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Review

Continuous-Flow Left Ventricular Assist Devices and Valvular Heart Disease: A Comprehensive Review

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ABSTRACT

Mechanical circulatory support with implantable durable continuous-flow left ventricular assist devices (CF-LVADs) represents an established surgical treatment option for patients with advanced heart failure refractory to guideline-directed medical therapy. CF-LVAD therapy has been demonstrated to offer significant survival, functional, and quality-of-life benefits. However, nearly one-half of patients with advanced heart failure undergoing implantation of a CF-LVAD have important valvular heart disease (VHD) present at the time of device implantation or develop VHD during support that can lead to worsening right or left ventricular dysfunction and result in development of recurrent heart failure, more frequent adverse events, and higher

RÉSUMÉ

L'assistance circulatoire mécanique avec des dispositifs d'assistance ventriculaire gauche (DAVG) implantables et durables à flux continu constitue une option de traitement chirurgical établie pour les patients atteints d'insuffisance cardiaque avancée et réfractaire au traitement médical selon les directives. Il a été démontré que le traitement par DAVG à flux continu offrait des avantages significatifs en termes de survie, d'efficacité fonctionnelle et de qualité de vie. Cependant, près de la moitié des patients atteints d'insuffisance cardiaque avancée subissant une implantation d'un DAVG à flux continu présentent une cardiopathie valvulaire (CPV) importante au moment de l'implantation du dispositif, ou développeront une CPV au cours du traitement, ce qui

Continuous-flow left ventricular assist device (CF-LVAD) therapy is recommended for selected patients with end-stage or advanced heart failure (class IIa, level of evidence B).[1,2] The most frequent indications for CF-LVAD implantation are nonsuitability for heart transplantation (HT; destination therapy [DT]) and end-stage heart failure whose state is declining despite maximal medical treatment and a heart donor is not available (bridge-to-transplant [BTT] or bridge-to-candidacy [BTC]). Thanks to the ongoing development of newer pump technologies, survival is steadily improving and now reaches 86% and 79% at 1 and 2 years, respectively, in selected patients,[3] which is close to the rates observed in early HT survival.[4] Another notable fact is the proportional increase of patients implanted for DT: now averaging 50% according to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).[5] These 2 facts along with a donor shortage mean that the number of patients receiving mechanical circulatory support as well as the duration of support will continue to increase. In this context, time-related complications such as valvular disease are anticipated to increase and are concerning, particularly for aortic valve insufficiency (AI) and for patients under long-term support. The first International Society for Heart and Lung Transplantation (ISHLT) guidelines for mechanical circulatory support were published in 2013 and provided recommendations for the management of associated valvular heart disease (VHD) in CF-LVAD patients.[6] Since then, several studies have been published and provide greater granularity to better tailor the approach to VHD in the setting of CF-LVAD support.

In the present review, we aim to address 3 questions related to HVD in patients supported with a CF-LVAD: 1) Does the

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mortality. In this review, we summarize the recent evidence related to the pathophysiology and treatment of VHD in the setting of CF-LAVD support and include a review of the specific valve pathologies of aortic insufficiency (AI), mitral regurgitation (MR), and tricuspid regurgitation (TR). Recent data demonstrate an increasing appreciation and understanding of how VHD may adversely affect the hemodynamic benefits of CF-LVAD support. This is particularly relevant for MR, where increasing evidence now demonstrates that persistent MR after CF-LVAD implantation can contribute to worsening right heart failure and recurrent heart failure symptoms. Standard surgical interventions and novel percutaneous approaches for treatment of VHD in the setting of CF-LVAD support, such as transcatheter aortic valve replacement or transcatheter mitral valve repair, are available, and indications to intervene for VHD in the setting of CF-LVAD support continue to evolve.

peut entraîner une aggravation de la dysfonction ventriculaire gauche ou droite, au développement d'une insuffisance cardiaque récurrente, à des événements indésirables plus fréquents et à une mortalité plus élevée. Dans cette revue, nous résumons les preuves récentes liées à la physiopathologie et au traitement de la CPV chez les patients traités avec un DAVG à flux continu. Nous ciblons les pathologies valvulaires spécifiques de l'insuffisance aortique (IA), de l'insuffisance mitrale (IM) et tricuspide (IT). Des données récentes démontrent une appréciation et une compréhension croissantes de l'impact potentiel de ces pathologies sur les avantages hémodynamiques du support par DAVG à flux continu. Ceci est particulièrement vrai pour l'IM, où de plus en plus de preuves démontrent désormais que l'IM persistant après l'implantation d'un DAVG à flux continu peut contribuer à aggraver l'insuffisance cardiaque droite et les symptômes récurrents d'insuffisance cardiaque. Des interventions chirurgicales simples et de nouvelles approches percutanées pour le traitement de la CPV, telles que le remplacement valvulaire aortique par cathéter ou la réparation de la valve mitrale par cathéter, sont disponibles et les indications pour intervenir continuent d'évoluer.

presence of valve disease impact hemodynamic and clinical outcomes in CF-LVAD patients? 2) When should we perform concomitant valve surgery at the time of CF-LVAD implantation? and 3) How should we address surgically heart valve disease in CF-LVAD patients?

We will focus mainly on the most commonly used pumps, the Heartmate II (Abbott, Chicago, IL), Heartmate 3 (Abbott, Chicago, IL), and HVAD (Medtronic, Minneapolis, MN). The first part is dedicated to the aortic valve (AV), the second part to the mitral valve (MV), and the third part to the tricuspid valve (TV).

De Novo Aortic Valve Disease During Long-term Continuous-Flow Left Ventricular Assist Device Support

Incidence, physiopathology, and risk factors for development of de novo AI during CF-LVAD support

Aortic insufficiency is now a well documented time-related complication in patients supported with long-term CF-LVAD. From 15% to 52% of patients supported with a CF-LVAD develop significant AI by 1-2 years.[7-22] A recent analysis from INTERMACS showed that more than 50% of CF-LVAD patients had mild AI after 2 years of support. When stratified according to the preoperative severity of AI, 11% of patients without any AI before implantation developed moderate-to-severe AI at 1 year, and 55% and 19% of patients with mild AI at the time of CF-LVAD implantation developed, respectively, mild and moderate-to-severe AI at 6 months.

The mechanisms of *de novo* AI are likely multifactorial and remain controversial. A CF-LVAD induces many changes in aortic blood flow dynamics and kinetics as well as in AV physiology.[21,23-31] The constant increase of afterload (in diastole and systole), combined with the decrease of LV end-diastolic pressure, increases the transvalvular gradient and decompression of the LV, both leading to AV closure (intermittent or permanent) and tissue stretching.[8,26] The continuous apposition of the leaflets associated with turbulent backflow and high blood velocities in the root from the outflow cannula might induce pathologic changes in the leaflets, the aortic wall, and the root dimensions. Two distinct features of AV degeneration have been described, leading to either aortic stenosis or regurgitation. Some authors have described valve thickening and fusion of the commissures (complete or partial) associated with a fibrinous and myxoid thickening of the aortic side of the leaflets.[27] Others have reported a thinning of the leaflets with partial fusion, along with a shortening of the leaflets secondary to curling.[29,30] One hypothesis is that long-term CF-LVAD support might cause an ischemia-induced involution of the ventricularis layer of the aortic cusps.[21,30] Changes in aortic wall dimensions and structure also have been reported by some authors, who describe an increase in aortic wall thickness, collagen, and smooth muscle content, although others authors have reported no change in the thickness of the aortic intima or media.[23,26] Aortic annulus and aortic root dilation, increase in the sinotubular junction diameter and sinus of Valsalva diameter, and aortic wall atrophy with a decrease in medial aortic thickness have all been observed in CF-LVAD patients. Fine et al.[32] measured aortic root and ascending aorta dimensions in 162 CF-LVAD patients supported for more than 6 months. They found that a small increase in the aortic root size occurred mostly within the first 6 months after CF-LVAD implantation and was associated with AI development.

