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ORIGINAL ARTICLE

Impact of progressive aortic regurgitation on outcomes after left ventricular assist device implantation

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Abstract
Aortic regurgitation (AR) following continuous flow left ventricular assist device implantation (cf-LVAD) may adversely impact outcomes. We aimed to assess the incidence and impact of progressive AR after cf-LVAD on prognosis, biomarkers, functional capacity and echocardiographic findings. In an analysis of the PCHF-VAD database encompassing 12 European heart failure centers, patients were dichotomized according to the progression of AR following LVAD implantation. Patients with de-novo AR or AR progression (AR_1) were compared to patients without worsening AR (AR_0). Among 396 patients (mean age 53 ± 12 years, 82% male), 153 (39%) experienced progression of AR over a median of 1.4 years on LVAD support. Before LVAD implantation, AR_1 patients were less frequently diabetic, had lower body mass indices and higher baseline NT-proBNP values. Progressive AR did not adversely impact mortality (26% in both groups, HR 0.91 [95% CI 0.61–1.36]; $P = 0.65$). No intergroup variability was observed in NT-proBNP values and 6-minute walk test results at index hospitalization discharge and at 6-month follow-up. However, AR_1 patients were more likely to remain in NYHA class III and had worse right ventricular function at 6-month follow-up. Lack of aortic valve opening was related to de-novo or worsening AR ($P < 0.001$), irrespective of systolic blood pressure ($P = 0.67$). Patients commonly experience de-novo or worsening AR when exposed to continuous flow of contemporary LVADs. While reducing effective forward flow, worsening AR did not influence survival. However, less complete functional recovery and worse RV performance among AR_1 patients were observed. Lack of aortic valve opening was associated with progressive AR.

Keywords Aortic regurgitation · Left ventricular assist device · Outcome

Introduction

The contemporary burden of advanced heart failure is extensive and is projected to escalate further [1]. Continuous-flow left ventricular assist devices (cf-LVAD) have fundamentally changed the management and prognosis of this syndrome. Notwithstanding their benefits, cf-LVADs are associated with complications arising from either the interaction between internal device components with blood elements, or rheological properties of non-pulsatile flow [2]. Aortic regurgitation (AR) develops and progresses insidiously in approximately a third of cf-LVAD recipients [3–5]. The pathological correlates of non-pulsatile flow at the level of the aortic valve (AoV) are commissural fusion and leaflet thinning [6]. These changes are accentuated in the absence of AoV opening and the ensuing continuous exposure to an increased transvalvular gradient [7]. The net result of alterations in AoV morphology is progressive valvular dysfunction [6]. Conventional semiquantitative echocardiography underestimates the severity of AR, as it does not take into account its pancyclic nature. Ostensibly small regurgitant orifices may therefore translate into significant AR, and potentially induce clinically relevant hemodynamic sequelae [4]. The importance of AR induced reduction of forward flow is proportional to the duration of support [3]. Other predictors of de-novo AR include absence of AoV opening,

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older age, female gender, systemic hypertension and suboptimal outflow graft anastomosis angles [3, 8]. The impact of de-novo AR on long-term LVAD survival is unknown, and there is an acute need for more data on the subject. An increase in LVAD output may counteract the adverse effects of inefficient flow, but this may come at the expense of reduced durability of older generation devices [9]. The clinical impact of AR after cf-LVAD support is subject to debate and remains a moving target, as does the appropriate management. The aims of the present study were to identify the mortality burden of progressive AR and its impact on the clinical and functional status in patients receiving cf-LVADs.

