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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Development of de novo aortic valve incompetence in patients with the continuous-flow HeartWare ventricular assist device

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KEYWORDS:
HVAD;
HeartWare;
VAD;
aortic regurgitation;
aortic incompetence;
aortic root;
echocardiogram

BACKGROUND: In this study we investigated the development of aortic incompetence (AI) and change in aortic root and left ventricular dimensions after implantation of the continuous-flow HeartWare ventricular assist device (HVAD) in our adult patient cohort.

METHODS: A retrospective analysis of serial echocardiograms was performed on patients implanted with an HVAD between July 2009 and July 2013. Data from echocardiograms performed before and at 1 and 2 years (±3 months) were analyzed. Patients with native aortic valves (AoVs) with no previous intervention and HVAD in situ for ≥6 months were included.

RESULTS: A total of 73 HVADs in 71 patients with a mean duration of support of 624 ± 359 days were included in our study. One patient developed moderate AI at 1 year (1.9%). Mild or greater AI was more likely in those with a closed or intermittently opening AoV at 1 year ($p = 0.005$). Aortic annulus dimensions increased significantly at 1 and 2 years, regardless of extent of AI. At 2 years, in those with mild or worse AI, the sinuses of Valsalva were also larger ($p = 0.002$). Left ventricular end-diastolic dimension (LVEDD) was significantly reduced in those with no or trace AI at 1 and 2 years ($p = 0.012$ and $p = 0.008$, respectively), but remained unchanged in those with AI at both time-points.

CONCLUSIONS: The development of more than mild AI is rare in HVAD patients at our center. When encountered, it is more common with a closed AoV. Dilation of the aortic annulus, and root dilation in those with mild or more AI, is seen with HVAD support over time.

J Heart Lung Transplant 2016;35:312–319

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Worldwide, continuous-flow left ventricular assist devices (cfLVADs) comprise >95% of implants.[1] Long-term left ventricular assist devices (LVADs) are frequently used as destination therapy (DT).[2] Currently in the UK, LVADs are licensed only as bridge-to-transplant (BTT) therapy for patients with refractory heart failure (HF).[3] In an era of seemingly declining numbers of available organs, these devices provide an important means of prolonging survival and improving patient symptoms and quality of life while awaiting organ transplantation. In the UK, the rate of BTT at 12 months is approximately 10%.[4]

De novo aortic incompetence (AI) in patients with cfLVADs results in the development of a wasteful

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http://dx.doi.org/10.1016/j.healun.2015.10.022

recirculation circuit, which, if significant, over the course of time can result in adverse hemodynamics. This is due to reduced effective pump flow, increasing pump work and reduced systemic perfusion.[5] Pathologic changes in the native valve have been thought to be causative in the development of de novo AI. The aortic valve (AoV) in patients with LVADs has been found to be thinner, with partial fusion of leaflets along with leaflet shortening secondary to curling seen on pathologic examination.[6–8] The commissural fusion has been to shown to be secondary to a non-inflammatory process.[9]

The HeartWare LVAD (HVAD; HeartWare, Framingham, MA) is a third-generation cfLVAD that has been commercially available in Europe (CE approval in 2009) and Australia (TGA approval 2011) before being approved in November 2012 by the Food and Drug Administration for use in the USA. The published literature to date on the development of new AI in patients supported with cfLVADs has been based predominantly on data from experience with the HeartMate XVE (HM-XVE; Thoratec Corporation, Pleasanton, CA) and HeartMate II (HMII; Thoratec) cfLVADs.[10–16] The number of patients with HVADs has been limited in previous studies.

The HVAD software for the European market has the facility to enable or disable the Lavare cycle. This feature is not available in North America. The Lavare cycle occurs at 60-second intervals and lasts for 3 seconds (Figures 1 and 2). During this cycle, the pump speed is lowered by 200 rpm below baseline for 2 seconds, then increased by 200 rpm above baseline before returning to baseline (refer to instructions for use of the HeartWare VAD, Rev0208/13 EN). This may have an impact on the long-term development of AoV pathology.