With AI being a time-related complication, the duration of CF-LVAD support and DT are important risk factors. Two major studies identified old age (> 60 years), low body surface area (BSA), female sex, AV closure, mild preoperative AI, peripheral vascular disease, and ischemic cardiomyopathy as risk factors (Table 1).[15,33] The loss of pulsatility and AV opening with CF-LVAD seems to be detrimental to AV physiology, and studies have clearly demonstrated that patients with intermittent AV opening during CF-LVAD support are less likely to develop AI.[7,10-13,15,16,34-36] We may think that the use of an intermittent low-speed algorithm, such as the one present in the Jarvik 2000 (Jarvik Heart, New

Table 1. Risk factors for *de novo* aortic insufficiency (AI) during continuous-flow left ventricular assist device (CF-LVAD) support and strategies for prevention or mitigation

Period	Risk factors for AI	Preventive strategy
Before CF-LVAD implantation		
	Age > 60 y; Female; Low body surface area	Pump speed optimization under echocardiographic guidance before hospital discharge (lowest pump speed tolerated to obtain a good LV unloading, mid-line position of the interventricular septum and AV opening).
	Destination therapy; Duration of support > 1 year	If mild AI, consider repair or AV replacement
During surgery		
	Outflow cannula angulation and position of the anastomosis in ascending aorta	Position of the anastomosis: at least 1-2 cm above sinotubular junction; Outflow cannula angulation: 90° transversally, 60°-120° in the coronal plane
	Aortic root or annulus dilation	If mild AI, consider repair or aortic valve replacement
After surgery		
	Systemic arterial hypertension Persistent AV closure	Mean arterial pressure target ≤ 80 mm Hg Pump speed optimization under echocardiographic guidance before hospital discharge (lowest pump speed tolerated to obtain a good LV unloading, midline position of the interventricular septum, and AV opening). Intermittent low speed algorithm?

AV, aortic valve; LV, left ventricle.

York, NY), the Heartmate 3, or the HVAD, could decrease the rate of *de novo* AI. Two studies including only patients supported with the HVAD reported 1.9% and 3% incidences of moderate AI and no severe AI after 1 year.[7,37] Surgical considerations such as position and angulation of the outflow graft are also important. Experimental and computational fluid dynamic studies have demonstrated that a large angle between the aorta and the outflow graft can increase the blood recirculation due to AI while decreasing the coronary artery flow. Furthermore, a too high anastomosis on the aorta with a too small angulation could increase the shear stress on the aortic root and AV.[38-41]

Does the presence of aortic valve disease affect hemodynamic and clinical outcomes in CF-LVAD patients?

The hemodynamic effects of AI in patients on CF-LVAD support are well documented in *in vitro* and *in vivo* echocardiographic and hemodynamic ramp studies.[8,42,43] In the setting of a CF-LVAD, AI creates a circulatory shunt or a "closed-circulatory loop" between the pump, the AV, the left ventricle, and back to the pump again[8] (Fig. 1, A and B). This phenomenon ultimately reduces pump efficiency and decreases left ventricular (LV) unloading, cardiac output, and organ perfusion. For a given pump speed, AI induces an increase in LV end-diastolic volume, and pressure, as well as an increase in degree of MR, and causes the recurrence of heart failure symptoms.[9-12,18,42] Sayer et al. demonstrated that, at basal speed, CF-LVAD patients with moderate or more AI had higher right and left ventricular filling pressures, lower pulmonary artery pulsatility index (PAPI), similar cardiac index (CI), and similar right ventricular (RV) stroke work index compared with patients without AI.[42] Those investigators also showed that increasing pump speed increased the severity of AI but could normalize CI and postcapillary wedge pressure (PCWP) in most patients with AI. However, PAPI did not improve after increasing the pump's speed.

The presence of AI is likely detrimental to RV function, especially in patients with moderate to severe preoperative right ventricular failure (RVF). The incomplete unloading of the LV increases RV afterload and worsens RVF. Therefore, it is important to perform a careful preoperatively assessment of the patient to check for AI by means of transesophageal echocardiography and to have a low threshold for concomitant AV repair or replacement.[44,45]

AI is also of concern in patients implanted for BTC in the setting of elevated pulmonary artery pressures. The chronically increased LV pressure could lead to worsening pulmonary hypertension and a rise in pulmonary vascular resistance, which can compromise eligibility for HT. The potential of recovery after CF-LVAD implantation could also be jeopardized by the hemodynamic effects of AI. For patients with elevated left-side filling pressure and associated secondary severe pulmonary hypertension, we typically would correct any AI greater than mild to optimize pump function and reduce pulmonary hypertension.[45]

For many years, the impact of any significant AI on survival and clinical outcomes after CF-LVAD implantation remained controversial, likely because of the underpowering of clinical studies.[12,14,16] Some authors showed a decrease in survival or an increase in adverse cardiac events,[15,18,19,34] and others did not notice such effects.[12,16] In a pooled analysis from 3 retrospective studies, Deo et al. demonstrated that the overall survival was similar in patients with and without *de novo* AI.[14] In a recent analysis of the INTERMACS database, Trudy et al. were the first to clearly demonstrate the negative impact of AI on CF-LVAD patients.[33,45] Those authors showed a significant reduction in survival after 1 year for patients who displayed progression to significant AI compared with patients who did not develop AI (77.2% vs 71.4% at 2 years; $P = 0.005$). They also showed that moderate-to-severe AI was associated with a higher LV end-diastolic diameter, reduced cardiac output, lower blood pressure (BP), higher

