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Third Annual Report From the ISHLT Mechanically Assisted Circulatory Support Registry: A comparison of centrifugal and axial continuous-flow left ventricular assist devices

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mechanical circulatory support;
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continuous-flow left ventricular assist devices;
axial flow;
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BACKGROUND: The IMACS Registry compiles and analyzes worldwide data from patients undergoing implantation of durable left ventricular assist devices.
METHODS: Data encompassing 16,286 LVAD recipients from 4 collectives and 24 individual hospitals was collected and analyzed. In this 3rd annual report we compare and contrast outcomes, adverse events and risks factors between axial flow and centrifugal flow device recipients.
RESULTS: Significant differences were found in the baseline characteristics of axial vs centrifugal flow LVAD recipients. Survival was similar between pump types. INTERMACS profile 1-3 constitute 85% of implants. A survival gap persists in destination therapy compared to bridge patients. RVAD need and delay impact survival dramatically. Centrifugal flow outperforms axial flow recipients in regards to GI bleeding and freedom from hemocompatibility related adverse events. No significant difference in the actuarial freedom from all strokes or either stroke subtype (hemorrhagic or ischemic) was seen among the two types of pumps. New end points to guide decision making are proposed.
CONCLUSIONS: We demonstrate a transition from axial to centrifugal flow with four-year survival that approximates 60%. A high frequency of adverse events remains an impediment to the wider adoption of these technologies. In the future, composite study endpoints examining life quality and adverse events beyond survival may help in shared decision making prior to MCS implant, and may provide the requisite data to support extension of MCS therapy into the lesser ill heart failure population.
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Since its inception on January 1, 2013, the International Society for Heart and Lung Transplantation (ISHLT) Mechanically Assisted Circulatory Support (IMACS) Registry has sought to collect and analyze data

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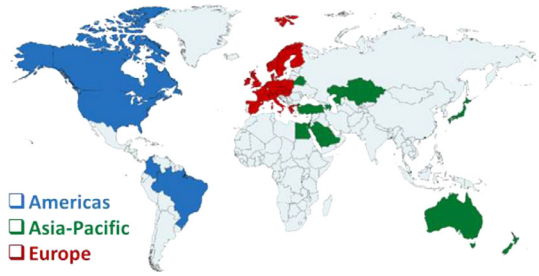


Figure 1 Distribution of countries in (n =35).

globally from patients undergoing durable ventricular assist device implantation with the goal of enhancing knowledge regarding outcomes and adverse events and developing risk models to advance the field worldwide. IMACS is currently comprised of 4 large collectives (Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS], USA; EUROMACS, Europe; JMACS, Japan; and the UK Registry, UK). An additional 24 hospitals provide data directly to the Registry. Uploads from all collectives and hospitals occur yearly and are merged into the Registry for analysis.

To use the worldwide Registry to meet the stated goals, the steering committee has approved regional comparisons of demographics, adverse events, and outcomes as a whole as well as stratified by pump type. This major achievement will provide the unprecedented ability to contrast the MCS experiences worldwide and thereby serve as a platform for new academic exploration, knowledge-sharing, and, possibly, establishment of best practices. To this effect, the world map has been divided into 3 major regions from which investigators will be allowed to use coalesced data for comparisons (Figure 1). Importantly, single-country, single-collective data (i.e., EUROMACS) and specific device brand data (i.e., HeartMate II) will *not* be available for said comparisons.

Patients and pumps

A total of 16,286 individual patients have been entered into the Registry through December 31, 2017, a 15.8% increase since last year's annual report. It should be noted that oversight of the INTERMACS Registry—the major collective contributing to IMACS—transitioned from the National Heart, Lung, and Blood Institute (NHLBI) to the Society for Thoracic Surgeons (STS) on January 1, 2018. INTERMACS data sharing negotiations between ISHLT and STS are ongoing at the time of this writing and, hence, the information included in this report is limited to the NHLBI data set.

Figure 2 depicts the relative distribution of continuous-flow left ventricular assist devices (CF-LVADs)—centrifugal vs axial flow—since the launch of the Registry in 2013. Notably, in 2017, centrifugal-flow pumps overtook axial-flow devices as the predominant choice for durable support. Parenthetically, during these 5 years, 306 patients received a total artificial heart, 815 underwent simultaneous placement of biventricular VADs (BiVADs, defined as durable LVAD plus any device for right VAD [RVAD] at time of index implant), and 28 received an isolated RVAD. Discussion of these alternative pumps and configurations is beyond the scope of this report.