We have implanted HVADs at our institution since 2009 and now have a growing cohort of patients with longer term devices. This has provided a unique opportunity to study the development of de novo AI. The aim of this study was to examine the development of new AI after implantation of the HVAD in our adult patients and, using echocardiography, document changes in the aortic root and left ventricular dimensions over time.

Methods

A retrospective review of echocardiograms was performed in patients who had an HVAD implanted at our institution between July 1, 2009 and July 31, 2013. Patients were excluded if they had previous AoV surgery, or if surgery on the AoV was carried out at the time of HVAD implant. Only those who had an HVAD in situ for at least 6 months were included in the subsequent analysis.

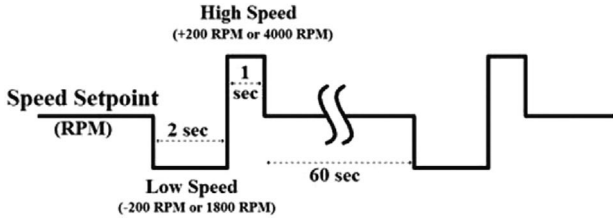

Figure 1 LAVARE™ Cycle. Reprinted with permission from HeartWare, Inc.

Surgical implantation technique

Implantation of the HVAD was carried out via median sternotomy on cardiopulmonary bypass using cannulation of the ascending aorta, and a 2-stage venous cannula via the right atrium (RA) or selective cannulation of the superior and inferior vena cava, respectively. Device implantation was carried out according to a standard technique recommended by the manufacturer. The outflow graft was attached to the right side of the middle part of the ascending aorta using a side-biting clamp. A simple 10-mm aortotomy was performed and the anastomosis was carried out end-to-side using a 5-0 Prolene continuous suture line. The length of the outflow graft was adjusted according to the size of the right ventricle (RV) and RA; that is, particular care was taken to ensure sufficient length to allow positioning of the graft entirely at the lowest level of the pericardium around the RV and the RA. Therefore, at the time of chest closure, the graft was visible only in the area of the anastomosis to ascending aorta. All patients had the Lavare cycle enabled before discharge from hospital. This was not disabled at any time-point, even if the patient was re-admitted with suspected HVAD thrombus.

Echocardiographic analysis

Echocardiograms performed within 3 months of implant were considered baseline. Thereafter, echocardiograms performed at 12, 24 and 36 months (± 3 months) post-implant were reviewed. These were performed by experienced cardiac sonographers and reported according to standards of the British Society of Echocardiography. The echocardiograms were further reviewed by the authors (S.B. and C.B.) for the purposes of this study. AI was assessed visually in the parasternal long- and short-axis views. A graded scale was used to report the grade of severity of AI as follows: none; trace; mild; mild–moderate; moderate; or worse. Opening of the AoV was assessed visually over a 3-beat cycle. The aortic annulus, the sinus of Valsalva (SoV) and the left ventricular end-diastolic dimension (LVEDD) and end-systolic dimension (LVESD) were all measured using the parasternal long-axis window.

Statistical analysis

SIGMAPLOT for Windows version 11.0 (Systat Software, Inc., San Jose, CA) and Microsoft EXCEL 2007 were used for data analysis. With normally distributed data, results are presented as mean ± standard deviation of the mean (SD). If data were not normally distributed, median and interquartile ranges (IQRs) are reported. Groups were compared using Fisher's exact test for categorical variables and Student's *t*-test or the Mann–Whitney rank sum test for numerical variables. To evaluate trends in results over time using matched data, repeated-measures analysis of variance (ANOVA) on ranks or Friedman's repeated-measures ANOVA was employed. $p < 0.05$ was considered statistically significant.

This study adhered to the terms of the UK Data and Protection Act and Freedom of Information Act, and was approved to obtain confidential information by the local Caldicott Guardian.