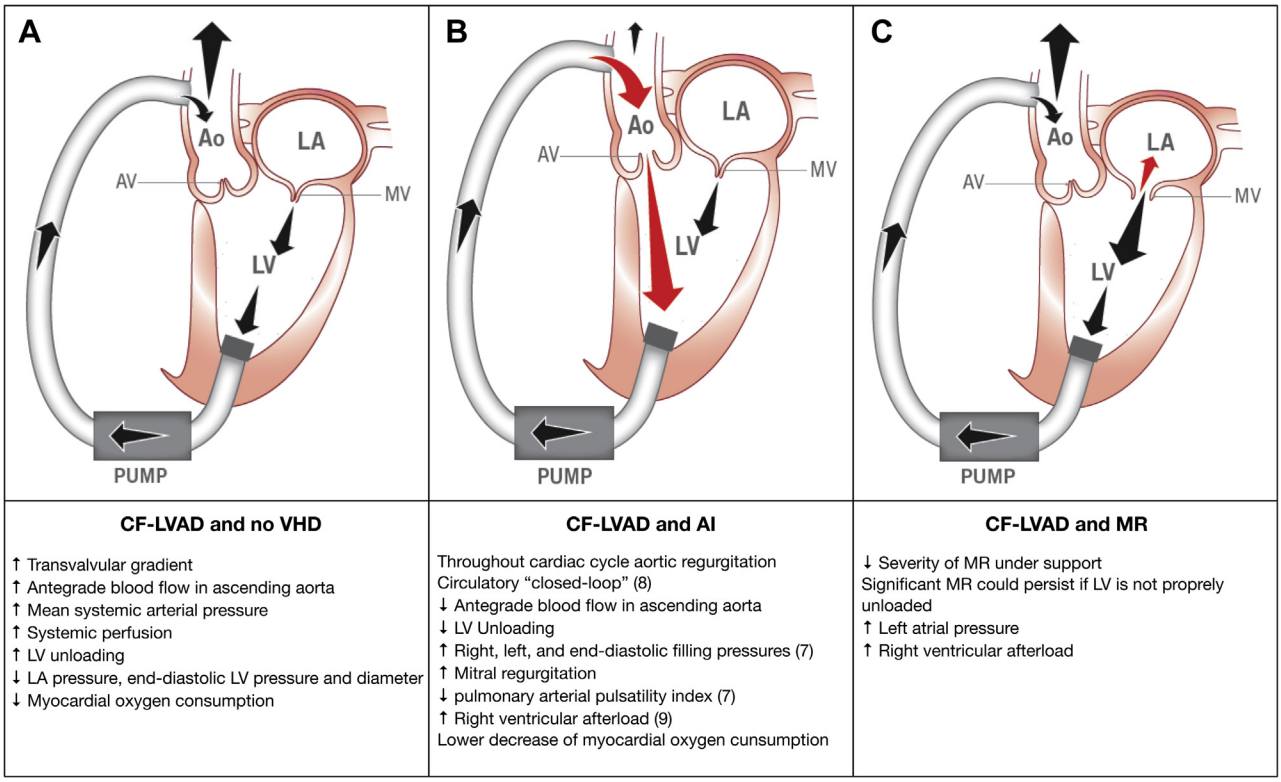

Figure 1. Schemas of hemodynamic effects of continuous-flow left ventricular assist device (CF-LVAD) (**A**) without valvular heart disease (VHD), (**B**) with aortic insufficiency (AI), and (**C**) with mitral regurgitation (MR). Ao, ascending aorta; AV, aortic valve; LV, left ventricle; MV, mitral valve; LA, left atrium.

B-type natriuretic peptide, higher readmission rate, and lower functional status. These findings are consistent with the anticipated outcomes induced by the hemodynamic consequences of AI, reflecting the closed blood recirculation loop and the decrease in LV unloading. Furthermore, they found a higher rate of rehospitalization, a higher mortality rate at 2 years, and a lower functional status in patients with significant AI. No association between AI and device malfunction, thromboembolism event, stroke, arrhythmia, or gastrointestinal bleeding was reported. The impact of AI during CF-LVAD support on outcomes after transplantation remains to be determined. The most important studies published since the ISHLT guidelines were published in 2013 are summarized in Table 3.

When should we perform a concomitant aortic valve procedure at the time of CF-LVAD implantation?

Assessment of the AV is part of the work-up before any CF-LVAD implantation. Importantly, the AV must be assessed under physiologic conditions in a transthoracic echocardiography laboratory to avoid any underestimation of AI severity when the patient is under general anaesthesia. AI before CF-LVAD implantation is defined and quantified in the same manner as for any non-VAD patient. A complete evaluation including anatomy of the AV, the aortic root and the ascending aorta, quantification of the AI severity, and description of the underlying mechanism of AI is mandatory for tailored management. Because the severity of AI progresses in at least 25% of cases, and because of the negative hemodynamic and clinical consequences of AI in CF-LVAD patients, it is recommended to treat any AI more severe than mild at the time of implantation and when the anticipated duration of support is more than 1 year (Consensus Guidelines published in 2013 and 2015; class I, level of evidence C).[6,11] According to the INTERMACS Registry, 3% of patients had a concomitant AV procedure at the time of CF-LVAD implantation.[33] This is probably underestimated, because 3% of patients remained with untreated moderate-to-severe AI at the time of CF-LVAD implantation.[45] In a retrospective study of 281 patients, Pal et al. reported a prevalence of 4% of moderate-to-severe AI before CF-LVAD implantation.[46] Patients with mild AI and risk factors for secondary AI during CF-LVAD support (female sex, age > 60 years, low BSA, ischemic cardiomyopathy) should also be considered for an AV procedure at the time of the CF-LVAD implantation, particularly patients in whom prolonged duration of support is anticipated (DT). Some authors advocate that patients with mild AI who have large BSA-indexed aortic roots may be the best candidates for central AV closure at the time of device implantation, whereas those with small aortic roots may forgo a repair.[47]

According to the ISHLT guidelines,[6] patients presenting with aortic stenosis (AS) of any degree associated with more than mild AI should be promptly considered for a bioprosthetic AV replacement (class I, level of evidence C) and patients with severe AS may be considered for AV replacement regardless of the degree of concomitant AI (class IIb, level of

Table 2. Summary of suggested indications or considerations for valvular procedure at the time of continuous-flow left ventricular assist device (CF-LVAD) implantation

Suggested indications for concomitant valve procedure at the time of CF-LVAD implantation	Suggested procedure
Aortic valve (AV)	
Mild AI with associated risk factor of AI progression under CF-LVAD	AV repair (partial closure); Bioprosthesis if repair not feasible
More than mild AI	
Mechanical valve already in place	Patch closure
Aortic stenosis	Bioprosthesis
Mitral valve (MV)	
Severe mitral stenosis	Bioprosthesis; Leaflet resection
Severe MR: • With pulmonary hypertension • Destination therapy • Bridge to candidacy because of elevated PAP • Posterior displacement of the coaptation point	MV repair: • Annuloplasty • Alfieri stitch • Leaflet resection • Neochords
Tricuspid valve (TV)	
Tricuspid annulus dilation > 43 mm with or without TR?	Annuloplasty; de Vega TV annuloplasty;
Severe tricuspid regurgitation and risk of right heart failure after CF-LVAD implantation	TV replacement (tissue valve)

AI, aortic insufficiency; MR, mitral regurgitation; PAP, pulmonary arterial pressure; TR, tricuspid regurgitation.

evidence C) to potentially optimize chances of recovery. We suggest considering concomitant AV procedures in selected situations, as summarized in Table 2.

How should we address important aortic valve disease at the time of CF-LVAD implantation?

