calculated using an annular diameter obtained from a transesophageal echocardiogram. [c] AR was graded from 0 to 4: 0 = none, 1 = trace/minimal, 2 = mild, 3 = moderate, and 4 - severe.

11) who received urgent TAVR developed severe mitral regurgitation of unclear origin 3 days after TAVR. THV migration and interaction of the THV with the anterior mitral leaflet were investigated as potential causes of the mitral regurgitation but did not appear to be significant contributors. This patient died from refractory cardiogenic shock during his post-TAVR hospitalization.

Outcomes

Nine (81.8%) of 11 patients were discharged home after a median length of stay of 14 days (interquartile range, 9-18 days) (Table 4). Only 1 (9.1%) patient was hospitalized for HF within 12 months of TAVR. Eight (72.7%) patients survived to 12 months after TAVR (Supplemental

Table 4. Patient outcomes after transcatheter aortic valve replacement.

Patient	Survived procedure	Complication	LOS (d)	Survived to discharge	Survival to 1 mo	12-mo hospitalization for HF	Survival to 12 mo	Time on LVAD support at death (mo)	Status as of July 1, 2021
All[a]	10 (90.9%)		14 (9-18)	9 (81.9%)	9 (81.9%)	1 (9.1%)	8 (72.7%)	44 (39-64)	
1	Yes	None	12	Yes	Yes	No	Yes	39	Died at 18 mo after TAVR from OHCA
2	Yes	LFA hematoma	15	Yes	Yes	No	Yes	84	Died at 44 mo after TAVR from pneumonia
3	No	Death	N/A	No	No	N/A	No	52	Died during TAVR
4	Yes	LFA/RFA hematomas	8	Yes	Yes	No	Yes	69	Alive at 66 mo after TAVR; DT
5	Yes	None	13	Yes	Yes	No	Yes	39	HT 32 mo after TAVR
6	Yes	None	15	Yes	Yes	No	Yes	43	Died at 40 mo after TAVR from mechanical fall and ICH
7	Yes	Stroke (subarachnoid hemorrhage)	24	Yes	Yes[b]	Yes[b]	No	68	Died at 3 mo after TAVR[b]
8	Yes	Rectus sheath hematoma	36	Yes	Yes	No	Yes	23	Died at 16 mo after TAVR from RV failure
9	Yes	None	9	Yes	Yes	No	Yes	45	Alive at 22 mo after TAVR; BTT
10	Yes	None	4	Yes	Yes	No	Yes	17	Died at 13 mo after TAVR from HF progression
11	Yes	None	19	No[c]	No	N/A	No	19	Died before discharge after TAVR from persistent cardiogenic shock[c]

BTT, bridge to transplant; DT, destination therapy; HF, heart failure; HT, heart transplantation; ICH, intracranial hemorrhage; LFA, left femoral artery; LOS, length of stay; LVAD, left ventricular assist device; N/A, not applicable; OHCA, out-of-hospital cardiac arrest; RFA, right femoral artery; RV, right ventricle; TAVR, transcatheter aortic valve replacement.
[a] Reported as median (interquartile range) or frequency and percentage. [b] Rehospitalized at 1 month after discharge for LVAD pump thrombosis requiring pump exchange. The patient died at 3 months after TAVR from RV failure after pump exchange. [c] Died after TAVR but before hospital discharge from persistent cardiogenic shock and severe mitral regurgitation, thought to be due to underlying cardiomyopathy. Late transcatheter heart valve migration and acute ischemia were not thought to be contributing to mitral pathology.

Table 5. Functional and structural outcomes in 12-month survivors (N = 8).

Patient	NYHA functional class (I-IV)	KCCQ-OS	BNP (pg/mL)	AR grade[a]	LVEDd (mm)	LVAD flow requirement (L/min)
1	II	96	303	1	48	3.8
2	II	N/A	230	0	59	4.7
4	II	74	387	0	39	3.2
5	I	63	228	0	69	4.6
6	I	N/A	230	0	48	1.9
8	II	90	421	0	43	2.7
9	I	84	182	0	56	3.5
10	II	50	63	0	59	4.3

AR, aortic regurgitation; BNP, B-type natriuretic peptide; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall score; LVAD, left ventricular assist device; LVEDd, left ventricular end-diastolic diameter; N/A, not applicable; NYHA, New York Heart Association.