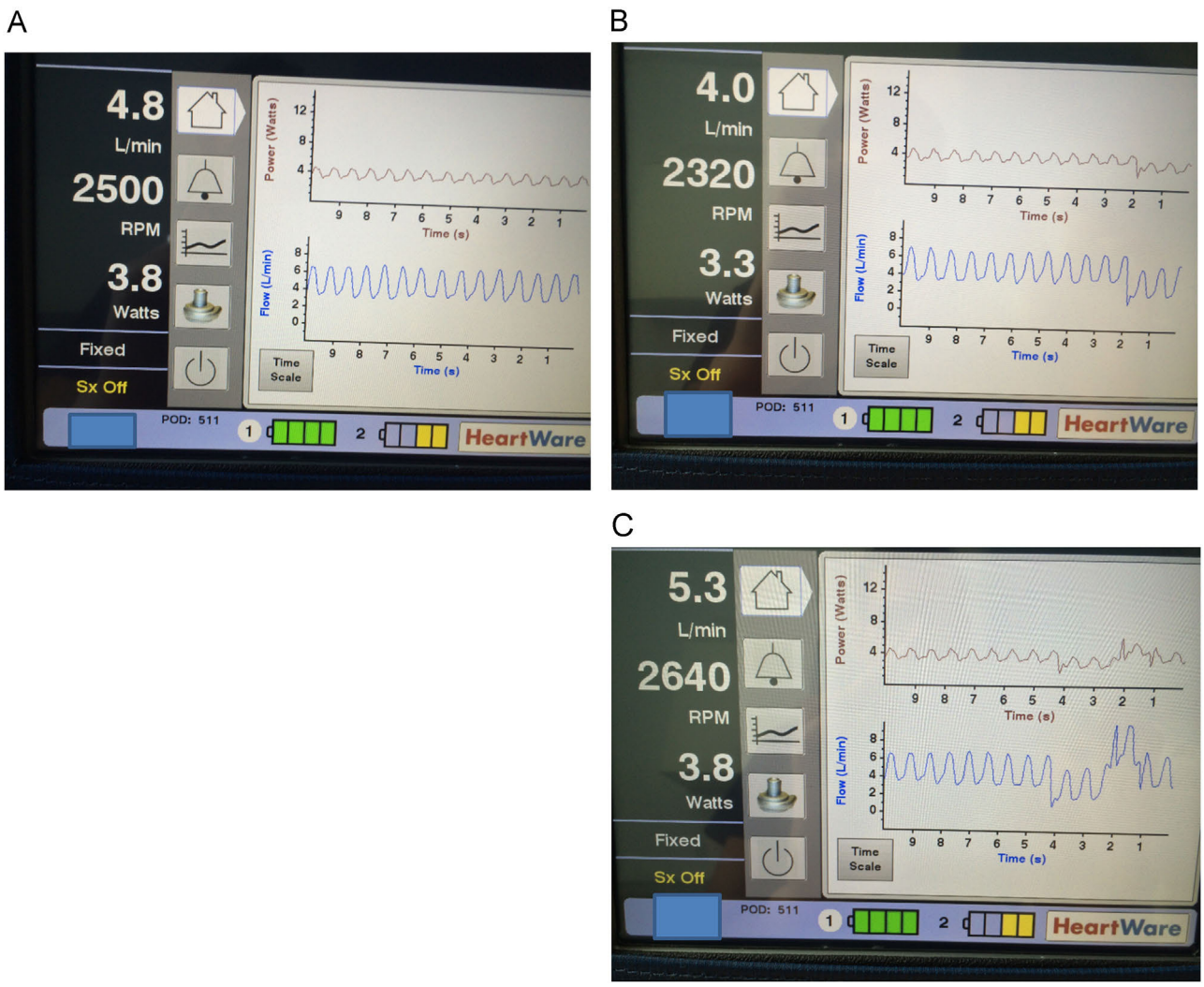

Figure 2 (A) Baseline pump power and flow; (B) Lavare cycle with reduction in pump speed by 180 rpm; (C) Lavare cycle with increase in pump speed by 180 rpm.

Results

We identified a total of 101 HVADs implanted in 96 patients in the aforementioned time period. Five patients had 2 implants each. Twenty patients were excluded due to a follow-up of <6 months. The remaining 71 patients (73 implants) and the corresponding 155 echocardiograms were included for analysis (Figure 3).

