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REVIEW ARTICLE

Managing valvular pathology during LVAD implantation

Michael J. Carr[1] · Susan Ansley Smith[1] · Mark S. Slaughter[1] · Siddharth Pahwa[1]

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Abstract

Since the time of their invention, implantable continuous flow left ventricular assist devices (LVADs) have improved the quality of life and extended survival for patients with advanced heart failure. The decision surgeons and their physician colleagues make with these patients to undergo implantation must come with full understanding of the immediate, short-term, and long-term implications of such a life-changing procedure. The presence of pathology regarding the aortic, mitral, and tricuspid valves introduces particularly complex problems for the surgical treatment strategy. Concomitant valve repair or replacement increases cardiopulmonary bypass and cross clamp times, and could potentially lead to worse outcomes in the perioperative setting. Following perioperative recovery, valvular pathology may worsen or arise de novo given the often drastic immediate physiologic changes in blood flow, septal function, and, over time, ventricular remodeling. Over the past two decades, there has been vast improvement in the device manufacturing, surgical techniques, and medical management surrounding LVAD implantation. Yet, addressing concomitant valvular pathology remains a complex question with no perfect solutions. This review aims to briefly describe the evolution of approach to valvular pathology in the LVAD patient and offer our opinion and treatment rationale.

Keywords Heart failure · Aortic valve · Mitral valve · Tricuspid valve

Background

Mechanical circulatory support for patients with advanced heart failure continues to evolve and improve in design and durability with continuous-flow left ventricular assist devices (LVADs) offering improved survival and better quality of life [1]. With the Food and Drug Administration approval for use as destination therapy (DT), the period for which these devices provide support has been increasing. A greater proportion of patients received LVAD therapy as DT from 2017–2021 compared to 2012–2016 (66% versus 47%, respectively) [2]. Native disease of the mitral and tricuspid valves is more common in heart failure patients evaluated for LVAD therapy. Aortic valves undergo significant alterations in hemodynamics during and after LVAD placement, which lead to structural changes. Native valvular heart disease was once considered a contraindication to LVAD implantation, particularly in regard to mechanical valves and risk of thromboembolism. Yet, it does not significantly increase peri-operative risk [3]. Valve surgery at the time of LVAD implantation is now considered common, but recent clinical trials show that it increases patient morbidity when compared to LVAD implantation alone.

In the International Society for Heart and Lung Transplantation (ISHLT) Registry for Mechanically Assisted Support (IMACS), 12% of patients undergo a valve procedure at the time of LVAD implantation [4]. A similar incidence of 19% was found in the European Registry for patients with Mechanical Circulatory Support (EUROMACS) [5]. In a study of patients undergoing HeartMate II (HMII) LVAD implantation, 22% underwent a concomitant valvular procedure (CVP). When compared to those who received HMII alone, 30-day mortality was significantly higher in patients undergoing CVPs (10% versus 4.8%, respectively) and even higher in those who had two or more CVPs (14%) [6]. In the ADVANCE bridge-to-transplant trial, 20% of patients underwent CVP; there was no significant difference in survival between groups but CVPs were associated with increased unadjusted early right heart failure [7]. In patients with HeartMate III (HMIII) implanted during the MOMENTUM 3 trial, 22% underwent CVP. While no difference was found in 30-day mortality or 2-year survival, the CVP cohort was

✉ Siddharth Pahwa
Siddharth.pahwa@uoflhealth.org

[1] Department of Cardiovascular and Thoracic Surgery, University of Louisville, Louisville, KY, USA

found to have an increased incidence of both stroke (4.9% versus 2.4%) and right heart failure (42% versus 30%) [8]. EUROMACS data found no significant difference in 1-year survival between groups (68% versus 66%) [5]. These data are important to consider with the acknowledgement that patients undergoing CVPs had higher acuity Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles and due to the additional procedures were subjected to longer cardiopulmonary bypass times.

Aortic valvular disease (Table 1)

Aortic stenosis (AS) typically does not require correction concomitantly with LVAD implantation as patients are not dependent on antegrade flow through the aortic valve (AV). The LVAD will decompress the left ventricle and provide the majority of cardiac output. As the LVAD transvalvular pressure gradient persists, this hemodynamic change may cause worsening fusion of the AV commissures, thus increasing the degree of AS.

LVAD implantation diverts blood flow from the left ventricle to the aorta, increasing cardiac output in heart failure and decreasing left ventricular pressure and wall stress which, in turn, boost reverse remodeling and reduce ventricular cavity size. Transvalvular pressure across the AV is increased with an increase in pressure at the aortic root which prolongs the diastolic period for the AV. During periods of high LVAD support, this causes the AV to be continuously closed [9]. With these physiological changes come mechanical changes in leaflet deterioration, commissure fusion, and aortic annulus dilation which may lead to worsening of baseline function or new-onset AS and aortic insufficiency (AI).