The choice of the procedure should be tailored according to the patient's surgical risk, the mechanism of AI, the anatomy of the AV and the aortic root, and the anticipated duration of support. There is no consensus regarding the safest and most appropriate intervention.[6,11] In an INTERMACS study including 5344 CF-LVAD patients, the most common concomitant procedure was AV closure (2.3%), followed by AV repair or partial oversewing (1.7%) and AV replacement (1.6%).[48]

Partial closure with a single central stitch (Park stitch) and modified Park stitch. The approximation of the 3 nodules of Arantius by a pledgeted 4-0 Prolene stitch was first described by Park et al. (Fig. 2A).[49] When the leaflet tissue is adequate,[50] it is the simplest technique to repair leaflet prolapse or malcoaptation. Because this type of closure is only partial, it allows blood ejection through the AV. Durability is the main concern and the technique should be avoided when the leaflets are thin and fragile. Several studies have demonstrated that adverse events and overall survival were similar between patients with and without central AV closure at the time of CF-LVAD implantation.[47,48,51-53] Jorde et al. reported recurrence rates at 1 year of 2.3% for mild AI, 2.3% for moderate-to-severe AI, and 2.3% for severe AI[18] and a freedom from significant AI at 2 years of 66% after repair.[47,51] The efficacy and the durability of repair seems to be more evident in DT patients or in patients with risk factors for AI, with a 69% decrease in the odds of significant AI compared with patients without AV repair. In an INTERMACS database analysis, Robertson et al. reported 18% of moderate to severe AI at 12 months after an AV repair concomitant with CF-LVAD implantation.[48]

Partial closure of AV with the modified Park stitch consists of an additional 5-0 Prolene pledgeted mattress suture on each side of the central stitch between the central pledget and each commissure for reinforcement and to relieve tension on the central stitch (Fig. 2B).[54] This technique can be used in case of degenerative AV disease, with an important prolapse, or when the tissue is fragile. The blood can pass through the AV, but the risk of stenosis is higher. In cases of recovery, the AV must then be replaced. The superiority of this technique over the central stitch alone and its durability remain to be determined.

Complete closure of the left ventriculo-aortic junction. Two different techniques have been described to completely close the left ventriculo-aortic junction: 1) direct suture of the native AV with the use of felt strips along the free edge of the leaflets (Fig. 2C); and 2) sewing a circular patch (Dacron, Gore-Tex, autologous pericardium, bovine pericardium), directly in the native annulus or in the sewing ring of a prosthesis already in place.[55] AV closure is efficient and is associated with a low rate of AI recurrence. This approach, however, leaves the patient completely dependent on the pump, and adverse events such as pump thrombosis or malfunction could be devastating. This technique is contraindicated when myocardial function recovery is possible or expected.[6,11] The 2 largest studies looking at the outcomes after concomitant AV procedures provide controversial results.[48,56] Using the data of the Heartmate 2 pivotal trials for BTT and DT indications, John et al. found that patients with concomitant AV procedures (n = 80 patients, divided into AV repair [n = 18], closure [n = 32], and replacement [n = 30]) were sicker and had higher early mortality and RVF rates.[56] In that study, 30-day mortality was lowest for AV closure (6.3%), followed by AV replacement (13%) and AV repair (18%). Survival rates at 1 and 2 years were also lower after AV closure than after AV repair or replacement (84.1% vs 70.9%, 75% vs 57%, and 64% vs 43%, respectively; $P < 0.001$).

In an INTERMACS database analysis (n = 305 patients, divided into AV repair [n = 125], closure [n = 95], and replacement [n = 85]), Robertson et al. reported increased mortality associated with complete oversewing of the valve, with most deaths occurring early after the procedure.[48] One-year survival was lower after AV closure compared with AV repair or replacement (81% for patients who did not undergo an AV procedure, 79% for patients who underwent an AV repair, 72% for patients with an AV replacement, and 64% for those with AV closure ($P = 0.003$)). Even if it is unclear whether the deaths were related to the AV closure, complete oversewing has become less popular. This technique is now mainly used when a mechanical valve is already in place, to avoid a redo AV replacement with the use of a bioprosthesis.

Table 3. Impact of aortic insufficiency (AI) under continuous-flow left ventricular assist device (CF-LVAD) and impact of aortic valve (AV) surgery at the time of CF-LVAD implantation: summary of the main studies published after 2013

Study and design	No. of patients	Impact of AI under CF-LVAD	Impact of concomitant AV surgery at time of CF-LVAD implantation	New message and suggested therapy
Cowger et al.[12] Retrospective, single center	166	No impact of AI on mitral regurgitation, pump thrombosis, device exchange, and survival. Patients with preexisting RV dysfunction poorly tolerated significant AI.	NA	*What is new:* No significant clinical effect from AI development was observed in this study, except for patients with previous RV dysfunction. *Suggested therapy:* Careful monitoring and pump speed optimization may provide benefit in patients with RV dysfunction if wedge pressures are not allowed to rise after LVAD speed reduction.
Robertson et al.[48] Retrospective, INTERMACS	5344	NA	AV closure significantly increased mortality. No impact on long-term survival.	*What is new:* AV repair did not increase operative mortality and did not impair long-term survival. *Suggested therapy:* AV closure should be avoided if possible, particularly in INTERMACS profile 1 and 2 patients.
Holley et al.[16] Retrospective, single center	210	Development of moderate or more AI did not correlate with decreased survival.	NA	*What is new:* AI development did not appear to impact long-term mortality. *Suggested therapy:* Pump speed optimization.
Trudy et al.[33] Retrospective, INTERMACS	10,603; 1399 developed moderate-to-severe AI	Moderate to severe AI had a negative impact on hemodynamics, hospitalizations, and survival on CF-LVAD support: • Higher left ventricular end-diastolic diameter • Reduced cardiac output • Low blood pressure • Higher BNP • Higher rate of readmission	NA	*What is new:* First clear demonstration of negative impact of AI in CF-LVAD patients. Confirmation of previously described risk factors for AI under CF-LVAD support. *Suggested therapy:* Concomitant AV procedure might be considered in patients with mild AI and risk factors for progression of AI under CF-LVAD support. Patients with moderate AI should be considered for concurrent AV procedures at the time of CF-LVAD implantation, especially if they have risk factors for AI.

BNP, B-type natriuretic peptide; NA, not applicable; RV, right ventricular.