[a] AR was graded from 0 to 4: 0 = none, 1 = trace/minimal, 2 = mild, 3 = moderate, and 4 = severe.

Figure S1 and Supplemental Table S4). Table 5 shows structural and functional outcomes in 12-month survivors. There was a durable reduction in AR grade on echocardiographic follow-up for all survivors and improvements in the NYHA functional class and KCCQ-OS (Figure 1). A large improvement (>20 points) in KCCQ-OS was seen in all survivors with available pre- and post-TAVR KCCQ data. Reductions were also observed in LV end-diastolic diameters (a mean reduction of 6.8 ± 4.4 mm), serum B-type natriuretic peptide levels (a mean reduction of 601 ± 216 pg/mL), and LVAD flows (from 4.4 ± 0.6 L/min before TAVR to 3.6 ± 1.0 L/min at 12 months after TAVR). One patient (patient 10) developed THV thrombus, which was managed with a higher international normalized ratio goal of 2.0 to 3.0 (previously 1.5-2.5 because of epistaxis), and they had no further sequelae of thrombus formation. No patient developed greater than mild or trace paravalvular regurgitation. One patient (patient 5) underwent HT 32 months after TAVR.

Discussion

This single-center report of TAVR for AR in patients with LVADs has 3 principal findings. First, TAVR in this population is technically challenging and requires careful preprocedural planning, with reduction in LVAD flows during computed tomography imaging to ensure accurate anatomic measurements and THV sizing. Second, despite careful preprocedural planning, these patients are at a high risk of THV migration during the procedure, with a third of patients requiring multiple THV prostheses owing to migration of the initial device. Third, although technically challenging with high procedural complexity and complication risk, we demonstrate a relatively high rate of survival in carefully selected patients and durable improvements in AR severity, functional status, and quality of life among survivors of the TAVR hospitalization.

This report comprises a contemporary LVAD population, with most patients having centrifugal CF devices. Our cohort was high risk for open surgical AV replacement, and the majority of our patients were evaluated for TAVR urgently as a final therapeutic option for AR-related decompensation. Eight (88.9%) of 9 patients discharged to home were alive at 12 months, with sustained echocardiographic improvement in AR. The impact of AR reduction is demonstrated by reductions in LV end-diastolic diameter and natriuretic peptide levels, indicating favorable ventricular remodeling and ventricular filling pressures.[1-4] Moreover, we observed reductions in LVAD flow commensurate with near complete or complete resolution of AR.

The finding of favorable outcomes after TAVR in LVAD recipients mirrors the prior success of off-label TAVR for AR in high-risk, inoperable patients with amenable anatomy not on LVAD support.[14,15] Prior series in patients with LVADs have demonstrated reduction in AR at short-term follow-up after TAVR,[16,18] and our report demonstrates the durability and long-term efficacy of echocardiographic and structural findings with a relatively high rate of postdischarge survival. In addition to these technical outcomes, patients in our study experienced substantial clinical improvement at 1 year, with an average 2 class reduction in the NYHA functional class and large improvements (>20 points) in their KCCQ-OSs. AR is a well-established cause of congestion and symptomatic HF,[1-4] and our findings establish favorable improvements in functional status and symptom burden that coincides with sustained echocardiographic and structural outcomes after TAVR.