Demographics stratified by pump type are shown in Table 1. Salient and clinically significant differences included older age, more frequent concomitant surgery, more destination therapy as treatment strategy, and less preoperative extracorporeal membrane oxygenation (ECMO) among axial-flow pump recipients. Given the multiple disparities in baseline data between pump types, attribution of advantage or superiority of one device type over another is not warranted.

Figure 3 illustrates the distribution of device strategy by year. Destination therapy remains the most common

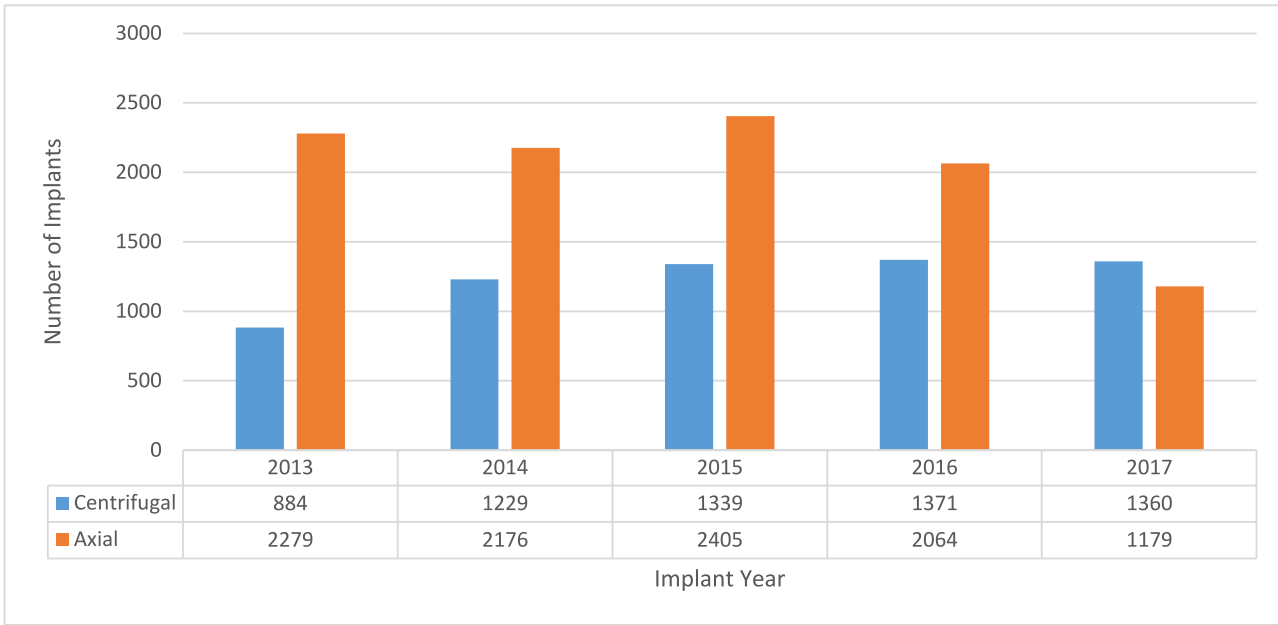


Figure 2 Distribution by year of device type in isolated continuous-flow LVADs. Asterisk indicates that reduction of nearly 900 implants in 2017* is related to the enrollment in the United States of patients into the MOMENTUM 3 continued access protocol.