Patients and methods

Data acquisition and eligibility criteria

We reviewed the PCHF-VAD registry which accumulated data from 12 European heart failure centers and investigators of the Postgraduate Course in Heart Failure (PCHF) of the Heart Failure Association of the European Society of Cardiology and the European Heart Academy registry [10]. Institutional review boards of participating centers approved the study, with a waiver of informed consent in some instances. Inclusion criteria were met by patients with first-time cf-LVAD implantation in whom the temporal dynamics of echocardiographic AR descriptors were available for review. Exclusion criteria were prior or concomitant AoV surgery and lack of paired echocardiographic data. Aortic regurgitation was quantized into none, mild, moderate and severe per center-specific protocols, predominantly assessed visually or by vena contracta [11]. Patients were dichotomized into two groups based on echocardiographic evidence of AR progression during the course of follow-up. Patients in group AR_1 either developed de-novo AR or had evidence of AR progression by at least one grade. Patients in whom AoV competence was preserved were assigned to the AR_0 group. Data were recorded using REDCap (Research Electronic Data Capture) capture tools, hosted at the University of Zagreb School of Medicine [12]. Ethical standards were adhered to while conducting this research.

Outcome definitions

The main outcome was all-cause mortality. The secondary outcomes were cardiovascular death, heart failure hospitalization, right ventricular failure, life-threatening ventricular arrhythmias, intracranial and non-cerebral bleeding events after LVAD implantation [10]. We performed an intergroup comparison of N-terminal fragment of B-type natriuretic peptide (NT-proBNP) at three time points: baseline, discharge from index hospitalization and at 6 months post VAD implantation. Follow up assessments of functional, hemodynamic, echocardiographic and electrocardiographic data were performed. Where available, additional information on the functional status was provided by an intergroup comparison of 6-minute walk tests (6MWT) and NYHA class.

Statistical analysis

Continuous data are presented as means with standard deviations or medians with interquartile ranges for non-normally distributed variables. Categorical variables are presented as absolute numbers with percentages. Measures of association were derived from Fisher's exact or chi square tests. The Shapiro–Wilk test was used to determine whether a continuous outcome could be modeled by a normal distribution. ANOVA was used for analyzing normally distributed variables, while the Kruskal–Wallis or Mann–Whitney U tests were used for nonparametric variables.

For survival analyses, the time of LVAD implantation was considered as the index date; the time of follow-up was defined as time to last contact, weaning from LVAD, heart transplant, or death. Time-to-event estimates were calculated using the Kaplan–Meier method. Probability values were obtained from the log-rank test. The hazard ratios (HR) were estimated using the Cox proportional hazards model with the group of patients with no progression of aortic regurgitation post-LVAD serving as the referent group. A Cox regression model based on a forward stepwise selection process, with a significance level of 0.05 and 0.10 for entry and removal thresholds, was used to test the association of progression of AR with 6 baseline covariates that significantly differed between the two patient groups at baseline (LVAD type, LVAD intention, diabetes mellitus, BMI, diastolic pulmonary artery pressure, and NT-proBNP value).

In patients in whom BNP values, but not NT-proBNP values, were available for review we used a previously validated formula to convert the former into the latter [13]. This method was used for 49 NT-proBNP datapoints pre-LVAD implantation, 27 datapoints at index hospitalization discharge and 26 NT-proBNP datapoints at 6-month follow-up. Logarithmic transformation was used to address the skewness of data. A two-tailed P value <0.05 was considered significant for all statistics. The data were processed using the Stata version 14 (StataCorp, College Station, TX, USA).

Results

Study population

Data from 583 patients were assessed for eligibility. Of these, 396 fulfilled the inclusion criteria. The study flow

diagram is detailed in Fig. 1. Baseline demographic and clinical profiles are shown in Table 1. In brief, patients in group AR_1 were comparable to group AR_0 with respect to age, gender, INTERMACS profile, prior stroke, renal function or atrial fibrillation. Pre-LVAD temporary mechanical circulatory support use did not differ between the groups. A lower body mass index (24 [22–28] vs. 26 [23–29], $P<0.01$), lower prevalence of diabetes (14% vs. 26%, $P=0.01$), and higher NT-proBNP (5181 [3004, 10098] vs. 3820 [2345, 7440] pg/ml, $P<0.01$) were observed in group AR_1. Patients in the AR_1 group were more likely to have received a HeartMate II device and less likely to have received a HeartWare device; they were more likely to have been bridged to transplantation than the control group (Table 1).