The incidence of clinically significant AR will likely increase with current LVAD systems because of the improved long-term survival of such patients.[23-25] Potential AR therapies, such as TAVR, are particularly important in patients with LVADs for DT, a group which constitutes a majority and rising proportion of LVAD recipients.[26] For this large and growing population, HT is not an option for the treatment of AR; thus, minimally invasive treatments, such as TAVR, are important treatment options. However, contrary to patients with LVADs for DT, patients with significant AR with LVADs as a BTT are eligible for higher HT listing status in the current version of the heart allocation policy,[27] and immediate TAVR may not be desired in patients stable enough to await HT. Therefore, it is notable that most patients in our cohort undergoing TAVR had an LVAD implanted as a BTT, with 4 patients with a BTT LVAD

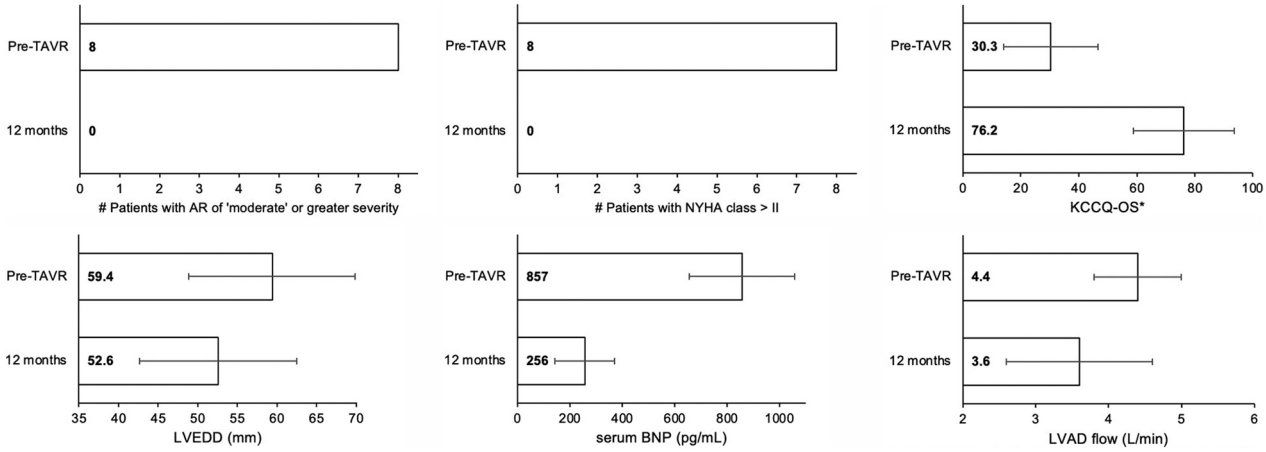


Figure 1.
Aggregate echocardiographic, biochemical, and functional outcomes in 12-month survivors (N = 8). Kansas City Cardiomyopathy Questionnaire overall score (KCCQ-OS), B-type natriuretic peptide (BNP), left ventricular end-diastolic diameter (LVEDD), and left ventricular assist device (LVAD) flow are presented as mean and standard deviation. Aortic regurgitation (AR) severity and New York Heart Association (NYHA) class are presented as number of patients. *Only 5 patients had available KCCQ data both pre-procedure and 12 months post-procedure. TAVR, transcatheter aortic valve replacement.

undergoing TAVR urgently and 1 patient successfully bridged to HT 32 months after TAVR. This strengthens the role of TAVR as an important therapeutic option for patients with DT and BTT LVADs.

We demonstrate the technical challenges of TAVR in this population, most importantly the high risk of THV migration related to continuous LVAD flow, large annulus, and lack of annular calcification. We believe that the high rate of THV migration is due to the unique hemodynamic environment of LVAD support with continuous flow, annular dilation, and aortic remodeling. This was evidenced by near-immediate migration in several patients despite generous THV oversizing and rigorous preprocedural testing for suitability. We describe several techniques to improve THV stability, and we have found that protocolized anatomic measurements, prosthesis oversizing, and LVAD pump variation during imaging and deployment are particularly critical to success. Unfortunately, treatment of AR alone may not fully alter the long-term prognosis of the patient's underlying cardiomyopathy. This was evidenced by high mortality rates unrelated to AR beyond 1 year, with only 4 patients alive at 24 months after TAVR (Supplemental Figure S1).