Table 1 Comparison of Baseline Characteristics Among Isolated CF-VAD Recipients

Baseline characteristics	Centrifugal ($n = 6,183$)	Axial ($n = 10,103$)	p-value
Demographics			
Age (years)	53.4 ±12.6	57.6 ± 13.1	<0.0001
Male (%)	77.8	80.1	0.0007
Blood Type O (%)	45.1	45.1	0.95
Body mass index (kg/m^2)	27 ± 5.8	28.3 ± 6.6	<0.0001
Body surface area (m^2)	2.01 ± 0.3	2.07 ± 0.3	<0.0001
Continent: Europe (%)	26.5	4.4	<0.0001
Continent: Americas (%)	69.2	90.6	<0.0001
Continent: Asia-Pacific (%)	4.3	4.9	0.09
Diabetes (%)	8.7	10.8	<0.0001
Peripheral vascular disease (%)	2.9	4.7	<0.0001
Active smoking (%)	5.2	6	0.02
Ischemic myopathy (%)	39.9	46.9	<0.0001
Idiopathic myopathy (%)	33.6	30	<0.0001
Acute myocardial infarction (%)	7.3	6.8	0.23
Clinical status			
Pre-operative ventilator (%)	13.9	11.7	<0.0001
Pre-operative ECMO (%)	8.3	4.7	<0.0001
Pre-operative IABP (%)	26.8	29.3	0.001
Pre-operative inotropes (%)	78.4	81.9	<0.0001
Pre-operative dialysis (%)	3.4	2.7	0.0084
INTERMACS Profile 1 to 3 (%)	83.8	84.4	0.3
Bridge to transplant (%)	50.3	16.1	<0.0001
Bridge ot candidacy (%)	34	23.4	<0.0001
Destination therapy (%)	13.4	59.9	<0.0001
Laboratory values			
BUN (mg/dl)	32 ± 22	29 ± 17	<0.0001
Creatinine (mg/dl)	1.4 ± 0.7	1.4 ± 0.6	0.41
INR	1.4 ± 0.5	1.3 ± 0.4	<0.0001
AST (U/liter)	40 ± 26	36 ± 23	<0.0001
ALT (U/liter)	40 ± 29	37 ± 27	<0.0001
Sodium (mEq/liter)	135 ± 5	135 ± 5	0.02
Total bilirubin (mg/dl)	1.4 ± 1.1	1.3 ± 1	<0.0001
White blood cell count ($\times 10/\mu l$)	9 ± 5	9 ± 4	<0.0001
Hemodynamics			
Central venous pressure (mm Hg)	11.2 ± 6	10.6 ± 6	<0.0001
Pulmonary wedge pressure (mm Hg)	25 ± 9	25 ± 9	0.45
Cardiac index (liters/min/m^2)	2 ± 0.7	2 ± 0.7	0.36
Pulmonary artery systolic pressure (mm Hg)	50 ± 15	50 ± 15	0.08
Pulmonary artery diastolic pressure (mm Hg)	25 ± 9	25 ± 9	0.0001
Echocardiographic parameters			
LVEF <20% (%)	66	68	<0.0001
Tricuspid regurgitation moderate/severe (%)	42	41	0.12
Mitral regurgitation moderate/severe (%)	57	57	0.68
Aortic regurgitation moderate/severe (%)	3.9	4.8	0.01
Concomitant surgery (%)			
Any concomitant surgery	37	43	<0.0001
CABG	1.3	1.5	0.41
Patent foramen ovale closure	4.7	5.4	0.06
AV repair/replace	4.5	5.6	0.002
Tricuspid valve (TV) repair/replace	3.4	3.6	0.54
Mitral valve (MV) repair/replace	2.1	4.2	<0.0001

ALT, alanine aminotransferase; AST, aspartate aminotransferase; AV, atrioventricular; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; INR, international normalized ratio; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEF, left ventricular ejection fraction; MV, mitral valve; TV, tricuspid valve.