With constant exposure to high transvalvular pressure from LVAD implantation, known AI will worsen over time, resulting in a non-propagating loop of blood flow returning from the outflow graft of the LVAD back through the incompetent AV. The high pressure at the aortic root and decreased pressure within the left ventricle favors retrograde flow across the AV into the left ventricle, reducing left ventricular unloading and decreasing systemic perfusion, increasing right ventricular afterload, and eventually leading to recurrence of heart failure [10].

One of the largest retrospective studies between 2006 and 2016 identified on the INTERMACS registry found that 67% ($n=7362$) of patients had no AI at the time of implantation, 31% had ($n=3241$) mild AI, and 3% ($n=322$) had moderate to severe AI [10]. Within the IMACS registry, mild AI was present in 41% and moderate to severe AI in 4.5% of patients at the time of LVAD implantation [4, 11]. The incidence of AI at the time of LVAD implantation has also been described in several smaller series, together suggesting that 20–30% of heart failure patients receiving LVAD therapy have mild AI at baseline with 3–12% having moderate to severe AI [12, 13]. Of the 10,925 patients studied on the INTERMACS registry who had no AI at implantation, 1399 patients developed moderate to severe AI on LVAD support. This was also associated with higher rates of rehospitalization and mortality up to 1 year [10]. Patients who develop moderate to severe AI after LVAD implantation demonstrate higher left ventricular end diastolic diameter and reduced cardiac output. Current consensus guidelines recommend consideration of surgical correction of moderate or greater AI during LVAD implantation [14].

Aortic valvular intervention

As progression of valvular degeneration is common after LVAD implantation, surgical replacement with bioprosthetic AV should be considered, especially if the LVAD is placed with the goal of ventricular recovery. Other interventions to consider with LVAD implantation include oversewing of the native valve or obliteration of the AV [25]. In select patients, isolated AS is well tolerated with proper device function within the left ventricle and some native ejection through the AV opening may benefit patient exercise tolerance during increased left ventricular filling [26]. Choosing to defer AV closure also provides an outlet for cardiac output should LVAD malfunction occur and device flow cease. Among patients who underwent LVAD implantation with aortic CVPs in INTERMACS between 2006 and 2012, improved survival was found with repair or replacement compared to valve closure, suggesting a benefit in maintaining a patent outflow tract [20]. CVPs may be accomplished through several approaches broadly classified as valve replacement, valve repair, or complete closure of the valve.

Valve replacement with bioprosthesis has been suggested to be preferable for patients in which native ventricular ejection is desired. However, valve replacement is time-consuming, requiring cross-clamping and cardiopulmonary bypass. Additionally, bioprosthetic valves have been associated with thrombosis, embolization, and complete sclerosis leading to commissural fusion and closure [27, 28].

Percutaneous valve replacement with transcatheter aortic valve replacement (TAVR) has emerged as a safe treatment method in LVAD patients with reduction in morbidity and no difference in mortality when compared with surgical repair [29, 30], though data are currently limited regarding route of catheterization and timing for TAVR with respect to pre-, concomitant, or post-LVAD implantation.

Valvular repair via leaflet coaptation using a single central Park's stitch [31] creates a partial closure of the AV cusps whereby preventing stasis and thrombosis in the aortic root while still allowing blood flow through the commissures. Although this also requires aorta

Table 1 Key studies reporting on LVAD implantation and AV disease

Objectives	Authors	Study groups	Results
Development of AI in LVAD-supported patients and consequences during long-term support	Cowger et al. [12] (2010) Cowger et al. [15] (2014)	$n=78$ $n=166$	■ Pre-operative median AI of grade 0 (2010) and mild or less in 94% (2014) ■ Progression after LVAD to mild-moderate AI in 42%, and moderate-severe in 11% at 6 months; to moderate-severe AI in 22–26% at 9–12 months; and to moderate-severe AI in 51% at 18 months ■ No significant difference in overall survival at 2 years in moderate or worse AI vs less severe AI
Compare the prevalence of AI after LVAD implantation and assess the role of aortic root diameter and AV opening	Pak et al. [16] (2010)	HMI, $n=67$ HMII, $n=63$	■ At 6 months, 95% HMI and 84% HMII were free from mild-moderate AI, while at 12 months, 89% HMI and 75% HMII were free of mild-moderate AI ■ Aortic root diameters at baseline and follow-up trended to be larger in patients who developed AI ■ Post-transplant aortic root circumferences were larger in HMII patients who developed AI ■ AI was more common in patients whose aortic valve did not open
Investigate the occurrence of de novo AI during LVAD support	Toda et al. [17] (2011) Hiraoka et al. [18] (2015)	$n=47$ $n=99$	■ De novo AI developed in 38–52% ■ Pre-operative functional MR, smaller body surface area, larger aortic root diameter, higher pulmonary artery systolic pressure, and post-operative AV opening were identified as risk factors for de novo AI ■ Overall survival was significantly worse with development of de novo AI ■ No significant mortality difference related to preoperative or de novo AI
Comparison of AI development and progression of after LVAD implantation versus no surgical intervention	Rajagopal et al. [13] (2013)	LVAD recipients, $n=184$ Non-surgical patients, $n=132$	■ LVAD implantation associated with worsening AI compared to nonsurgical patients ■ AI developed or progressed to moderate-severe disease after LVAD implantation in 11%
Concomitant AV procedures in patients undergoing implantation of LVAD	Dranishnikov et al. [19] (2012) Robertson et al. [20] (2015)	Replacement, $n=19$ Closure, $n=125$ Repair, $n=95$ Replacement, $n=85$; INTERMACS registry analysis	■ At 6–12 months, moderate-severe AI developed in 5% (closure), 19% (repair), 9% (replacement), and 10% (no intervention) ■ AV closure associated with increased mortality when compared with repair or replacement ■ ICU stay, duration of mechanical ventilation, and in-hospital mortality of patients with IM score* of 1–2 was significantly higher in concomitant AV replacement group ■ Similar outcomes in patients with IM score* of 3–4 between concomitant AV replacement and control group