Given these risks, TAVR recipients should be carefully selected with attention to symptom severity, medical therapy optimization, transplant listing, and anatomic suitability. This off-label treatment should be considered and performed at centers with significant experience with TAVR given the complexity, complication risk, and requirement for careful planning with multimodality imaging. We recommend a multidisciplinary approach centered around the patient and involving structural heart cardiac surgeons, cardiac surgeons experienced in LVAD implantation and management, HF cardiologists, cardiovascular imaging specialists, and structural heart interventional cardiologists for a comprehensive approach to the management of AR in patients with LVADs.

This study should be interpreted in the context of several important limitations. First, this is a single-center study at an institution with significant experience with TAVR and LVAD implantation/management, and our findings may not be generalizable to other centers. Second, the procedural success noted here is biased by the selection of patients with LVADs that we believed were anatomically suitable to undergo TAVR and too high-risk to undergo repeat cardiac surgery. Specifically, these cases were discussed at our multidisciplinary Heart Team meeting, where the optimal treatment modality for the patient's AR was discussed. Third, traditional TTE measures often underestimate AR severity and hemodynamic significance of moderate grade or lower AR in the unique hemodynamic environment of CF-LVAD support, where AR can be continuous throughout the cardiac cycle and eccentric.[28-30] Using traditional echocardiographic indices may not capture all patients with hemodynamically significant AR that would potentially benefit from TAVR.

The observed benefit of TAVR for AR in patients with LVADs warrants prospective trials in a larger sample. These studies may assess the severity of AR using novel echocardiographic parameters developed specifically for AR quantification on CF-LVAD support.[28,29] Importantly, advancements in THV technologies and implantation technique may address the unique risks in this population. For instance, the JenaValve Trilogy Heart Valve System (JenaValve Technology Inc) is a novel THV under investigation designed for the treatment of aortic stenosis and AR that employs AV leaflet–clasping mechanisms and does not require annular calcification for THV anchoring.[31] These new designs may offer a safe and effective treatment option for AR in patients with LVADs.

Conclusion

In conclusion, TAVR for the treatment of AR in patients with LVADs is technically challenging but feasible in select patients and resulted in durable improvements in AR severity, functional status, and quality of life. TAVR may be an appropriate off-label treatment for carefully selected high-risk patients with LVADs with significant hemodynamic and symptomatic AR at select centers.

Declaration of competing interest

Dr Stanley J. Chetcuti has received consulting fees from Medtronic and research fees from Medtronic, Boston Scientific, Edwards Lifesciences, Gore Medical, Abbott Laboratories, and JenaValve Technologies. Dr Francis D. Pagani is a noncompensated scientific advisor for Medtronic, Abbott Laboratories, FineHeart, and CH Biomedical and is on the Data Safety Monitoring Board for the Carmat Total Artificial Heart and the National Heart, Lung, and Blood Institute PumpKIN Study. Dr Michael Grossman has received consulting fees from Medtronic; research fees from Medtronic, CSI, and Edwards Lifesciences; and support from the Blue Cross Blue Shield of Michigan for his role in quality improvement for the Michigan Structural Heart Consortium quality improvement collaborative. Dr G. Michael Deeb is an independent consultant for third party measurements on computed tomography scans for the Medtronic SMall Annuli Randomized To Evolut or SAPIEN Trial (SMART). Dr Daniel P. Menees has a nonmonetary disclosure with Medtronic. Dr Keith D. Aaronson has received consulting fees from Medtronic and Abbott Laboratories. Dr Devraj Sukul has received salary support from the Blue Cross Blue Shield of Michigan for his role in quality improvement for the Blue Cross Blue Shield of Michigan Cardiovascular Consortium. Drs Keerthi T. Gondi, Marty C. Tam, Jonathan W. Haft, and Himanshu J. Patel have no relevant disclosures or financial conflicts of interest.

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Ethics statement and patient consent

All data were deidentified and accessible only to investigators. This study was approved by the institutional review board at the University of Michigan. Requirement for informed consent was waived due to the retrospective nature of this analysis. This study was conducted in accordance with local and international guidelines for ethically conducted research.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at https://doi.org/10.1016/j.jscai.2022.100530.

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