Primary outcome

The median time on LVAD support was 1.4 [0.8, 2.6] years. All-cause death occurred in 62 (26%) patients in the AR_0 group and in 39 (26%) patients in the AR_1 group (Table 2). The unadjusted HR demonstrated a nominally, but statistically non-significant, lower risk of all-cause mortality implantation in the AR_1 group (HR 0.91; 95% CI 0.61–1.36, $P=0.65$) (Fig. 2). Using stepwise regression, LVAD type was established as an independent predictor of all-cause death. After

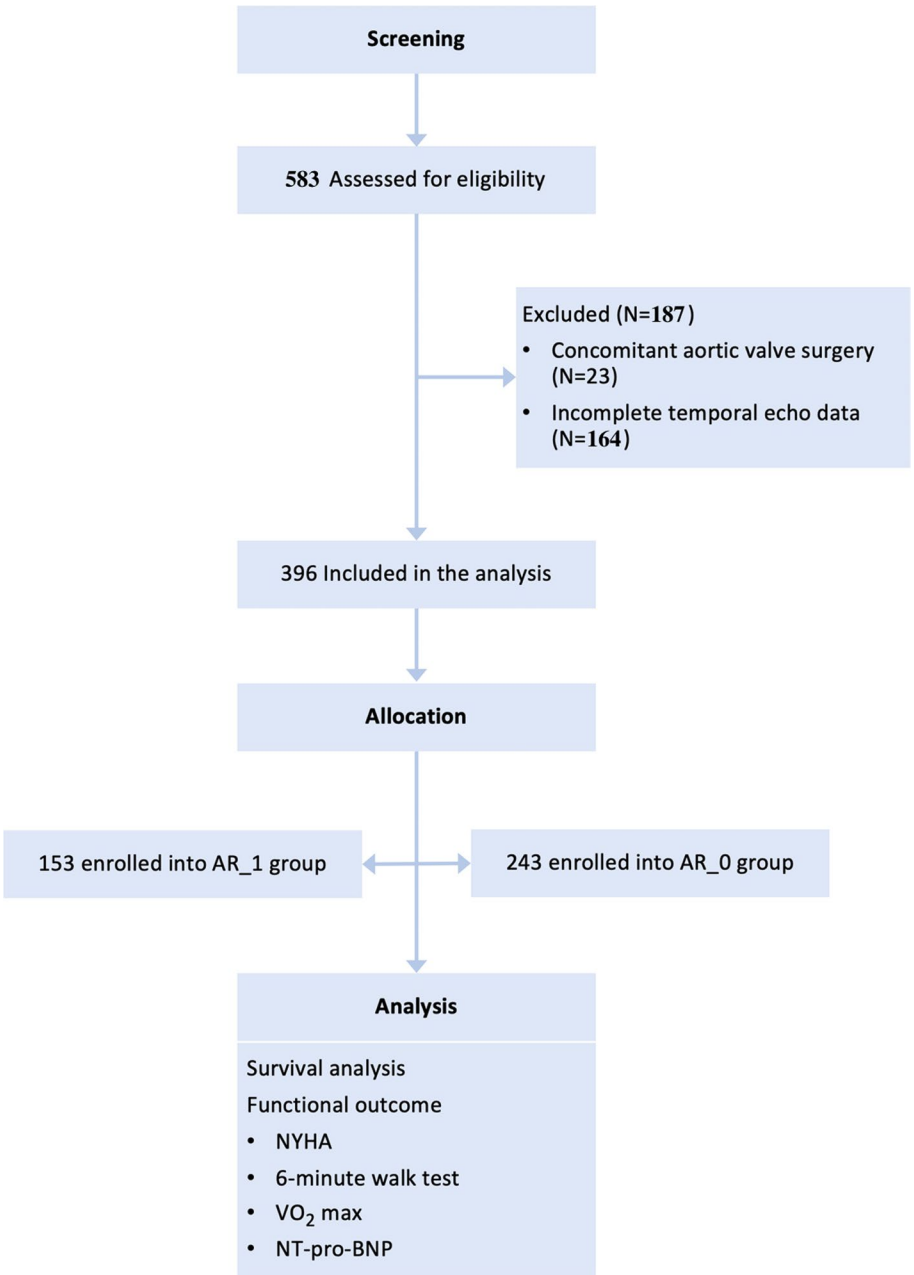

Fig. 1 Study flowchart summarizing patient eligibility, allocation and analysis. *RVAD* right ventricular assist device, *BiVAD* biventricular assist device