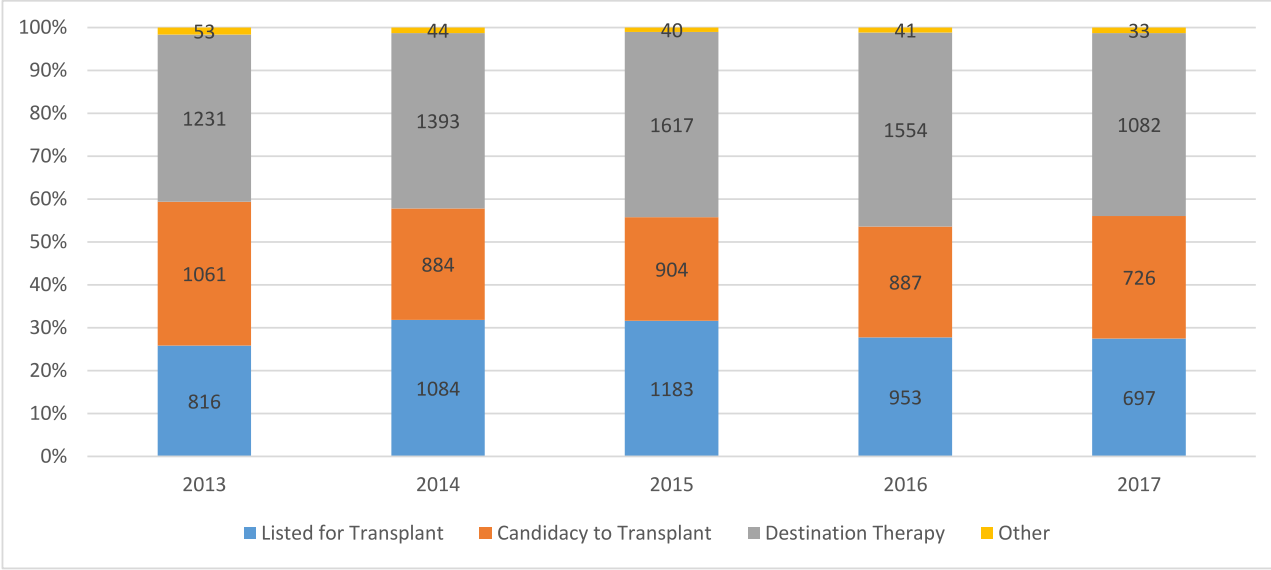


Figure 3 Distribution of device strategy by year in isolated continuous-flow LVADs.

Table 2 Distribution of INTERMACS patient profiles by year of implant

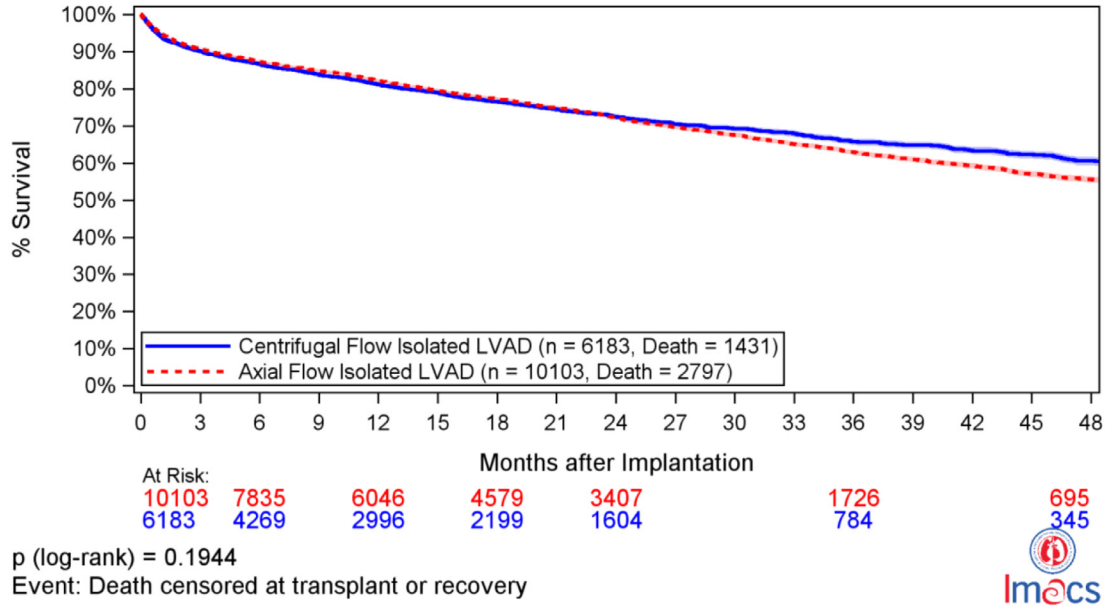
	INTERMACS profile							
Implant year	1	2	3	4	5	6	7	Total
2013	467 (15%)	1,030 (33%)	979 (31%)	523 (17%)	92 (3%)	25 (1%)	24 (1%)	3,140 (100%)
2014	521 (15%)	1,193 (35%)	1,107 (33%)	440 (13%)	86 (3%)	22 (1%)	12 (0%)	3,381 (100%)
2015	605 (16%)	1,240 (33%)	1,334 (36%)	445 (12%)	65 (2%)	18 (0%)	19 (1%)	3,726 (100%)
2016	633 (19%)	1,096 (32%)	1,239 (36%)	371 (11%)	48 (1%)	19 (1%)	15 (0%)	3,421 (100%)
2017[a]	535 (21%)	831 (33%)	823 (33%)	265 (10%)	42 (2%)	18 (1%)	12 (0%)	2,526 (100%)
Total	2,761 (17%)	5,390 (33%)	5,482 (34%)	2,044 (13%)	333 (2%)	102 (1%)	82 (1%)	16,194 (100%)