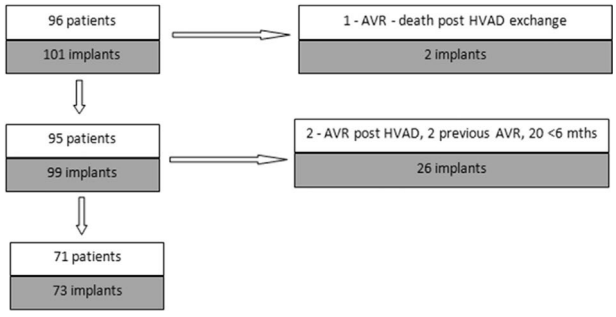

Figure 3 Patient inclusion to the study algorithm.

Demographics

Eighty-five percent of our implants were males, with just over half (53.5%) having heart failure due to dilated cardiomyopathy (DCM). Mean age at implant was 47 years. The LV pre-HVAD was moderately dilated at 6.8 cm in diastole, with a normal-sized aortic annulus and SoV. The mean duration of HVAD support was 1.7 years. Baseline demographic data including HVAD pump speeds are reported in Table 1. Pump speeds were optimized before hospital discharge and rarely changed after implantation. They are reflective of the mean speed at the time of echocardiography.

Development of AI in HVAD patients over the study period: Development of more than mild AI is infrequent

Pre-implant only 3 patients (4.1%) had mild AI. The remainder had no AI. Among the 53 implants who were supported with an HVAD for 1 year, only 1 (1.9%)

Table 1 Baseline Demographics

Patient characteristics ($n = 71$)	
Male (n)	60 (84.5)
Age (years)	47 ± 12.6
Etiology of heart failure	
Dilated cardiomyopathy	38 (53.5)
Ischemic cardiomyopathy	28 (39.4)
Congenital heart disease	4 (5.6)
Other	1 (1.4)
Body mass index (kg/m^2)	26.9 ± 5.3
Mean duration of HVAD support (days)	624 ± 359
Mean HVAD speed (rpm)	2,660 ± 217
LVESD (cm)	6.0 ± 1.1
LVEDD (cm)	6.8 ± 0.9
Aortic annulus (cm)	2.1 ± 0.3
Sinus of Valsalva (cm)	2.9 ± 0.3

Data expressed as number (%) or mean ± SD. HVAD, HeartMate ventricular assist device; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension.

developed moderate AI. For this individual the moderate AI was associated with pulmonary edema. The patient went on to be successfully transplanted on the urgent list. In the group supported beyond 1 year, none developed moderate or worse AI (Table 2).

Patient characteristics and development of AI

The etiology of HF and gender were not related to the development of de novo AI (Tables 3a,b,c).

AI and relationship to valve opening status: AI is more likely to develop in those with a closed or intermittently opening AoV

We then examined the relationship between the AoV opening status at the time of echocardiogram (open, closed or intermittently opening) to the severity of AI. We found that mild or more AI was more likely to occur in those with a closed or intermittently opening AoV (Figure 4). This was statistically significant among those supported to 1 year ($p = 0.005$), but not in the group supported beyond 1 year, although numbers in the subsequent group were small (Tables 3a,b,c).

Changes in aortic root size in those supported to 1 and 2 years: Aortic root size dilates irrespective of extent of AI

The aortic annulus was found to dilate significantly over both time-points (1 year and 2 years) in those with mild or greater AI ($p = 0.05$ and 0.013, respectively) and in those with trace or no AI ($p = 0.006$ and 0.008). In comparison, the SoV was found only to dilate in those supported out to 2 years. This met statistical significance in those with mild or greater AI ($p = 0.002$) and trended toward significance in those without AI ($p = 0.056$), as shown in Tables 4a and 4b.

Changes in LV dimensions in those supported out to 1 and 2 years: LV dimensions decrease only in those without AI

The LVEDD was significantly smaller in patients with no or trace AI. This was found in those supported out to 1 and 2 years ($p = 0.008$ and $p = 0.012$, respectively); however, the same reduction in LVEDD was not seen in those with mild or worse AI. In the group with none or trace AI supported to 1 year, LVESD was significantly smaller compared with baseline ($p = 0.024$). No reduction in the LVESD was found in those with mild or worse AI at either time-point (Tables 4a and 4b).