Table 1 Baseline demographic and clinical profiles of the study population

	Overall ($n=396$)	AR_0 group ($n=243$)	AR_1 group ($n=153$)	*P*-value
Age	53 ± 12	53 ± 12	54 ± 11	0.41
Male gender, *n* (%)	325(82)	203(84)	122(80)	0.34
Etiology of heart failure, *n* (%)				0.26
Dilated cardiomyopathy	184(47)	106(44)	78(51)	
Ischemic cardiomyopathy	181(46)	115(47)	66(43)	
Other	31(8)	22(9)	9(6)	
Arterial hypertension, *n* (%)	93(24)	58(24)	35(23)	0.82
Diabetes mellitus, *n* (%)	85(22)	63(26)	22(14)	0.01
Chronic kidney disease, *n* (%)	97(25)	59(24)	38(25)	0.90
Coronary artery disease, *n* (%)	100(25)	65(27)	35(23)	0.39
Chronic obstructive pulmonary disease, *n* (%)	36(9)	25(10)	11(7)	0.30
Atrial fibrillation/flutter, *n* (%)	122(31)	77(32)	45(29)	0.63
Ventricular arrhythmia, *n* (%)	102(26)	60(25)	42(28)	0.54
Cerebrovascular event, *n* (%)	31(8)	16(7)	15(10)	0.25
LVAD type, *n* (%)				0.04
HeartMate 3	124(31)	74(31)	50(33)	
HeartMate II	175(44)	98(40)	77(50)	
HeartWare	83(21)	62(26)	21(14)	
Other	14(4)	9(4)	5(3)	
LVAD intention, *n* (%)				0.02
Bridge to transplantation	254(68)	143(62)	111(76)	
Bridge to decision	56(15)	40(17)	16(11)	
Destination therapy	66(18)	47(20)	19(13)	
INTERMACS class, *n* (%)				0.63
Class 1	49(13)	33(14)	16(11)	
Class 2	102(26)	62(26)	40(27)	
Class 3	140(36)	82(34)	58(39)	
Class 4–7	100(26)	65(27)	35(24)	
Life support prior to LVAD implant, *n* (%)				0.17
None	301(78)	187(80)	114(76)	
ECMO	21(6)	15(6)	6(4)	
IABP	41(11)	19(8)	22(15)	
Temporary BiVAD	1(0.3)	1(0.4)	0(0)	
Temporary LVAD	3(1)	3(1)	0(0)	
Other	17(4)	9(4)	8(5)	
Prior cardiac surgery, *n* (%)	39(10)	22(9)	17(11)	0.50
Concomitant procedure with LVAD implant, *n* (%)	54(14)	38(16)	16(11)	0.14
Systolic blood pressure, mmHg	99 ± 14	99 ± 14	100 ± 14	0.64
Diastolic blood pressure, mmHg	64 ± 11	64 ± 10	65 ± 11	0.76
Heart rate, bpm	84 ± 19	84 ± 19	83 ± 21	0.58
Body mass index, kg/m2	26 [23–29]	26 [23–29]	24 [22–28]	< 0.01
NYHA class				0.52
II	11(3)	8(3)	3(2)	
III	226(58)	142(59)	84(56)	
IV	152(39)	89(37)	63(42)	
Creatinine, umol/L	116 [92–150]	112 [90–145]	122 [97–152]	0.55
Bilirubin, umol/L	24 ± 21	24 ± 22	23 ± 18	0.63
LVIDD, mm	71 [63–79]	71 [64–78]	72 [63–80]	0.28
LVEF, %	19 ± 7	19 ± 7	19 ± 7	0.82