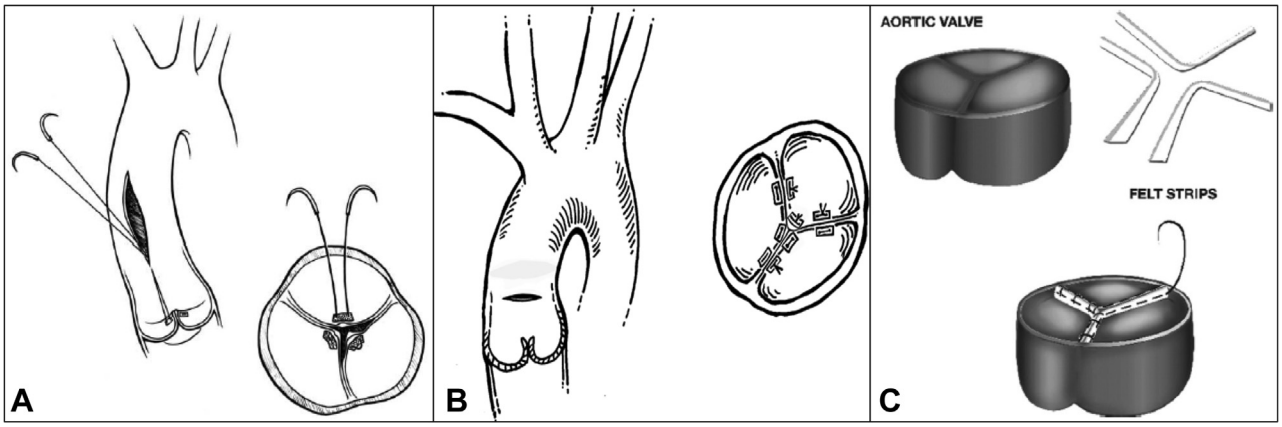

Figure 2. Various surgical techniques to deal with aortic valve insufficiency at the time of continuous-flow left ventricular assist device implantation. (**A**) Park stitch: pledgeted 4-0 Prolene sutures are applied to approximate the 3 nodules of Arantius to create a coaptation stitch. Reproduced from Park et al.[49] with permission from Elsevier. (**B**) Modified central closure technique. Reproduced from Morgan and Brewer[54] with permission from Wolters Kluwer Health. (**C**) Suture technique for aortic valve closure with felt strips with a second layer of over-and-over stitch anchored to the aortic wall. Reproduced from Adamson et al.[55] with permission from Elsevier.

Replacement with a bioprosthetic valve. Bioprosthetic valve replacement is the procedure of choice when the AV is calcified or stenotic or when a partial closure will not provide satisfactory results.[48] Its potential benefits must be weighed against the risk of a prolonged cross-clamp time. The long-term competency and superiority of bioprosthetic valve replacement compared with oversewing of the AV is unknown. In the INTERMACS analysis,[48] at 1 year after AV replacement at the time of CF-LVAD implantation, survival was 72% and no AI recurrence was observed. In stable DT patients (ie, INTERMACS profile 3 and higher), some authors had increasingly favoured bioprosthetic replacement, which definitively addresses the insufficiency for the short term.[57] However, valve fusion, fibrosis, subvalvular thrombi, and obstruction have been reported early after CF-LVAD implantation,[58] and there is probably an increased rate of bioprosthetic failure in these patients owing to the increased and abnormal loading conditions.[58] For this reason, if a bioprosthetic valve is already in place at the time of CF-LVAD implantation, its complete integrity must be verified. If the prosthetic valve has been in place for more than 5 years or has signs of structural degeneration, the recommended procedure—and the simplest—is to oversew the valve.[11] However, with the increasing availability of transcatheter aortic valve replacement (TAVR) and its feasibility in CF-LVAD patients, this recommendation might change in the future and TAVR could be an option later in the patient's course of treatment. Several reports with a limited number of patients have demonstrated the feasibility of TAVR as a successful treatment modality for CF-LVAD patients who develop severe AI or concomitant to CF-LVAD implantation, in either the native AV or a failing bioprosthesis.[59-61]

Because of its thromboembolic risk, a mechanical prosthesis in the setting of a CF-LVAD is strongly discouraged. When an aortic mechanical valve is already in place, the choice is to replace the mechanical prosthesis with a tissue prosthesis, to oversew the valve with a patch (pericardium, Gore-Tex, or Dacron), or to use a plug as described by Cohn et al.[55]

How and when should we address de novo aortic valve insufficiency after CF-LVAD implantation?

Preventive strategy—patients without AI or with asymptomatic AI. Because the nonopening of the AV at the time of discharge from the initial CF-LVAD implant is strongly associated with the development of AI, speed pump optimization to maintain AV opening is of pivotal importance for preventive treatment if feasible.[11,18] Numerous authors advocate for systematic ramped-speed studies before a patient's discharge.[18] Lowering the pump's speed under echocardiographic guidance might reduce the transvalvular gradient and promote AV opening. However, the primary objectives of CF-LVAD support must be pursued, and pump settings must allow adequate LV unloading guided by the LV size and the midline position of the interventricular septum and degree of MR. Jorde et al. reported the results of a prospective speed optimization study in 35 patients.[18] AV opening was noted in only one-half of the patients but, surprisingly, only 1 patient among the 17 without AV opening developed AI after 1 year. When this strategy is used, a close clinical follow-up is needed to ensure that heart failure, end-organ dysfunction, or pump thrombosis do not develop because of reduced CF-LVAD support.

Afterload reduction, volume management and fluid balance control are part of the routine care of CF-LVAD patients. The negative impact of high BP in CF-LVAD patients is well known, particularly because of its association with pump thrombosis. However, the relation between blood pressure and AI occurrence is more controversial. Patil et al. suggested that the BP control achieved at 3 and 6 months after surgery plays an important role in influencing the development of AI.[62] In their retrospective study of 119 patients with CF-LVAD, systolic BP was an independent predictor of AI under support. However, such an association was not found in many other studies.[15,34] The ISHLT guidelines recommended a mean arterial pressure target of $\leq$ 80 mm Hg (class IIb, level of evidence C). Once patients become ambulatory and are discharged from the hospital, a combination of diuretics, angiotensin-converting enzyme inhibitors,

β-blockers, and angiotensin receptor blockers is usually prescribed for medical management of BP.

Severe AI does not necessarily result in clinical heart failure or elevated filing pressures. Owing to a lack of data, there are no recommendations regarding the best time to intervene or the best way to manage asymptomatic patients with significant AI under CF-LVAD support.[11] The management should essentially be based on BP control and echocardiography-guided pump speed optimization, with the goal of preventing any progression toward clinically significant AI. Such patients must be closely followed with the use of echocardiography, with N-terminal pro—B-type natriuretic peptide serums levels, and right heart catheterization.

Patients with significant AI and heart failure symptoms. The aim of the treatment is to reduce congestion and cure AI itself. Medical treatment is always the first step of management to achieve symptomatic relief. Diuretics and vasodilators are the first line of treatment to decrease congestion and control blood pressure. Symptomatic patients with AI who fail to improve after echocardiography-guided optimization should undergo right heart catheterization with simultaneous echocardiography.[11] An increase in pump speed might be considered to increase cardiac output and end-organ perfusion, but at the expense of worsening AI.[42] We must keep in mind that this strategy is only palliative and effective in the short term. If medical management fails to decrease the symptoms and stabilize AI, more invasive alternatives must then be considered. There is no clear recommendation regarding the most appropriate surgical or interventional modality to manage such patients. If the patient is a candidate for heart transplantation, listing or upgrade on the waiting lists might be the first option.

Surgical procedures (AV replacement or repair, LV outflow tract closure) are feasible but have high risks of complications.[63] Percutaneous procedures—either TAVR or AV closure with Amplatzer[64]—have been reported with equivalent satisfying immediate hemodynamic results.[61] However, device migration, hemolysis, and mid-term and long-term outcomes remain of concern with these approaches. Future studies assessing larger patient cohorts are required to sufficiently evaluate the efficacy of these techniques.