Table 1 (continued)

Objectives	Authors	Study groups	Results
Evaluate impact of AI progression during LVAD support on clinical outcomes	Holley et al. [21] (2017) Truby et al. [10] (2018) Jimenez Contreras et al. [22] (2022)	$n = 237$ $n = 10{,}603$, INTERMACS registry analysis $n = 836$	■ Moderate-severe AI developed in 10–32% with increase in prevalence over time ■ Predictors of AI included older age, female gender, smaller body mass index, pre-operative AI, longer duration of LVAD support, and destination therapy designation ■ Overall survival 78% at 1 year, 71–77% at 2 years, 59% at 3 years, 42% at 5 years
Impact of uncorrected mild AI at the time of LVAD implantation	Tanaka et al. [23] (2020)	Propensity score match: Mild AI, $n = 101$ No AI, $n = 101$	■ 44% of mild AI and 9% of no AI groups developed ≥ moderate AI ■ Higher heart failure rehospitalization in mild AI ■ Overall survival 74% vs 71% at 1 year, 64% vs 67% at 3 years, 59% vs 63% at 5 years (mild AI vs no AI, respectively)

AV aortic valve, *AI* aortic insufficiency, *MR* mitral regurgitation, *LVAD* left ventricular assist device, *IM* INTERMACS, *HMI* HeartMate I, *HMII* HeartMate II, *HMIII* HeartMate III

* "IM score": INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) patient profiles 1–6 detail clinical stages of New York Heart Association class IV, where profile 1 patients are in critical cardiogenic shock, 2 in progressive decline, 3 are stable but inotrope dependent, and 4–7 considered to have ambulatory heart failure [24]

cross-clamping and cardiopulmonary bypass, central leaflet coaptation takes less time than valve replacement. In the event of considerable thinning or friability of the aortic leaflet tissue, a modified Park's stitch has been described with a single additional stitch on each side of the central stitch between the central pledget and each commissure [32]. Over a median follow-up of 312 days where no patient had more than mild AI immediately following LVAD placement, severity of AI progression was significantly less in the Park's stitch group compared to no repair (0%, $n = 18$, versus 18%, $n = 105$, respectively) [31]. Schechter et al. also assessed long-term outcomes with central leaflet coaptation, with median follow-up of 560 days reporting 95% ($n = 19$) of patients with greater than mild AI at time of LVAD implant had none or trace AI postoperatively and no significant increase in AI for the duration of follow-up [33].

Depending on the individual patient, outflow tract closure may be required and is accomplished using a bovine pericardial patch or suture closure of the AV leaflet lines of coaptation [34]. Adamson et al. provide a case series which describes complete suture closure with felt strip reinforcement which resulted in no subsequent development of AI or distal embolization. Improved survival was noted at 1 and 3 years in comparison to patients without AI intervention [35]. Although closure definitively eliminates AI, acute malfunction of the device may leave no course for native cardiac output and become rapidly fatal as previously discussed. Additionally, complete outflow tract closure should not be given consideration if myocardial recovery is possible.

A more recent study from the IMACS registry ($n = 15{,}267$) over 2013–2017 reported significantly reduced survival with aortic CVP as compared to no AV surgery, with AV repair having better outcomes than AV replacement. Yet, repeated analysis in patients with moderate to severe AI at time of LVAD implantation revealed no difference in survival between the three groups, suggesting a benefit to CVPs in patients with increasing disease severity [11].

Rajagopal et al. reported a comparison of patients with AI who underwent LVAD implantation versus those treated only with medical therapy and found a significantly higher risk of developing AI or progression of native AI after LVAD implantation. This risk difference was not associated with pre-operative AI grade [13].

It is important to note that if CVP is deemed a requirement, then mechanical valves are not recommended due to the decreased valvular opening, which increases the risk of thrombosis and possible subsequent embolization. Given the general consensus that AI will worsen over time following LVAD implantation, consideration of repair or replacement of mild AI may be appropriate in patients undergoing LVAD implantation as destination therapy.