Discussion

Our center has exclusively implanted the HVAD for continuous-flow support. This has provided us with a large cohort of patients for the study of de novo AI. We have demonstrated in our HVAD population, with a mean duration of device support of 1.7 years, that the development of clinically significant de novo AI is a rare occurrence, and more likely to be found in those with a closed or intermittently opening AoV.

The precise etiology of de novo AI post-LVAD is unknown. Several possible contributing mechanisms have been suggested. After LVAD implantation there is a higher transvalvular gradient across the valve as the LV is decompressed and left ventricular end-diastolic pressure (LVEDP) falls, whereas pressure in the aorta is higher than at pre-implantation. Pathologic studies of the AoV itself have shown degenerative valvular change with leaflet

Table 2 AI in HVAD Patients Over Time, N (%).

			Degree of aortic incompetence							
	Implants	Echo	None	Trace	Mild	Mild to moderate	Moderate	Moderate to severe	Severe	Unable to assess
Pre-implant	73 (100)	73 (100)	50 (68.5)	18 (24.6)	3 (4.1)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2.7)
1 year	53 (100)	48 (90.6)	25 (47.2)	9 (16.9)	12 (22.6)	0 (0)	1 (1.9)	0 (0)	0 (0)	1 (1.9)
2 years	31 (100)	27 (87.1)	12 (38.7)	5 (16.1)	5 (16.1)	3 (9.7)	0 (0)	0 (0)	0 (0)	2 (6.4)
3 years	7 (100)	7 (100)	5 (71)	0 (0)	1 (14)	1 (14)	0 (0)	0 (0)	0 (0)	0 (0)

AI, aortic incompetence; HVAD, HeartMate ventricular assist device.

Table 3a Demographics, Etiology of Heart Failure and Aortic Valve Status in Patients With None or Trace AI Compared to Those With Mild or Worse AI Pre-implant

Pre-implant (implants = 73, echo = 73)	None or trace AI pre-HVAD (%) [median (IQR), mean ± SD], echo = 70 (100%)	Mild or more AI pre- HVAD (%) [median (IQR) or mean ± SD], echo = 3 (100%)	*p*-value
Demographics			
Age (years)	51.5 (39 to 57)	38 (36.5 to 38)	NA
Male gender	61 (87.1)	1 (33.3)	
BMI (kg/m^2)	27.1 ± 5.2	25.2 ± 6.8	
Etiology of HF			
Ischemic	27 (38.6)	1 (33.3)	NA
Dilated	38 (54.3)	1 (33.3)	
Congenital	4 (5.7)	1 (33.3)	
Other	1 (1.5)	0 (0)	
Aortic valve status			NA
Opening	70 (100)	3 (100)	
Intermittent	0 (0)	0 (0)	
Closed	0 (0)	0 (0)	

Due to the small numbers with aortic incompetence (AI), no statistics have been performed. BMI, body mass index; HF, heart failure; HVAD, HeartMate ventricular assist device; IQR, interquartile range; NA, not applicable.

Table 3b Demographics, Etiology of Heart Failure and Aortic Valve Status in Patients With None or Trace AI Compared to Those With Mild or Worse AI in Those With HVAD Support for 1 Year applicable

One year: (implants = 53, echo = 48)	None or trace AI 1 year HVAD support (%) [median (IQR) or mean ± SD], echo = 35 (100%)	Mild or more AI 1-year HVAD support (%) [median (IQR) or mean ± SD], echo = 13 (100%)	*p*-value
Demographics			
Male gender	30 (85.7)	11 (84.6)	0.4
BMI	27.7 ± 4.8	24.1 ± 4.8	**0.05**
Etiology of HF			
Ischemic	15 (42.8)	4 (30.8)	1.0
Dilated	18 (51.4)	8 (61.5)	0.1
Congenital	1 (2.8)	1 (7.7)	1.0
Other	1 (2.8)	0 (0)	NS
Aortic valve status			
Opening	25 (71.4)	4 (30.8)	0.2
Intermittent	3 (8.6)	1 (7.7)	0.2
Closed	7 (2)	8 (61.5)	**0.005**

Bold *p*-values are statistically significant. See Table 3a for other abbreviations.