Mitral Valve Disease and Long-term CF-LVAD

Does the presence of mitral valve regurgitation affect hemodynamic and clinical outcomes in patients on CF-LVAD support?

Significant MR is frequent in advanced heart failure patients and is associated with a bad prognosis.[65,66] More than 50% of CF-LVAD candidates have at least moderate MR at the time of CF-LVAD implantation.[67,68] Secondary or functional MR is the most common feature associated with heart failure and LV dilation: impairment of leaflet coaptation results from MV annulus dilation or dislocation of the papillary muscle and chordae tendinae (type I or type IIIb in Carpentier's classification). The CF-LVAD decompresses the LV, decreases LV end-diastolic pressure, LV dimensions, and left atrial volume, and can increase mitral leaflet coaptation, all these elements contributing to decrease the severity of MR (Fig. 1C).[69] Several studies have highlighted the beneficial role of CF-LVAD alone by decreasing the severity of MR.[67,69] In a multicentre study, Stulak et al. reported better survival in patients with preoperative significant MR, suggesting the lack of value of addressing moderate to severe MR at the time of CF-LVAD implantation.[70] However, in patients with MR and with suboptimal LV decompression (inflow cannula toward the septum, AI, low pump speed because of suction events and small LV cavity, fluid overload), significant MR could persist. As shown in several studies, persistent MR in CF-LVAD patients can have detrimental hemodynamic and clinical effects, and is associated with persistent pulmonary hypertension, worse RV function, and death.[71,72] The negative impact of MR seems to be more pronounced in patients undergoing CF-LVAD support for DT. In a retrospective single-centre study of 91 patients implanted with a Heartmate 2 for DT, Okoh et al. found a significantly lower survival rate in patients with more than moderate MR.[68] Of note, more patients in this group also showed significant tricuspid regurgitation (TR), which might also have an impact on survival. These results are consistent with an INTERMACS database analysis by Robertson et al., who demonstrated lower survival in DT patients with uncorrected moderate-to-severe MR (73% in MV repair group vs 64% in no mitral procedure group; $P = 0.09$).[67] Thus, the impact of moderate and severe MR on survival in CF-LVAD remains controversial and may be accounted for by patients being "good responders" or "nonresponders" to CF-LVAD unloading. Mechanisms of MR and the geometry of the MV are important predicting factors of failure after MV repair.[73] We can extrapolate that such parameters may have an effect in CF-LVAD patients with significant MR. Very few studies address this aspect. Kitada et al. nicely demonstrated that a posterior displacement of the mitral leaflets' coaptation point was significantly associated with significant MR after CF-LVAD implantation and might be considered as an indication for MV repair.[74] More recently, Kassis et al. reported a trend for this association.[71] The most important studies published since the ISHLT guidelines were published in 2013 are summarized in Table 4.

When should a concomitant mitral valve procedure be performed at the time of the CF-LVAD implantation?

If the benefit of a concomitant AV procedure in CF-LVAD patients with more than mild AI is well admitted, the same has not yet been established for MR. In the absence of prospective or randomized studies, the necessity for correction of an MV disease at the time of CF-LVAD implantation remains unclear.[6] As discussed above, the benefit of concomitant MV procedures is still debated. Indeed, studies have demonstrated that, on the one hand, uncorrected MR at the time of CF-LVAD implantation had no impact on survival.[70,75-77] On the other hand, a concomitant MV procedure showed the highest trend toward early mortality compared with results obtained from the AV and TV data.[56] For these reasons, current guidelines do not recommend routine MV repair or replacement for severe MR at the time of CF-LVAD implantation (class III, level of evidence C).[6]

Table 4. Impact of mitral valve regurgitation (MR) under continuous-flow left ventricular assist device (CF-LVAD) and impact of mitral valve (MV) surgery at the time of CF-LVAD implantation: summary of the main studies published after 2013

Study and design	No. of patients	Impact of MR under CF-LVAD	Impact of concomitant MV surgery at the time of CF-LVAD implant	New message and suggested therapy
Goodwin et al.[103] Retrospective, single center	238: < moderate MR: 195; ≥ moderate MR: 43	LV unloading after CF-LVAD implantation was immediate regardless of preoperative MR severity. MR did not influence RV function. No significant difference of survival with uncorrected MR between the 2 groups.	NA	*What is new:* LV unloading was immediate regardless of preoperative MR severity. Preoperative MR had no impact on postoperative outcomes. *Suggested therapy:* Concomitant MV repair or replacement at the time of CF-LVAD implantation might be unnecessary.
Dobrovie et al.[104] Retrospective, single center	128: severe MR: 65; ≤ moderate MR: 63	Decrease of severe MR prevalence from 51% to 6% after CF-LVAD implantation. No difference in clinical outcomes and survival between the 2 groups. Similar functional status, complication rates. and survival.	NA	*What is new:* Durable decrease of MR severity after CF-LVAD implantation (3 years). *Suggested therapy:* Concomitant MV repair or replacement at the time of CF-LVAD implantation might be unnecessary.
Okoh et al.[68] Retrospective, single center	91: < moderate MR: 29; ≥ moderate MR: 62	Lower survival at 2 years in patients with severe MR(47% vs 17%; $P = 0.001$). Survival was the lowest in patients with combined moderate-to-severe MR and TR	NA	*What is new:* In DT patients, uncorrected moderate-to-severe MR was associated with the worst clinical outcomes and survival after CF-LVAD implantation. *Suggested therapy:* Tailored approached in patients with expected support duration > 1 year.
Roberson et al.[67] Retrospective, INTERMACS	4930: no MV procedure: 4667; MV repair: 252; MV replacement: 11	Reduction of MR severity: 18% of patients with moderate or severe MR under CF-LVAD support.	Undergoing an MV procedure did not improve mortality, but was associated with a trend toward increased long-term survival in patients receiving a CF-LVAD for DT. Concomitant MV procedure may have benefits in terms of improving quality of life and reducing hospital readmissions.	*What is new:* Undergoing an MV procedure did not improve mortality, but was associated with a trend toward increased long-term survival in patients receiving a CF-LVAD for DT. Concomitant MV procedure may have benefits in terms of improving quality of life and reducing hospital readmissions. *Suggested therapy:* Some patients may benefit from MV repair in terms of quality of life and a reduction in the likelihood of hospital readmission and, possibly, mortality when DT is anticipated.

Kawabori et al.[77] Retrospective, single center	108 with preoperative severe MR: MV procedure: 26; no MV procedure: 82	NA	No difference in overall survival. Similar postoperative complication rates.	*Suggested therapy:* Authors suggested that concomitant MV procedure does not further reduce severe residual MR after CF-LVAD implantation or its associated effects.
Hata et al.[105] Retrospective, single center	74	Significant LV reverse remodelling in all patients regardless of MR severity before CF-LVAD implantation	NA	*Suggested therapy:* Significant MR might not require routine surgical repair at the time of LVAD implantation. MV repair should be considered for patients with possibility of cardiac recovery or with severe pulmonary hypertension and depressed right ventricle.
Choi et al.[76] Systematic review	8 studies; 445 patients; concomitant MV surgery: 113	NA	No difference in perioperative outcomes. No difference of survival between the 2 groups.	*What is new:* Concomitant MV procedures seem to be safe and did not increase operative mortality. However, no benefit in survival was observed. *Suggested therapy:* Significant MR might not require routine surgical repair at the time of LVAD implantation.