Presence of existing mechanical aortic valve

Regarding patients who have had prior mechanical AV replacement, a patch or plug closure of the left ventricular outflow tract has been described in limited experience [36, 37], while most groups prefer conversion of mechanical valve to a bioprosthetic valve.

"How we do it"

The authors advocate AV replacement with a stented bioprosthesis for AS that is moderate or greater and for AI that is greater than mild in severity. The authors are also currently exploring the use of TAVR in the early post-operative setting. Should a patient have a mechanical AV, this is replaced by a tissue bioprosthesis during LVAD implant.

Mitral valvular disease (Table 2)

Mitral stenosis impairs left ventricular filling which in turn prevents optimal functioning of the LVAD implant. As such, mitral valve replacement with a bioprosthetic valve is recommended with moderate to severe mitral stenosis and considered in any mitral valve (MV) area less than 1.5 cm^2 [14]. The most common valvular pathology at the time of LVAD implantation is mitral regurgitation (MR). Mitral valve function is closely linked to left ventricular size and contractility, and functional MR is among the most common etiologies of heart failure. Pathologic left ventricular remodeling leads to MV annular dilatation resulting in leaflet coaptation failure. Impaired contractility further worsens valve closing force and leads to leaflet tethering which increases volume loading of the left ventricle and initiates a feedback loop of failure. Pre-implantation echocardiographic features of posterior displacement of MV leaflets may be indicative of post-implantation significant MR, even after ventricular unloading under LVAD support [38].

In patients undergoing LVAD implantation, MR was found to be severe in 23% of patients within the INTERMACS registry [39], moderate to severe in 57% within the IMACS registry [4], and moderate to severe in 46% of patients enrolled in the MOMENTUM 3 trial [40]. Typically, LVAD implantation alone functions to offload the left ventricle, reduce pulmonary arterial pressures, and promote reverse remodeling; thus, MR improves in the majority of patients across all severity levels [41]. Morgan et al. observed a significant reduction of moderate to severe MR, from 76% pre-operatively to 8% post-LVAD implant at 1 month and 11% at 6 months [42].

When moderate to severe MR persists after implantation, the impact has thus far been inconsistent in published reports. In INTERMACS, persistent moderate to severe MR was present in 19% of patients at a median of 15 months after LVAD implantation, and was associated with a higher prevalence of right heart failure and renal failure [43]. However, of 44% patients in the MOMENTUM 3 trial with at least moderate MR prior to implantation, persistent MR at 1 month was found in only 6.2% of patients with HMIII and 14% of patients with HMII, and it did not significantly worsen or impact mortality at 2 years [40]. Those with severe baseline MR, larger left ventricular dimension, and implantation with HMII versus HMIII were each independently associated with increased likelihood of post-implant persistent MR [40]. Mitral valve repair with leaflet resection, debridement, and commissurotomy has been suggested due to the shorter duration of the procedure compared to valve replacement and the ability to perform repair through the apical incision, which ultimately serves as LVAD implantation site [3]. One type of MV repair is the valve leaflet edge-to-edge repair (Alfieri stitch [44]), which anchors the free edge of the anterior and posterior leaflets, creating a double-orifice mitral valve [44]. The need for additional incisions, bicaval cannulation, and prolonged cardiopulmonary bypass times can be ameliorated through a transapical approach [45]. Although the edge-to-edge repair can be safely performed, there is concern for evidence of benefit. One study reported no difference in edge-to-edge repair vs LVAD alone [46], while a second reported recurrent MR in the early and mid-term [46, 47]. Success of a staged or hybrid procedure of bioprosthetic valve insertion and balloon valvulotomy through transcatheter approach has also been reported [48].

Mitral valvular intervention

Mitral valve repair with leaflet resection, debridement, and commissurotomy has been suggested due to the shorter duration of the procedure compared to valve replacement and the ability to perform repair through the apical incision which ultimately serves as LVAD implantation site [3]. One type of MV repair is the valve leaflet edge-to-edge repair (Alfieri stitch [44]), which anchors the free edge of the anterior and posterior leaflets, creating a double-orifice mitral valve [44]. The need for additional incisions, bicaval cannulation, and prolonged cardiopulmonary bypass times can be ameliorated through a transapical approach [45]. Although the edge-to-edge repair can be safely performed, there is concern for evidence of benefit. One study reported no difference in edge-to-edge repair vs LVAD alone [46], while a second reported recurrent MR in the early and mid-term [46, 47]. Success of a staged or hybrid procedure of bioprosthetic valve insertion and balloon valvulotomy through transcatheter approach has also been reported [48]. Among patients in the INTERMACS registry with moderate to severe MR, 5.3% underwent mitral CVP at the time of LVAD implantation, 96% of whom had mitral valve repair [51]. Notably, at