Table 3c Demographics, Etiology of Heart Failure and Aortic Valve Status in Patients With None or Trace AI Compared to Those With Mild or More AI in Those With HVAD Support for 2 Years

Two years (implants = 31, echo = 27)	None or trace AI 2 years HVAD support (%) [median (IQR) or mean ± SD], echo = 19 (100%)	Mild or more AI 2 years HVAD support (%) [median (IQR) or mean ± SD], echo = 8 (100%)	*p*-value
Demographics			
Male gender	17 (89.5)	6 (75)	1.0
BMI (kg/m^2)	27.2 ± 5.3	28.1 ± 5.4	0.7
Etiology of HF			
Ischemic	9 (47.4)	6 (75)	1.0
Dilated	10 (52.6)	2 (25)	1.0
Congenital	0 (0)	0 (0)	NA
Other	0 (0)	0 (0)	NA
Aortic valve status			
Opening	12 (63.1)	5 (62.5)	1.0
Intermittent	1 (5.2)	1 (12.5)	1.0
Closed	4 (21.1)	2 (25)	1.0

See Table 3a for abbreviations.

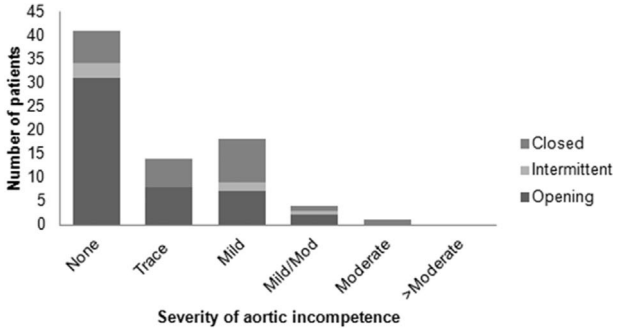

Figure 4 Aortic valve opening status and severity of aortic incompetence (all analyzed echocardiograms at 1, 2 and 3 years combined).

thinning and commissural fusion leading to incompetence.[6] These investigations have also shown thinning of the aortic root at a mean duration of device support of 961 days, but this was predominantly in extracorporeal pulsatile devices. It has also been suggested that excessive aortic root dilation leads to an alteration in geometry and valvular regurgitation.[15] It is currently unclear whether the development of de novo AI in cfLVAD patients affects long-term survival[10,17]; however recently published work has suggested that it does not significantly impact on survival unless there is concomitant right ventricular dysfunction.[18]

Pak et al investigated the prevalence of de novo AI in a cohort of 67 HM-XVE and 63 HMII patients. Their threshold for reporting significant AI was a grade of more than mild to moderate. Their prevalence of AI was 6% for the HM-XVE group and 14% for the HMII group.[15] This was over a comparatively shorter mean duration of device support at <1 year. A second study published in the same year comparing the aforementioned devices reported a high incidence of moderate or worse AI. At 1 year, 26% of the at-risk population had AI, with this increasing to 51% at 18 months.[11] From these reports, it was evident that significant AI was more commonly encountered in patients with a cfLVAD. A later study in a group of predominantly DT HMIIs reported a considerably higher incidence of mild or worse AI at around 6 months of 52%.[10] The most recent data from another UK center showed a 43% incidence of mild or worse AI for the HMII LVAD and a 66% incidence for the HVAD.[13] The investigators did not specify whether the Lavare cycle was enabled in their HVAD group, and the study was not propensity matched for a direct comparison of the two cfLVADs. Instead, the investigators compared variables between those who did and did not develop AI and found that AI was associated with a longer duration of support and AoV closure. They also found a sharp increase in the incidence of AI after 3 years. The numbers at risk in their cohort were 10 patients at 3 years and 3 patients at 4 years with freedom from moderate or worse AI 82.8% and 46.6%, respectively, but they did not detail the type of LVAD in each group.[13] In comparison, 7 patients in our cohort were supported out to 3 years, with none having moderate or worse AI. In comparison, we identified a 1-year incidence of mild or worse AI of 25% in our HVAD population, with a similar incidence in those supported for 2 years of 26%. It is possible that with even longer follow-up of our HVAD cohort the incidence of AI would increase due to the time-dependent nature of de novo AI.