[a]The marked drop in implants in 2017 compared with previous years likely reflects the enrollment of patients into the continued access protocol of the MOMENTUM 3 trial during this year. These patients received the study device and hence their data were not eligible for inclusion in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)/ISHLT Mechanically Assisted Circulatory Support (IMACS).

strategy, overwhelmingly due to the volumes of device implants in the United States. However, this trend favoring destination therapy has not occurred in Europe or in the Asia-Pacific region (data not shown). Table 2 provides a yearly breakdown of INTERMACS (IM) profile distribution; there has been a gradually increasing proportion of patients in critical cardiogenic shock (IM Profile 1) receiving durable support despite substantial evidence that these patients fare worse.[1,2] Two thirds of patients undergoing CF-LVAD support continue to be IM2 and 3. The share of ambulatory heart failure patients (IM4–7) undergoing LVAD implant has remained modest at <15%, and declined from 22% in 2013 to 13% in 2017. It is important to note that the substantial drop in implant volume in 2017 compared with earlier years likely reflects enrollment of patients into the continued access protocol of the MOMENTUM 3 clinical trial in the United States. These patients all received the study device and, as such, their data were not eligible for collection into the INTERMACS Registry. Approximately 40% of patients undergo a concomitant procedure at the time of index CF-LVAD implant.

Survival analyses and causes of death

The actuarial survival for all 16,286 isolated CF-LVAD recipients stratified by pump type is depicted in Figure 4. No difference in survival was identified between pump types. The survival hazard function demonstrates an early steep decrease in risk followed by a constant hazard at about 0.01 death/month starting at the 6-month time-point (refer to Figure S1 in the Supplementary Material available online at www.jhltonline.org/). Device strategy continues to be a differentiator for survival with the destination therapy cohort faring worse than bridge-to-transplant (BTT) or bridge-to-candidacy (BTC) groups (Figure 5). Another consistent observation has been the worse prognosis associated with IM1 profile compared with less-sick profiles (IM2, IM3, and IM4–7); indeed, over one third of IM1 patients succumb by 2 years. As expected, the curves separate early but become parallel after three months (Figure 6). When IM1 is stratified by pre-implant use of ECMO, a significant decrease in survival is seen among patients requiring ECMO support (see Figure S2 online).



Months after Implant	Centrifugal Flow Isolated LVAD	Axial Flow Isolated LVAD
1	94.1%	94.9%
6	86.6%	87.3%
12	81.1%	82.1%
24	72.4%	72.2%
36	65.8%	62.9%
48	60.5%	55.5%

Figure 4 Survival in centrifugal- or axial-flow isolated LVADs.

Need for RVAD support, whether at the time of index implant or at any time thereafter, is associated with a drastic reduction in survival when compared with isolated CF-LVAD placement. Importantly, survival worsens with increased delay in institution of RVAD support (Figure 7).

Neurologic dysfunction and multisystem organ failure dominate the causes of death, irrespective of pump type, followed next by right heart failure and infection (Table 3).

In an effort to identify factors associated with early and late mortality, 46 variables (demographics, hemodynamics, serological values, and type of concomitant surgery) were used to develop the multivariate risk model (see Table S1). Pre-operative end-organ dysfunction, defined as higher creatinine and higher bilirubin, were the 2 most powerful predictors of early mortality (hazard ratio [HR] 3.67 and 3.27, respectively), whereas higher sodium and higher pulmonary artery diastolic pressure had a protective effect (HR 0.77 and 0.82, respectively). Peripheral vascular disease, older age, and implant in the Americas stood out as highest risk for mortality in the constant phase period (Table 4).