Table 1 (continued)

	Overall ($n=396$)	AR_0 group ($n=243$)	AR_1 group ($n=153$)	*P*-value
Cardiac output, L/min	3.8 [3.1–4.5]	3.8 [3.1–4.5]	3.8 [3.0–4.3]	0.26
Prior concomitant therapy, *n* (%)				
Diuretic	350(92)	211(90)	139(94)	0.20
Beta blocker	240(67)	144(67)	96(67)	0.90
ACEi/ARB	163(45)	105(48)	58(41)	0.16
MRA	250(75)	149(75)	101(75)	0.86
ARNI	12(4)	7(4)	5(4)	0.90
Calcium channel blocker	1(0.3)	1(0.5)	0(0)	0.41
Ivabradine	37(12)	25(13)	12(10)	0.35
Inotrope	231(66)	137(63)	94(70)	0.23
Ultrafiltration	9(3)	7(4)	2(2)	0.26
NT-proBNP, pg/mL	4354 [2622, 8705]	3820 [2345, 7440]	5181 [3004, 10098]	< 0.01

LVAD Left ventricular assist device, *INTERMACS* Interagency registry for mechanically assisted circulatory support, *ECMO* Extracorporeal membrane oxygenation, I*ABP* Intra-aortic balloon pump, *NYHA* New York Heart Association, *LVIDD* Left ventricular internal diastolic diameter, *PA* Pulmonary artery, *ACEi/ARB* Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, *MRA* Mineralocorticoid receptor antagonists, *ARNI* Angiotensin receptor-neprilysin inhibitor, *NIV/cPAP* Non-Invasive ventilation/continuous positive airway pressure, *NT-proBNP* N-Terminal Pro B-Type Natriuretic Peptide

adjustment for this variable, AR progression or de-novo AR following LVAD was not significantly related to all-cause death (HR 0.95, 95% CI 0.63-1.43), *P*=0.82) (Table 3).

Secondary outcomes

Twenty-one patients in the AR_1 group (14%) and 36 patients in the AR_0 group (15%) suffered a cardiovascular death (HR 0.85; 95% CI 0.49-1.45, *P*=0.55). The incidence rates for cardiovascular mortality, heart failure hospitalization, right ventricular failure, ventricular arrhythmias, and bleeding events are presented in Table 2. Briefly, intergroup variations in non-fatal adverse events among patients with or without AR progression did not meet the prespecified thresholds of statistical significance.

Table 2 Incidence rates and hazard ratios for the primary and secondary endpoints by aortic regurgitation progression following LVAD implantation

	AR_0 group ($N=243$) Incidence Rate	AR_1 group ($N=153$) Incidence Rate	Hazard Ratio (95% CI), *P*-value	
			Unadjusted	Adjusted*
All-cause mortality (n of events = 101)	14.9 (11.6–19.1)	13.5 (9.9–18.5)	0.91 (0.61–1.36) $P=0.65$	0.95 (0.63–1.43) $P=0.82$
Cardiovascular mortality (n of events = 57)	8.7 (6.2–12.0)	7.3 (4.8–11.2)	0.85 (0.49–1.45) $P=0.55$	0.96 (0.55–1.67) $P=0.89$
Heart failure hospitalization (n of events = 91)	17.0 (13.2–21.9)	12.5 (8.8–17.8)	0.77 (0.50–1.18) $P=0.23$	0.88 (0.56–1.38) $P=0.58$
Right ventricular failure (n of events = 45)	8.1 (5.7–11.6)	6.1 (3.7–10.1)	0.78 (0.42–1.45) $P=0.43$	0.80 (0.43–1.51) $P=0.50$
Ventricular arrhythmias post-LVAD (n of events = 118)	19.8 (15.5–25.3)	26.1 (20.0–34.2)	1.35 (0.93–1.94) $P=0.11$	1.37 (0.94–1.98) $P=0.10$
Intracranial bleeding (n of events = 31)	3.9 (2.4–6.4)	5.3 (3.2–8.8)	1.38 (0.68–2.79) $P=0.37$	1.61 (0.78–3.32) $P=0.20$
Other bleeding (n of events = 81)	13.5 (10.2–17.9)	13.5 (9.5–19.1)	1.01 (0.65–1-58) $P=0.97$	1.03 (0.65–1.61) $P=0.91$