Table 2 Key studies reporting on LVAD implantation and MV disease

Objectives	Authors	Study groups	Results
Significance of residual MR after LVAD implantation	Kassis et al. [49] (2017) Jain et al. [43] (2022)	$n=69$ $n=8364$, INTERMACS registry analysis	■ 80% had ≤ mild MR post-implantation ■ Predictors of residual MR included younger age, female gender, non-ischemic heart failure, increased LVEDD, RV dysfunction, and severe baseline MR or TR ■ Significant residual MR post-implantation is associated with persistent pulmonary hypertension, increased right heart failure with worse RV size and function, renal failure, and time to first hospitalization and death
Evaluate outcomes of concomitant MV procedures in patients undergoing LVAD implantation	Fukuhara et al. [50] (2017) Robertson et al. [51] (2018)	Repair, $n=115$ Repair, $n=252$ Replacement, $n=11$ No intervention, n = 4667; INTERMACS registry analysis	■ Concomitant MV procedures performed in patients with higher pre-operative pulmonary vascular resistance and pulmonary artery pressures ■ MV repair more likely performed in destination therapy, and patients developed right heart failure less frequently than those without repair ■ Less frequent rehospitalization at 1 year post-implant with concomitant MV procedures ■ Repair or replacement did not impact early or late survival
Impact of baseline MR on outcomes after LVAD implantation as destination therapy	Okoh et al. [52] (2019)	< Moderate, $n=29$ Moderate-severe, $n=62$	■ Patients with moderate-severe MR were associated with pulmonary disease and TR ■ Survival of baseline moderate-severe MR significantly worse than less than moderate MR group
Comparison of MV repair versus no intervention for severe MR during LVAD implantation	Pawale et al. [53] (2019)	Repair, $n=78$ Historical controls, $n=28$	■ Mortality at 30 days similar between groups ■ MR at 3 months present in 0% of repair group, compared to 29% in control ■ Rehospitalizations due to heart failure less frequent in repair group
Evaluate the effect of clinically significant MR at 2 years after LVAD implantation	Kanwar et al. [40] (2020)	HMII, $n=466$ HMIII, $n=461$; MOMENTUM 3 trial	■ Baseline MR in 44% of HMII, 43% HMIII ■ Overall, clinically significant MR at 2 years present in 9.4% HMII, 6.9% HMIII ■ Baseline MR present in 15% HMII, 9.4% HMIII at 2 years ■ Implantation with HMIII decreased likelihood of persistent MR compared to HMII
Determine the prognostic impact of functional MR prior to LVAD implantation	Pausch et al. [54] (2022)	Uncorrected functional MR < 2, $n=43$ MR ≥ 2, $n=34$	■ No significant difference in overall survival or 1 year event free survival ■ Uncorrected functional MR ≥ 2 associated with increased right heart failure within 1 year (35% vs 12%)

MV mitral valve, *MR* mitral regurgitation, *LVAD* left ventricular assist device, *RV* right ventricle, *IM* INTERMACS, *HMI* HeartMate I, *HMII* HeartMate II, *HMIII* HeartMate III

3 months post-LVAD implantation, there was no significant difference in the prevalence or degree of MR, with moderate to severe MR seen in 20% of patients who underwent CVP and in 25% with LVAD alone. Additionally, there was no significant difference in survival between these groups or among those with moderate to severe MR, compared with none to mild MR at LVAD implantation [51]. Meta-analysis performed by Choi et al. on outcomes of mitral CVPs for significant baseline MR reported no significant difference in survival with CVPs [55].

Consensus guidelines provided by the ISHLT and American Association for Thoracic Surgery do not recommend routine CVP for severe MR [14]. However, more recent data has brought about interesting concerns, including a trend toward benefit with concomitant MR intervention in patients who received LVAD as destination therapy. This subgroup reported fewer rehospitalizations, particularly due to a reduction in right heart failure [51]. Additionally, studies have shown an improvement in quality of life and functional status with CVP [50, 51, 53]. Regarding specifically LVAD implantation as destination therapy and mitral CVPs, one study reported the presence of moderate-severe MR as an independent predictor of reduced survival at 30 days (90% vs 100%), 1 year (63% vs 90%), and at 2 years (52% vs 83%) when compared to those with less than moderate MR [52]. In comparison of MV repair to historical controls without intervention, over median 18 months follow-up, rehospitalizations due to heart failure were 7.1% with MV repair versus 20% in the control group [53]. In subset analysis of the INTERMACS registry, patients who received mitral CVPs reported improved quality of life at 1 year post-implant with fewer hospital re-admissions and trended toward higher rate of survival at 2 years [51].

While data presented in the MOMENTUM 3 trial confirmed durable resolution of MR in a large proportion of patients, opponents note the trial was not designed in a manner appropriate to power evaluation of mortality differences, especially in the small cohort of patients with persistent MR who underwent subset analysis. Kassis et al. reported that persistent MR is associated with significantly larger right ventricular size, worse right ventricular function, and higher pulmonary arterial pressures, resulting in shorter time to first hospitalization and death [49].