Previous work has shown that individuals are more likely to develop de novo AI with longer periods of device support,[10,11,13–15,19] and with persistent closure of the AoV. In the previously referenced work by Patil et al, 79.2% of patients with mild or worse AI had a permanently closed AoV, as compared with only 28.9% in the non-AI group. These data were not divided according to device type.[13] Aggarwal et al found that 82.9% of their patients with HMIIs, with mild or greater AI, had a closed AoV, compared with 39.5% with a closed valve in those without AI.[10] In another study with a smaller subgroup of 40 patients with both HM-XVE and HMII devices, 26 patients (65%) had a closed AoV, of whom 11 (42.3%) developed AI. AI developed in only 1 of 14 patients with an AoV that opened.[15]

We similarly found that mild or more AI is more likely to occur with a closed or intermittently opening AoV. The AoV opening status is determined by a combination of underlying ventricular function, LVAD speed and transvalvular gradient. With higher LVAD speeds, the left ventricle is fully decompressed by the device and hence very little, if any, blood is ejected through the valve itself. In addition, the continuous nature of blood flow in the aortic root over time may contribute to the valve becoming regurgitant. Our data are unique with all patients having the same device and surgical placement and, although patients were treated as BTT, overall they had a longer-than-anticipated duration of device support. At our institution, all HVAD patients have the Lavare cycle feature enabled. We run our HVADs at low speeds to provide an opportunity for the left ventricle to contribute to cardiac output and the AoV

Table 4a Change in Serial Aortic Root and Left Ventricular Dimensions in Patients Supported With HVAD Out to 1 Year

	None or trace AI ($n = 35$) [median (IQR), mean ± SD]			Mild or more AI ($n = 13$) (mean ± SD)		
Implants = 53, echo = 48	Pre-implant	1 year	*p*-value	Pre-implant	1 year	*p*-value
Aortic annulus (mm)	20 (20 to 22)	22 (21 to 24)	**0.006**	20.0 ± 2.8	22.6 ± 3.0	**0.05**
SoV (mm)	29.1 ± 3.0	28.9 ± 3.0	0.814	29.1 ± 2.3	30.1 ± 3.9	0.5
LVEDD (mm)	67.7 ± 9.6	60.2 ± 13.4	**0.012**	67.5 ± 10.5	64.1 ± 10.8	0.42
LVESD (mm)	60.0 ± 10.6	52.6 ± 14.3	**0.024**	60.3 ± 11.8	58.8 ± 13.0	0.79

Bold *p*-values are statistically significant. LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; SoV, sinus of Valsava.

Table 4b Change in Serial Aortic Root and Left Ventricular Dimensions in Patients Supported With HVAD Out to 2 Years

Implants = 31, echo = 27	None or trace AI ($n = 19$) [median (IQR) or mean ± SD]				Mild or more AI ($n = 8$) [mean ± SD (mm) or median (IQR)]			
	Pre-implant	1 year	2 years	*p*-value	Pre-implant	1 year	2 years	*p*-value
Aortic annulus (mm)	20.7 ± 2.9	22.7 ± 2.2	23.1 ± 3.0	**0.008**	20.3 ± 3.2	21.8 ± 3.1	23.1 ± 2.6	**0.013**
SoV (mm)	29.9 ± 3.6	30.5 ± 2.9	31.3 ± 3.7	0.056	29 ± 2.3	28.8 ± 5.5	31.9 ± 7	**0.002**
LVEDD	67.8 ± 9.0	61.4 ± 12.8	61.7 ± 12.7	**0.008**	65 (57.5 to 73)	59 (56 to 64)	57.5 (55 to 62)	0.96
LVESD	61 (51 to 65)	55 (39.5 to 65.5)	61 (44 to 67.5)	0.94	57 ± 9.9	57.8 ± 8.5	57.3 ± 8.3	0.95

See Table 4a for abbreviations. Bold *p*-values are statistically significant.

to open, without compromising decompression. Nevertheless, there were patients with a closed, or intermittently opening AoV, as shown in Figure 4, perhaps reflecting the severity of underlying LV dysfunction. To our knowledge, the HVAD in the USA does not have the Lavare cycle feature and, although we lack comparative data, the very nature of this in allowing the valve to intermittently open may have been contributory to the lower incidence de novo AI in our cohort. Furthermore, although every European HVAD has this feature available, the decision to enable it is at the discretion of the implanting institution.