The incidence rates are presented as number of events per 100-patient years (95% confidence interval)

LVAD Left ventricular assist device

*Adjusted for LVAD type

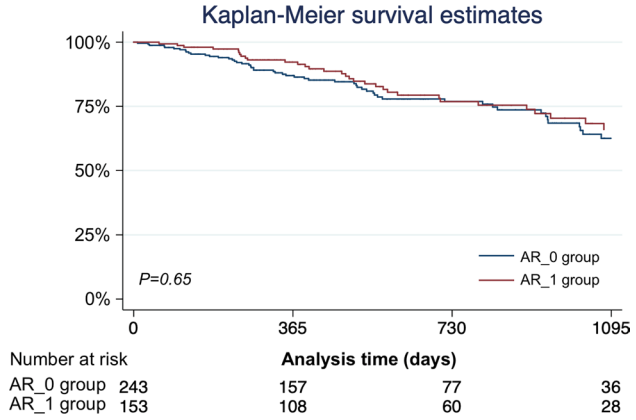

Fig. 2 Kaplan–Meier plot of time to all-cause survival, according to aortic regurgitation progression following left ventricular assist device LVAD implantation. The analysis begins at the time of LVAD implantation. *AR_0* no AR progression, *AR_1* de-novo AR or AR progression. *HR* hazard ratio

Table 3 Multivariate Cox regression model of risk factors for all-cause death following LVAD implantation

Variable	HR	95% CI	P value
Aortic regurgitation progression	0.95	0.63–1.43	0.82
LVAD type			0.03
Heart Mate 3	Referent		
Heart Mate II	2.04	1.14–3.64	
Heart Ware HVAD	2.65	1.40–5.00	
Other	1.62	0.54–4.90	

LVAD Left Ventricular Assist Device

Follow-up assessments-NT-proBNP values and metrics of functional outcome

There were no differences in the NT-proBNP values, NYHA class or 6MWT (Table 4) at the time of index hospitalization discharge between the AR_0 and AR_1 groups. Conversely, 15% of the patients in the AR_1 group were found to be in NYHA class I in comparison to 24% of patients in the AR_0 group, which was mirrored by a lower proportion of patients in NYHA class III among the AR_0 cohort than in the AR_1 cohort (10% vs. 18%, respectively, P=0.03). Variables associated with NYHA class at 6-month follow-up on univariate analysis were then entered into a multiple linear regression model. These included AR progression, age, hypertension and chronic obstructive pulmonary disease. Progression of AR was significantly associated with NYHA class at later follow-up in the multiple regression analysis (P=0.03), as was the presence of chronic obstructive pulmonary disease (P=0.01).

Table 4 Intergroup comparisons of follow-up assessments

	AR_0 group (N=243)	AR_1 group (N=153)	P
Assessments at index hospitalization discharge			
NYHA, *n* (%)			0.58
I	7(3)	1(1)	
II	144(64)	92(65)	
III	69(31)	49(35)	
IV	4(2)	0(0)	
LVIDD, mm	61 ± 13	61 ± 13	0.79
LVIDS, mm	53 ± 13	54 ± 13	0.83
TAPSE	12 [10, 16]	12 [10, 16]	1.0
6-min walk test, m[a]	383 ± 136	354 ± 132	0.39
NT-pro-BNP, pg/ml[b]	1962 [1302, 3272]	2275 [1300, 3662]	0.41
Assessments at 6-month follow-up			
NYHA, *n* (%)			0.03
I	49(24)	21(15)	
II	129(64)	91(66)	
III	21(10)	24(18)	
IV	4(2)	1(1)	
LVIDD, mm	63 ± 13	65 ± 12	0.26
LVIDS, mm	54 ± 14	58 ± 14	0.06
TAPSE	14 [12, 17]	10 [9, 14]	< 0.01
6-min walk test, m[d]	487 ± 158	415 ± 132	0.12
NT-pro-BNP, pg/ml[e]	1357 [770, 2207]	1483 [939, 2529]	0.30