Younger age, female gender, non-ischemic heart failure, increased left ventricular end diastolic diameter, right ventricular dysfunction, elevated right heart pressures, and severe MR or tricuspid regurgitation (TR) at the time of LVAD implantation have all been implicated as predictors of persistent MR. When present while on LVAD support, MR is associated with increased renal failure, almost twofold increase in right heart failure, and a trend toward increased mortality [43, 54]. One study also identified patients with persistent atrial fibrillation and larger atrial dimensions were less likely to have reduction in MR with LVAD implantation and had worse 2-year survival [56].

Presence of existing mitral valve prosthesis

Consensus guidelines do not recommend routine replacement of a properly functioning mechanical or bioprosthetic mitral valve at LVAD implantation. Flow across the mitral valve typically improves post-operatively; therefore, risk of thrombus formation and subsequent embolic event is thought to be low [4, 57].

"How we do it"

The authors recommend replacing the mitral valve with a tissue bioprosthesis for moderate or greater mitral stenosis. The authors also agree that careful consideration to mitral valve repair or replacement should be given in cases with moderate or greater mitral regurgitation. Reduction in risk of persistent MR after LVAD implantation may be achieved through appropriate inflow cannula alignment with the septum, hemodynamic optimization through selection of the pump speed most likely to reduce pulmonary capillary wedge pressures with maximized mechanical unloading, and guideline-directed heart failure medical therapy. However, in the authors' practice, if a patient is getting the LVAD as destination therapy, is younger in age (< 65 years), and has a dilated ventricle (> 6.5 cm), there is a low threshold to repair or replace the mitral valve for moderate or greater MR.

Tricuspid valvular disease (Table 3)

TR is also common in patients undergoing evaluation for LVAD implantation. Twelve percent of patients presented with severe TR at baseline in the INTERMACS registry [39] while 41% and 32% presented with moderate to severe TR in the IMACS [4] and EUROMACS registries, respectively [58]. Left ventricular systolic dysfunction or valvular pathology lead to pulmonary hypertension and consequential right ventricular remodeling. Change in ventricular dimensions may lead to tricuspid annulus dilatation and leaflet tethering resulting in functional TR. Subsequent increase in right ventricular preload worsens the degree of TR. Impairment of tricuspid leaflet coaptation may also be seen with implantable cardiac device leads crossing the valve area, which is common in patients with chronic heart failure [59].

LVAD function has the ability to unload the right ventricle and improve ventricular function as evidenced by a reduction in right ventricular end-diastolic dimension and TR as well as an increase in right ventricular ejection fraction, stroke work index, and tricuspid annular plane systolic excursion [60]. The decreased pulmonary vascular resistance and right ventricular afterload lead to right ventricular

Table 3 Key studies reporting on LVAD implantation and TV disease

Objectives	Authors	Study groups	Results
Explore the clinical impact and natural course of uncorrected TR in patients after LVAD implantation	Veen et al. [58] (2021)	$n=2496$; EUROMACS registry analysis	■ Baseline moderate-severe TR improved to none-mild TR immediately post-LVAD in 65% of patients ■ Uncorrected TR pre-LVAD and residual TR post-LVAD associated with increased early and late mortality
Compare outcomes of concomitant TV procedures in LVAD patients with moderate or worse TR versus	Robertson et al. [63] (2014)	Procedures, $n=588$ LVAD alone, $n=1608$; STS registry analysis	■ Concomitant TV procedures did not reduce early death or right VAD requirement ■ Concomitant TV procedures associated with increased risk post-operative renal failure, reoperation, greater transfusion requirement, and increased hospital length of stay
Compare clinical outcomes and quality of life in concomitant TV procedures versus LVAD implantation alone	Mullan et al. [64] (2020)	Mild TR, $n=8263$ Moderate, $n=4252$ Severe, $n=2100$; INTERMACS registry analysis	■ TV procedure rate increased with severity of TR: 8.6% of mild, 18% of moderate, and 44% of severe ■ TV procedures not associated with improved survival or quality of life in TR of any grade ■ TV procedures associated with increased risk of bleeding (HR 1.32), arrhythmia (HR 1.23), and stroke (HR 1.71) compared to LVAD implantation alone
Determine the durability of concomitant TV repair and the development of late right heart failure	Barac et al. [65] (2020)	$n=156$	■ Over mean follow-up of 23 months, 38% developed moderate-severe TR after concomitant repair ■ 36% of patients developed right heart failure ■ TV repair failure found to be independent predictor of late right heart failure (HR 2.6)
Identify whether concomitant TV procedures reduced the incidence of moderate or severe right heart failure within the first 6 months after LVAD	Mendiola et al. [66] (2022)	$n=60$; TVVAD trial interim analysis	■ No significant difference in incidence or severity of right heart failure at 6 months, post-operative mortality, or need for right ventricular assist device between TV procedure group versus no intervention

TV tricuspid valve, *TR* tricuspid regurgitation, *LVAD* left ventricular assist device, *IM* INTERMACS, *STS* Society of Thoracic Surgeons, *HMI* HeartMate I, *HMII* HeartMate II, *HMIII* HeartMate III, *HR* hazard ratio

remodeling, regression of tricuspid valvular annulus dilation, and subsequent resolution of functional TR.