DT, destination therapy; NA, not applicable; LV, left ventricular; RV, right ventricular; TR, tricuspid valve regurgitation.

However, recent studies have demonstrated the safety of concomitant MV procedures despite a potentially longer cross-clamp time,[76] better hemodynamics (decrease in pulmonary vascular resistances, increased freedom from recurrent MR),[72] and better clinical parameters (decrease in heart failure symptoms, survival) after MR correction at the time of CF-LVAD implantation[78,79] or a negative impact on survival in a subgroup of CF-LVAD patients with uncorrected MR.[67,68,71]

In a systematic review and meta-analysis of 8 retrospective single-centre studies including 445 patients with moderate-to-severe or severe MR at the time of CF-LVAD implantation and either undergoing a concomitant MV procedure or not, the authors did not note any differences in residual MR, perioperative outcomes, LV dimensions, and short- and long-term survival.[76] There was no information about adverse events, hospital readmission, or quality of life.

In a recent INTERMACS database analysis, Robertson et al. compared outcomes between concomitant MV procedures and managing moderate-to-severe MR with CF-LVAD implantation alone.[67] The first finding of that major study was that only a small proportion of the patients underwent concomitant MV procedures. Among the 4930 patients included in the analysis, only 3.9% and 7.7% of patients with preoperative moderate and severe MR underwent an MV procedure (263 patients in total). Among them, 252 patients underwent MV repair and 11 MV replacement. Patients with an MV procedure had more significant pulmonary hypertension, PCWP, and pulmonary vascular resistance and were more likely considered to be in BTC. The second important finding was that concomitant MV procedures did not increase postoperative morbidity or mortality. The need for right ventricular assist devices (RVADs), rate of neurologic events, and length of hospitalization were similar in both groups. Third, the study did not provide strong evidence for a survival benefit after concomitant MV procedure in the entire population. The authors could not find any association between the decision to perform an MV procedure or the degree of MR and an increased risk of mortality in either the early or the late phase. Although there were no differences in degree of MR at 3 months between patients who underwent MR correction and patients who did not, there was a trend toward a long-term survival advantage for DT patients with moderate-to-severe MR who had undergone MV repair. Furthermore, Kaplan-Meier analysis demonstrated that patients undergoing concomitant MV repair had significantly higher freedom from rehospitalization at both 1 and 2 years. In terms of quality of life, no difference could be observed, but the greatest changes in the 6-minute walk test were observed in patients who underwent MV repair. These findings might help to identify clinical situations and CF-LVAD patients who would benefit the most from a concomitant MV procedure.

Based on the Robertson et al. study,[67] we suggest considering concomitant MV procedures only in very selected situations, as summarized in Table 2. In our opinion, it might be reasonable to consider correction of severe MR for patients implanted as BTT or BTC with elevated pulmonary pressure, for DT patients with borderline RV function, and for patients implanted with potential bridge to recovery.

How should we address important mitral valve regurgitation at the time of CF-LVAD implantation?

In the setting of CF-LVAD, operative strategies to treat MV disease include MV repair, replacement, or complete excision of both the leaflets and the subvalvular apparatus (Table 2). The choice of strategy is based on surgeon experience. There are no data to support one of these techniques over another. Although outcomes prediction for patients with residual MR is difficult, the ideal surgical management and the appropriate surgical strategy for such patients remain without consensus. Fewer than 1% of CF-LVAD candidates have had a previous MV replacement. If a mechanical valve is already implanted, the current guidelines do not recommend its routine replacement as long as it functions well. However, most of the published series reported its replacement with a tissue valve to decrease the risk of thromboembolic complications.[80]

With the development of percutaneous transcatheter mitral valve procedures (ie, Mitraclip; Abbott Labs, Chicago, IL), more and more CF-LVAD candidates will likely have a mitral device in place at the time of CF-LVAD implantation. An increasing number of case reports have shown that CF-LVAD implantation after a previous Mitraclip procedure appears to be safe.[81,82]

Tricuspid Valve Disease and Long-term CF-LVAD

Does the presence of tricuspid valve regurgitation affect hemodynamic and clinical outcomes in CF-LVAD patients?

Moderate to severe functional TR is present in ~ 40%-50% of patients undergoing CF-LVAD implantation and persists in 23%-40% of patients.[83-87] Tricuspid regurgitation is usually secondary to annular dilation and leaflet tethering caused by RV dilation, pulmonary hypertension, and LV dysfunction. In patients with significant preoperative TR, tricuspid annulus enlargement and lower RV stroke work are more likely. In theory, mechanical unloading of the LV could reduce RV afterload and then decrease TR. However, Alturi et al. showed an early and sustained improvement in post-VAD pulmonary hypertension, RV function, and TR grade without TV procedure.[86] Nevertheless, the severity of TR does not always improve after CF-LVAD implantation. Indeed, the favourable effects of CF-LVAD unloading on the RV afterload might be counterbalanced by an increase in cardiac output, the leftward shift of the ventricular septum, and an increase of venous return and RV preload. In addition, the pulmonary vasculature of chronic heart failure patients might be remodelled, leading to a high or fixed increase in pulmonary vascular resistance and RV dysfunction associated with persistent TR. Another limitation to the improvement of TR under CF-LVAD is that tricuspid dilation alone, without severe regurgitation, is associated with RVF and adversely affects survival after CF-LVAD implantation.[84,88] Indeed, Kukucka et al. found that a tricuspid annulus dilation > 43 mm was associated with decreased survival and that CF-LVAD implantation did not correct TV annular dilation.[88]

In terms of the clinical impact of persistent TR, a study by Piacentiano et al. was one of the first to demonstrate the

negative impact of significant TR in CF-LVAD patients. In a retrospective analysis of 137 CF-LVAD patients, an early improvement of TR after CF-LVAD implantation alone was observed, but moderate or severe TR persisted in 30% of patients. The authors also showed that significant TR was associated with a longer duration of inotrope support, a higher rate of RVAD use, longer hospital stays, and a trend toward worse survival at 1.5 years.[89] Finally, Zhigalove et al. showed a decrease of survival in patients with significant TR, but a similar survival with or without TVR.[90] Table 5 summarizes the most important studies published since the publication of the ISHLT guidelines.

When should we perform a tricuspid valve procedure at the time of the CF-LVAD implantation?

Persistent moderate-to-severe TR seems to be detrimental to CF-LVAD patients, but the benefit of a concomitant TV procedure remains unclear. Although the ISHLT guidelines suggest that a moderate or severe TR should prompt consideration of surgical repair at the time of implantation (class IIa, level of evidence C),[6] studies conducted more recently either demonstrated no survival benefit from addressing significant TR[91] or showed an increase in postoperative morbidity or mortality.[92-94] No randomized study has yet been conducted.