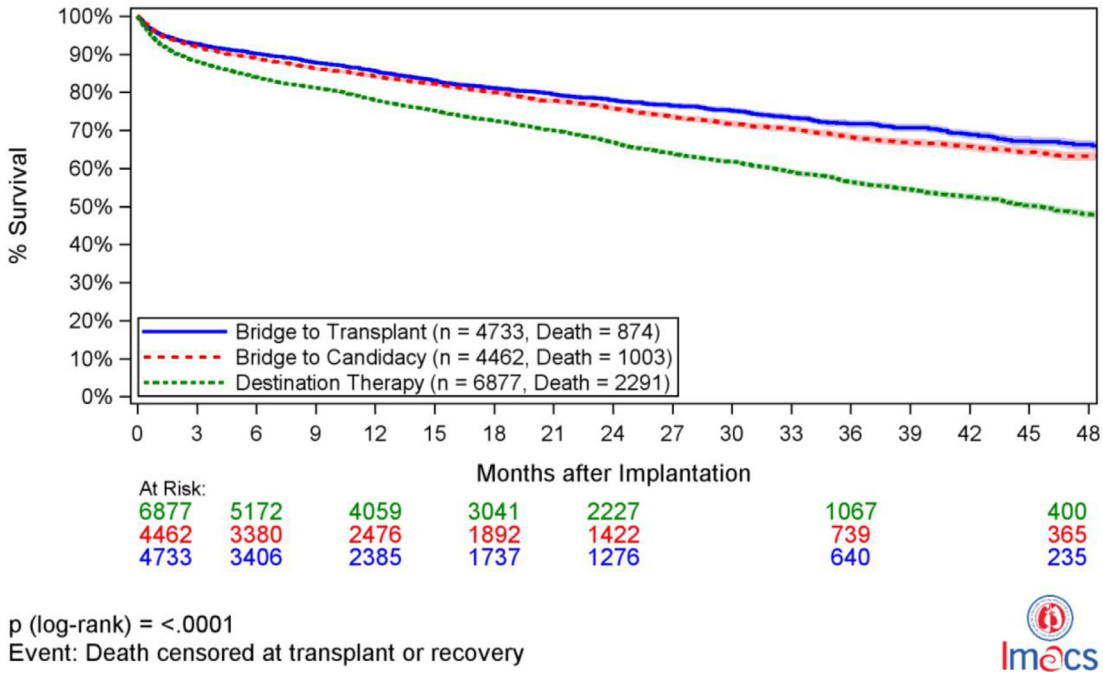
Adverse events

Complications after LVAD implantation continue to limit long-term success of durable MCS therapies. Early and late event rates for 4 key adverse events stratified by pump type are presented in Table 5. In general, these events appear to cluster with greater frequency in the first 3 months and decrease markedly thereafter. Gastrointestinal (GI) bleeding occurs with troubling frequency and is most often seen in axial-flow recipients. Device-specific infections are less prominent, both early and late, in centrifugal-flow pump patients, an observation that may be related to the intrapericardial location of the pump that avoids the large avascular pre-peritoneal pocket required by axial-flow technologies. On the other hand, the incidence of stroke appears to be higher for the centrifugal-flow pump cohort in the early post-operative period but drops and is similar to that seen in axial-flow recipients beyond 3 months.

Actuarial freedom from stroke, GI bleeding, and device-specific infection by pump type are depicted in Figures S3, S4, and S5 online. Freedom from hemorrhagic and ischemic strokes was similar between centrifugal- and axial-flow pump recipients up through 4-year follow-up (Figure 8a and b).

New analyses: Composite end-points

The MOMENTUM 3 clinical trial[3,4] expanded the traditional survival-only analyses that dominate the LVAD literature to include composite end-points to reflect the totality of important events. The primary end-point of the MOMENTUM 3 trial was survival free from a disabling



Months after Implant	Bridge to Transplant	Bridge to Candidacy	Destination Therapy
1	95.6%	95.6%	93.5%
6	90.1%	88.9%	84.0%
12	85.6%	84.1%	77.9%
24	77.9%	75.7%	66.9%
36	71.7%	68.3%	56.5%
48	66.2%	63.2%	47.9%

Figure 5 Survival in isolated CF-LVADs by device strategy.