Within the EUROMACS registry, uncorrected TR diminished after LVAD implantation, with a decrease of moderate-severe TR to none-mild TR seen in 65% of patients immediately post-LVAD implantation regardless of baseline right ventricular failure or pulmonary hypertension [58]. Other studies have noted similar results [61]. In one study of patients with uncorrected TR over longer follow-up of at least 1 year, significant persistent TR was found in 24% of patients and associated with age, preoperative tricuspid annular diameter, and residual MR. During mean follow-up of 21 months, patients with residual TR > 20% had significantly higher risk of mortality compared to those without (adjusted hazard ratio [HR] 4.0, $p < 0.001$) [62].

Pulmonary vascular resistance may remain elevated following LVAD implantation secondary to chronic pulmonary vascular remodeling, further contributing to right ventricular failure with increased right ventricular preload but without the expected reduction in afterload following implantation. Right ventricular contractility may also be compromised with leftward shift of the septum, decreasing the contribution of septal contraction and worsening TR with further dilation of the tricuspid valve annulus [60].

Tricuspid valvular intervention

Current guidelines advocate for the consideration of tricuspid CVPs if moderate to severe TR is present. A subset of patients that may benefit from tricuspid CVPs in those with less than moderate to severe TR include patients with pre-existing atrial fibrillation. Anwer et al. found a significant increase in early progression of TR after LVAD implantation in patients with atrial fibrillation, suggesting benefit of CVP in those with less than severe TR [67].

However, patients would not necessarily benefit from the additional procedure as TR may resolve with LVAD implantation alone. Among patients with moderate to severe TR in the INTERMACS registry, 17% underwent CVPs. Overall, tricuspid CVP was associated with slightly decreased survival (HR1.13) and significantly higher likelihood of stroke, bleeding, and arrhythmia [64]. In a propensity-matched study of patients within the EUROMACS registry, tricuspid CVPs had no significant difference in rehospitalization rate, right heart failure, or survival after LVAD implantation. Additionally, no difference was found in the prevalence of moderate to severe TR between patients who underwent intervention versus LVAD alone at 1 year [68].

Another single-center retrospective study showed that patients with moderate to severe TR at LVAD implantation receiving tricuspid CVPs had significantly increased risk of post-operative right heart failure and renal failure. No association with improved overall survival was found when compared to those who did not undergo a tricuspid CVP [69].

A recent prospective randomized controlled trial (Treatment of Tricuspid Valve Regurgitation in Patients Undergoing Left Ventricular Assist Device Implantation [TVVAD], NCT 03775759) studied patients with primary endpoint of incidence of right heart failure at 6 months, and assigned patients to tricuspid valve annuloplasty or replacement versus no intervention. The authors reported success in reduction of post-implantation TR, but no significant difference was seen in the primary or secondary endpoints including all-cause mortality and requirement for right ventricular assist device. The trial ended after enrollment of 60 patients due to futility in care [66].

Notably, CVP with ring annuloplasty has been shown to result in repair failure of 38%, defined as moderate to severe TR on post-procedure echocardiography. On intermediate follow-up, repair failure was independently associated with late onset right heart failure [65]. In a similar retrospective analysis of patients undergoing both ring annuloplasty and DeVega suture annuloplasty, repair failure occurred in 30% of patients with a trend toward lower rate of TR in the suture annuloplasty group [70]. In a smaller analysis of suture annuloplasty, 8.6% of patients had residual moderate TR at discharge and 17% had moderate to severe TR at 1 year [71].

"How we do it"

The authors agree that consideration should be given to repair moderate or greater TR with the intent to optimize right ventricular function, especially in the context of patients with pre-existing pulmonary hypertension. Our practice is to perform repair with suture or ring annuloplasty, as this does not significantly prolong time on cardiopulmonary bypass, can be performed without cross-clamping, and may improve right ventricular function post-operatively.

Multiple valvular pathologies

Pathologic deterioration of multiple valves is common in advanced heart failure, especially in patients undergoing evaluation for LVAD implantation. Limited studies are available for review and discussion to guide treatment pathways, but increasingly long cross clamp time and cardiopulmonary bypass are detrimental in this patient population (Table 4).