In a single-centre retrospective study, Saeed et al. did not find any benefit of concomitant TVR in patients with grade III or IV TR.[92] Extracting data from the Society of Thoracic Surgeons database, Robertson et al. analyzed the records of 2196 patients with moderate-to-severe preoperative TR who underwent CF-LVAD implantation, of whom 27% (588 patients) underwent a concomitant TV procedure.[93] After adjustments for between-group differences, the authors concluded that performing a concomitant TV procedure did not reduce the rate of early death or RVAD requirement and was associated with worse early postoperative outcomes (postoperative renal failure, greater transfusion requirement, reoperation, prolonged ventilation, prolonged intensive care unit stay, and prolonged hospital stay). The same findings were reported by Song et al. in an analysis of 2527 CF-LVAD patients from the INTERMACS database. Although significant TR was associated with a lower survival rate, TV repair did not confer improved survival. In a single high-volume centre, Han et al. showed that a concomitant TV procedure was protective against worsening TR during the first 2 years and was not associated with increased hospital mortality.[95] However, they reported a higher rate of postoperative complications and a survival rate similar to that of patients presenting with significant preoperative TR but who did not undergo a TV procedure. Again, concomitant TV procedures did not improve survival of CF-LVAD patients.

New studies are needed to identify the patients who will most benefit from TV procedures. Some surgeons have argued that TV annuloplasty is not only beneficial in reducing TR, but may also primarily decrease RV volume, which may help to improve overall RV performance.[96] Two studies have shown that TV repair or replacement was associated with a decrease of TR and an early reverse remodelling of the RV, despite a higher preoperative risk of RVF in such patients.[91,97] Others have found that concomitant TV procedures, unlike concomitant AV procedures, did not increase CF-LVAD procedural mortality.[46,98] One study with a small number of patients showed a survival benefit even after adjusting for preoperative characteristics.[99] All of those studies suggest that additional selection criteria are needed to identify the patients in whom concomitant TVR might prevent RVF.

Veen et al. tried to provide more evidence in a meta-analysis of 8 retrospective studies including 562 patients undergoing isolated CF-LVAD implantation and 303 CF-LVAD patients with concomitant TV procedures.[100] Patients with both TV procedures and LVAD implantation had a more severe clinical condition than patients who had isolated CF-LVAD. The authors observed no significant difference in early mortality, RVF, acute kidney injury, hospital stay, or RVAD implantation between groups. Late mortality and RVF were also similar. One of the interpretations of these findings could be that the sickest patients may benefit from TV procedures, because they have outcomes similar to less sick patients. They also raised very relevant questions: Does TR have an impact on outcomes by itself or is it merely a marker for the severity of RV dysfunction? and If so, does TVS improve RV function? To date, no definitive answer has been provided in the literature. The decision remains to be based on a multidisciplinary team discussion. Concomitant TV procedures might consequently be performed in the most severe patients with a high risk of RVF under CF-LVAD.

How should we address tricuspid valve insufficiency at the time of CF-LVAD implantation?

There is no recommendation to guide the surgeon's choice of procedure. In the current literature, ~ 80% of patients who underwent CF-LVAD implantation and concomitant TV procedures had TV repair with the use of an annuloplasty.[93,95,101] Only 1 study compared TV repair and replacement in this clinical setting.[101] Deo et al. did not find any difference between the 2 procedures and concluded that the choice of repair vs replacement did not affect clinical outcomes. Akhter et al. showed that a de Vega tricuspid valve annuloplasty was safe and provided a significant reduction of TR at 1 year in 90% of their patients.[102]

Conclusion

The presence of important valvular heart disease in patients with end-stage heart failure presenting for CF-LVAD consideration is common. Previously, there has been a lack of understanding and consensus on the adverse impact of VHD on patients receiving LVAD therapy, particularly for regurgitant TV and MV pathologies. Recent evidence demonstrates more consistent findings of an adverse impact of valvular pathologies on the hemodynamic benefit of CF-LVAD support, leading surgeons and cardiologists to advocate for more aggressive surgical correction. This is particularly true for AI. Safe and simple surgical approaches, such as partial central AV closure, are being used with satisfactory results.

MR was previously thought to resolve with CF-LVAD support, and few patients were considered for MV intervention at the time of CF-LVAD implantation. However, there is a greater appreciation that ~ 20%-30% of patients have persistent MV regurgitation after CV LVAD implantation

Table 5. Impact of tricuspid valve regurgitation (TR) under continuous-flow left ventricular assist device (CF-LVAD) and impact of tricuspid valve (TV) surgery at the time of CF-LVAD implantation: summary of the main studies published after 2013

Study and design	No. of patients	Impact of TR under CF-LVAD	Impact of concomitant TV surgery at the time of CF-LVAD implant	New message and suggested therapy
Robertson et al.[93] Retrospective, Society of Thoracic Surgeons database	2196	NA	Concomitant TV procedure did not affect the risk of postoperative need for RV support or death. TV procedure was associated with postoperative renal failure, reoperation, higher transfusion requirements, and prolonged length of stay.	*What is new:* Performing a concomitant TV procedure for CF-LVAD patients with moderate-to-severe TR did not reduce early death or RV assist device requirements and was associated with worse early postoperative outcomes. *Suggested therapy:* May not perform TV surgery based only on the degree of TR.
Song et al.[87] Retrospective, INTERMACS	2527; ≥ moderate TR: 989	Patients with moderate and severe TR had significantly poorer survival	Survival of patients with moderate-to-severe TR who underwent TV repair was not superior to those with moderate-to-severe TR who underwent no TV procedure.	*What is new:* Whereas significant TR at the time of LVAD implantation was associated with worse survival at late follow-up, concomitant TV repair did not appear to confer a survival benefit among patients with moderate-to-severe TR at the time of LVAD implantation. *Suggested therapy:* Not clear.
Veen et al.[100] Systematic review and meta-analysis	No TV procedure: 562; concomitant TV surgery: 303	NA	Patient who underwent TV surgery were sicker. No significant differences in early and late mortality, early and late RV failure, acute kidney failure, early RV assist device implantation, or length of hospital stay.	*What is new:* TV surgery was not associated with the worst perioperative outcomes. *Suggested therapy:* Current literature is unable to offer a definitive answer.
Zhiglov et al.[90] Retrospective, single center	124: < moderate TR: 88; ≥ moderate TR: 36	Lower survival in patients with moderate-to-severe TR	Higher rate of postoperative complications in the TV surgery group. No difference of survival in patients with or without concomitant TV surgery.	*What is new:* TV surgery was associated with the worst perioperative outcomes and similar mid-term survival. *Suggested therapy:* None.

NA, not applicable; RV, right ventricular.

that has an important adverse impact on outcomes. Our knowledge of which patients at risk for persistent MR after CF-LVAD implantation continues to evolve, as does the approach to address MR concomitant with or following CF-LVAD implantation. As with MR, our understanding of the impact of TR on CF-LVAD outcomes continues to evolve. At present, there is no clear benefit established for TV intervention, but patients with important TR tend to have worse outcomes.

Despite the lack of consensus on treatment of important VHD in the setting of CF-LVAD support, new insights continue to be developed that will have significant impact on how we treat VHD in the setting of CF-LVAD therapy in the future.

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