NYHA New York Heart Association, NT-proBNP *N-Terminal pro B-type natriuretic peptide*; *LVIDD* Left ventricular internal diastolic diameter, *LVIDS* Left ventricular internal diameter end systole, *TAPSE* Tricuspid annular plane systolic excursion

[a]N = 71

[b]N = 208

[d]N = 49

[e]N = 243

Hemodynamic and echocardiographic data

Postoperative mean arterial blood pressure data were similar between the groups at 6-month follow-up. Patients in the AR_1 group at 6-month follow-up were significantly more likely to have their AoV permanently closed on echocardiographic evaluation (55% vs. 38%, P<0.01, Fig. 3). In multivariate regression analysis, lack of AoV opening at 6-month follow up was related to the occurrence of worsening AR (those with AR_1 had less frequent AoV opening, P<0.001), irrespective of SBP value (P=0.67). Patients with progressive AR had less efficient LV unloading at 6-month follow-up, albeit not reaching statistical significance (Table 4). RV

function, quantified with tricuspid annular plane systolic excursion, deteriorated in the AR_1 group at 6-month follow-up (Table 4).

In a multivariate logistic regression model, an increase in log-transformed NT-proBNP increased the odds of developing de-novo or worsening AR (OR 1.50, 95% CI 1.12-2.02, *P*=0.008), while the presence of diabetes at baseline and LVAD as bridge to decision (vs. LVAD as bridge to transplantation) were both associated with lower odds (OR 0.40, 95% CI 0.21-0.78, *P*=0.007 and OR 0.39, 95% CI 0.17-0.88, P=0.023).

Discussion

We have shown that patients commonly experience worsening incompetence of their native AoV when exposed to the continuous flow of contemporary LVADs. Previous reports placed the incidence of significant AR at 25–34% of LVAD patients, which compares well with the 39% incidence among our 396 patients from 12 European centers [3–5]. Notwithstanding the reduced effective forward flow by recycling the regurgitant volume, worsening or de-novo AR was not significantly associated with survival in our study. We did, however, demonstrate an adverse association of progressive AR with NYHA status at 6-month follow-up. This finding was not corroborated by other measures of functional status. A marginal decline in the capacity of LVADs to decompress the LV was seen in patients with progressive AR. Incomplete LV unloading has been shown to increase RV afterload, and subsequently, impair RV function [14]. Our data substantiates this link, as patients with progression of AR also had a

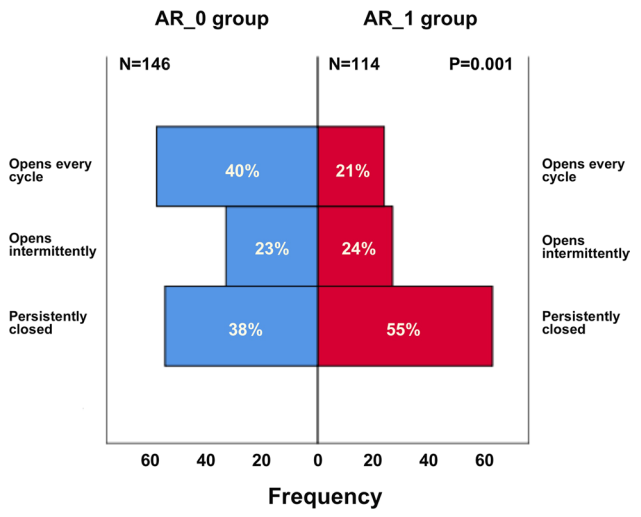

Fig. 3 Intergroup comparison of aortic valve mobility status. *AR_0* no progression of aortic regurgitation (AR), *AR_1* de-novo AR or AR progression