The MOMENTUM 3 trial provides the largest cohort of patients ($n = 85$) who had multiple valvular procedures during HMIII LVAD implantation. Patients undergoing a CVP had higher acuity INTERMACS profiles (score 1–2: 41% CVP vs 31% no valvular procedure, $p < 0.05$) and significantly increased cardiopulmonary bypass time (124 min vs 76 min, respectively, $p < 0.0001$). These patients encountered a higher incidence of short-term adverse events

Table 4 Key studies reporting on LVAD implantation and multiple valvular disease

Objectives	Authors	Study groups	Results
Examine the impact of performing single valve, multiple valves, or no valve procedures at the time of LVAD implantation	Maltais et al. [73] (2016) Sugiura et al. [72] (2019) John et al. [8] (2022)	Single, $n=190$ Multiple, $n=26$ No valve procedures, $n=398$ Single, $n=62$ Multiple, $n=29$ No valve procedures, $n=495$ Single, $n=325$ Multiple, $n=85$ No valve procedures, $n=1380$; MOMENTUM 3 trial analysis	■ Concomitant valve procedures associated with increased stroke, bleeding, and right heart failure up to 30 days ■ No significant difference in survival among groups regardless of procedure, device type, or indication for implant ■ Mortality associated with increased age, baseline creatinine, cardiopulmonary bypass time, and decreased body mass index ■ No significant difference in mortality found between groups up to 2 years

LVAD left ventricular assist device

including stroke (4.9% vs 2.4%, respectively), bleeding (34% vs 24%, respectively), infection (28 vs 20%, respectively), and right heart failure (42% vs 30%, respectively) at 30 days (all $p<0.01$). Additionally, no difference between groups was found in 30-day mortality (3.9% vs 3.3%, respectively) or 2-year survival (82% vs 81%, respectively) [8]. At 2-year follow-up, there was a less pronounced, but still significantly higher incidence of bleeding (53% vs 47%, $p=0.03$) and right heart failure (44% vs 33%, $p<0.001$) in the valvular procedure group, but again no difference in mortality (81% vs 82%, $p=0.87$) [8]. Other smaller studies also report no significant difference in mortality between groups [72, 73].

"How we do it"

The authors agree that longer bypass and cross clamp times may be detrimental in this already sick patient population. However, to have the best surgical outcome from the LVAD operation, it is imperative that valvular pathologies be addressed, if need be. In patients with multiple valvular pathologies, each valve is given consideration as an independent entity and addressed accordingly. It is our recommendation that, in these patients, it is essential that the surgical planning and implementation is precise to a fault and each valve is addressed on their own independent merit.

Discussion

Over the past two decades, there has been significant evolution in the technology of mechanical circulatory support with left ventricular assist devices now in their third generation of long-term continuous flow support. There seems to be a trend toward significant improvement in mortality risk associated with later generation devices in patients who undergo CVPs. Early studies reported 30 day mortality rates as high as 25% in HMII plus AV procedure [74], and later on 14% in patients with HMII plus two or more valvular procedures, and subsequently in HMII with mitral (12%), aortic (11%), or tricuspid (8.9%) alone [6]. Yet, more recent studies noted comparable survival between groups and elucidated predictors of mortality including age, cardiopulmonary bypass time, and baseline renal function [73]. Data from the MOMENTUM 3 trial found the HMIII to demonstrate higher efficiency hemodynamic unloading of clinical significant MR, with no influence of uncorrected baseline or residual MR on outcomes 2 years after implantation [40]. Furthermore, HMIII implantation and CVPs noted no difference in mortality at 30 days or 2 years, regardless of significantly worse INTERMACS profile and longer cardiopulmonary bypass time in the valvular procedure group [8]. The investigators of this pivotal trial suggest consideration of a randomized trial to assess CVPs during LVAD

implantation, and the authors of this manuscript agree in conjunction with transcatheter-based procedures.

Based on these findings, a growing body of literature has developed to influence decisions on which patients may benefit from CVPs. While concomitant procedures expose patients to short-term morbidity including stroke, bleeding, and right heart failure, no mortality difference has been assessed and CVPs are associated with benefits in terms of reduced hospital readmission and improved quality of life in select patients. The patients who need valvular repair are typically more sick at baseline, as many of the studies report a higher acuity in INTERMACS profile. In the increasing group of patients undergoing LVAD implantation as destination therapy, the short-term risk in morbidity may be worth a more aggressive stance in valvular correction to attain an increased likelihood of long-term survival. Whether patients benefit from higher risk implantation with CVPs may only be decided with additional randomized, prospective, and longer term study of specific cohorts, particularly in the destination therapy population.

Conclusion

Concomitant surgical intervention for valvular pathology at the time of LVAD implantation may expose the patient to higher cardiopulmonary bypass and cross clamp times and in turn to a higher risk of peri-operative morbidity and mortality. Yet, it seems that more contemporary studies support CVPs during LVAD implantation, especially as more long-term data emerges. Further research in larger cohorts with longer term follow-up is needed to provide answers for individualized evidence-based treatment strategies. Research regarding standardization of surgical techniques for addressing concomitant valvular pathologies may be interesting areas needing investigation, especially for patients who receive LVAD implantation as destination therapy.

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