Cowger et al showed that increasing aortic sinus diameter is correlated with worsening AI on serial echocardiographic studies.[11] Their work did not provide absolute values for baseline and follow-up dimensions to allow comparisons to be made with our data. Using echocardiography, Pak et al reported a larger baseline aortic root diameter in those who developed AI (3.42 ± 0.43 cm) and at follow-up (3.58 ± 0.54 cm). This difference was not statistically significant. Pathology reports for all 77 hearts explanted during transplant had aortic root circumference data, and in the HMII cohort there was a significantly larger aortic root circumference in those with AI (8.44 ± 1.06 cm) compared to those without AI (7.28 ± 1.02 cm).[15] Our data are similar to those of Patil et al, who showed no significant difference in the aortic root and LVEDD at baseline in patients with or without AI.[13] Their study did not go on to describe serial changes in the aortic root dimension or LVEDD.

It has also suggested that the changes in aortic blood flow after LVAD implantation may be partly responsible for the development of de novo AI.[11] The continuous flow of blood in the ascending aorta directed toward the AoV may play a role.[16] Herein we have shown a statistically relevant dilation of the aortic root irrespective of the presence or absence of AI over a 2-year period. We also found that the annulus dilated earlier than the sinuses. The proximity of the outflow graft insertion point to the aortic root with the constant strain of flow may partially explain these findings. It has been suggested that there may be some link to the position and anastomotic size[20] of the outflow graft in the ascending aorta. An area for further research could address whether changing the position of the insertion point of the outflow graft further away from the aortic root would impact the changing aortic dimensions over time and the development of AI.

With respect to left ventricular chamber dimensions, we found a reduction in LVEDD and LVESD in patients with none or trace AI at 1 year, and LVEDD at 2 years, suggesting adequate LV unloading. This was not seen in the AI group, where LV dimensions were unchanged at both time-points. However, we did not observe an increase in chamber dimensions. Rajagopal et al showed that the LVEDD in their group with moderate or worse AI did not change, in keeping with adequate off-loading despite regurgitation.[19] We acknowledge that LV dimensions are influenced by many variables, including concomitant medical therapy, volume status, remodeling and possible recovery, which were not accounted for.

Although published series to date have shown heterogeneity among centers regarding the reported rates of de novo AI, the overall incidence of de novo AI in our HVAD cohort appears lower. The reasons for this are perhaps multifactorial and may include patient demographics (as all BTT), use of intermittent low-flow software, surgical implantation techniques, and the aggressive medical management of heart failure post-implantation at our center. However, as this area of investigation continues to evolve, we hope to reach a better understanding of the mechanisms involved.

Limitations

This study was non-blinded, single-center, retrospective analysis of echocardiograms in our HVAD population. We are limited in our echocardiographic analysis by the image quality and had low event rates with which to demonstrate change. Our study lacks comparative data from our institution for patients with an alternative cfLVAD, such as the HMII, as we do not implant these devices. We also lack histopathologic information regarding the AoV and root to correspond with our echocardiographic findings.

In conclusion, to our knowledge, this is the largest study to date to examine de novo AI in patients with the HVAD. With longer term HVAD support at our center, the development of mild or worse, or clinically significant, AI is rare and more commonly seen in those with a closed or intermittently opening AoV. Further research and prospective studies are needed to determine whether this may be partly attributable to device settings and whether it has an influence on long-term survival.

Disclosure statement

Stephan Schueler and Neil Wrightson are proctors for the HeartWare VAD. The remaining authors have no conflicts of interest.

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