reduction in RV function. Less efficient LV unloading, coupled with the fact that the AoV was persistently closed in 55% of patients in the investigated group (AR_1), is likely to have a cumulative impact with increasing duration of LVAD support. Our survival analysis captured the entire follow-up period, but the functional outcomes were accumulated only for the first 6 postoperative months. The impact of AR progression on functional outcomes beyond that period is not reflected by the present data and may therefore underestimate long-term outcomes. The mechanism of AR in cf-LVAD recipients is multifactorial. Size mismatches between the outflow graft and native aorta result in high velocity jets that create mosaics of high pressure and shear stress [15]. These flow patterns manifest as chaotic eddy currents which may lead to aortic root dilatation and shortening of AoV coaptation lengths [15, 16]. Greater angles between the outflow graft and the aorta have also been associated with greater regurgitant volumes [17]. We have established an association between non-opening of the AoV and the development of de-novo or worsening AR. Attempts at optimizing cf-LVAD speeds have previously been proposed to allow for intermittent AoV opening [3, 16]. There is, however, no consensus on the optimal line of management of de-novo AR among LVAD recipients. Jorde et al. proposed a staged approach to symptomatic AR which initially included optimization of LVAD parameters under echocardiographic guidance, followed by hemodynamic studies in the absence of clinical improvement [18]. Interventional approaches were reserved for symptomatic patients in whom less invasive management failed to improve symptoms. Aortic regurgitation in a continuous flow system is mostly pancyclic, which makes parallels with diastolic AR seen in natural pulsatile flow patterns inherently flawed. The definition of AR in most published studies on patients with cf-LVADs is not based on quantifiable parameters and therefore lacks both uniformity and reproducibility [3]. Visual estimation of AR severity is limited in continuous flow settings, as well as in eccentric jets, which are both seen in LVAD recipients [5]. Recently, a novel Doppler echocardiographic approach obtained at the LVAD outflow cannula has been suggested for the quantification of AR in LVAD carriers [5, 19]. The authors demonstrated a better correlation with measured cardiac loading and have further shown that conventional visual estimation may underestimate AR severity. Imamura et al. have shown that 98% of patients in their series were initially found to have mild or less AR on visual estimation. This was contrasted by the results of their reevaluation based on novel echocardiographic parameters for quantifying AR, which identified 34% of patients as having at least moderate AR [5]. After reclassification, survival free from hemocompatibility events was significantly lower in those with significant AR which was also an independent predictor of death or hemocompatibility-related adverse events [5]. We grouped all patients with worsening aortic regurgitation into the AR_1 group, irrespective of the absolute degrees

of AR. Only 15 patients in the entire cohort had moderate AR by conventional semiquantitative evaluation. We believe that the paucity of patients quantified as having significant AR may be a failure of definition rather than a reflection of the rarity of these observations. The current practice of quantifying AR which equalizes hemodynamic conditions of pulsatile systems with continuous flow systems may be erroneous. This may explain why, in our study, more patients with AR progression were found to be in NYHA III class and had worsening RV function. The current strategy of AR quantification may be especially unsuitable for LVAD patients with permanently closed aortic valves, in whom AR is completely pancyclic. We feel that our study may provide an additional impetus for promoting management algorithms that allow for intermittent aortic valve opening in patients with continuous flow systems. Data on RV function in LVAD recipients in relation to AR progression has thus far been scarce. Our observations to that effect should be explored in future studies in more detail.

Limitations

Our retrospective and observational design is limited by the comprehensiveness of data input. Furthermore, evaluation of AoV insufficiency was based on semiquantitative data from transthoracic echocardiograms, which leads to underestimation of the true AR burden with cf-LVADs. Finally, associations observed in our study may be subject to unmeasured confounding.

Conclusion

We found that the competence of the AoV in cf-LVAD recipients deteriorates in a significant proportion of patients. While this observation did not translate into worse survival in this large cohort of patients, we have shown that it results in a discrete negative effect on midterm functional outcomes of device therapy. Other manifestations of AR progression were reduction in longitudinal RV function and less complete LV unloading. A clear association between persistently closed AoVs and progressive AR was also confirmed in our LVAD recipients.

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Declarations

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