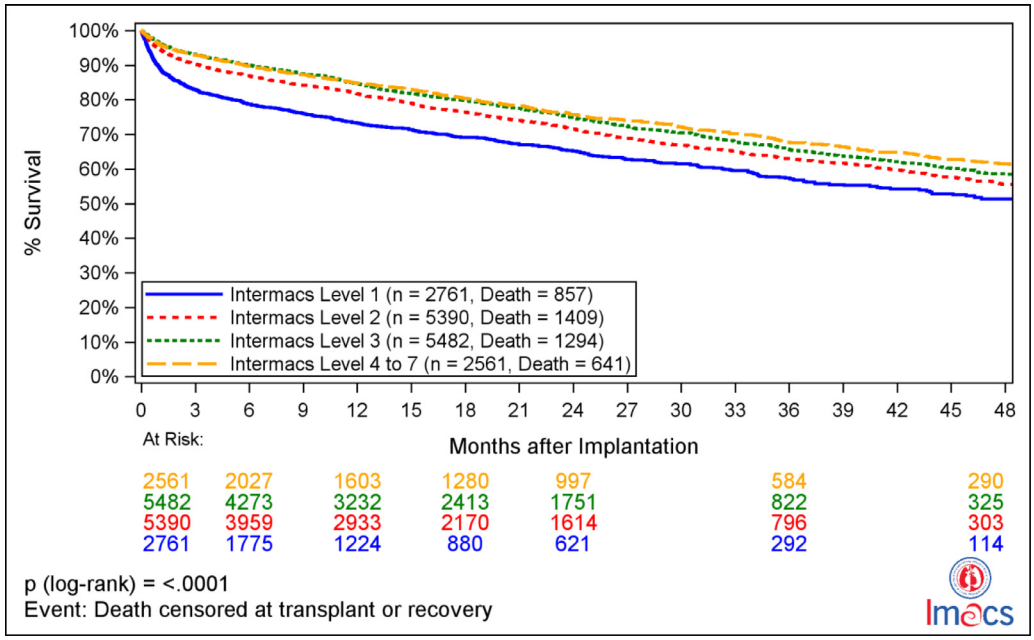
stroke or pump replacement or removal of a malfunctioning pump. Moreover, the recognition that bleeding and thrombotic events constitute the Achilles heel of MCS technologies led to the concept of hemocompatibility-related adverse events (HRAEs). These include stroke, peripheral thrombosis, pump thrombosis, and GI bleeding.[5] Freedom from HRAEs was thus defined as a new composite end-point. In an effort to expand our analyses, we incorporated similar (but retrospectively acquired) composite end-points and introduced 2 new composites designed to capture patient-centered outcomes. The latter may serve as additional information that can be shared with prospective LVAD candidates to aid in their decisionmaking process.

Figure 9 depicts the freedom from death, stroke, or pump exchange/removal, stratified by pump type. Although the curves for axial- and centrifugal-flow pumps are nearly superimposable through 15 months of support, they can be seen to diverge and separate by 4 years, favoring the centrifugal pump cohort (log rank, $p < 0.0001$). Perhaps even more interestingly, centrifugal pumps are associated with a much higher freedom from development of a HRAE, an effect that becomes apparent in the early post-operative period (log rank, $p < 0.0001$; Figure 10).

The first new composite we define as "uneventful implant" and it is described as freedom from death, stroke, bleeding requiring reoperation, RVAD, pump replacement, or device-related infection in the first 90 days post-implant (Figure 11). Nearly 75% of patients undergoing isolated CF-LVAD support in the Registry have met this end-point. The second composite, "living well at 1 year," is defined as freedom from the same adverse events at the 1-year time-point. More than half of the patients undergoing CF-LVAD implantation, according to this arbitrary definition, are living well at 1 year (Figure 12). On both composites, centrifugal devices outperformed axial devices.

Discussion

In this Third Annual Report, we have focused on an outcome analysis of 16,286 patients who underwent isolated CF-LVADs as they represent by far the most common mode and configuration of durable support worldwide. For the first time, we sought to stratify all comparisons by pump type to expand upon the information emanating from industry-sponsored trials.

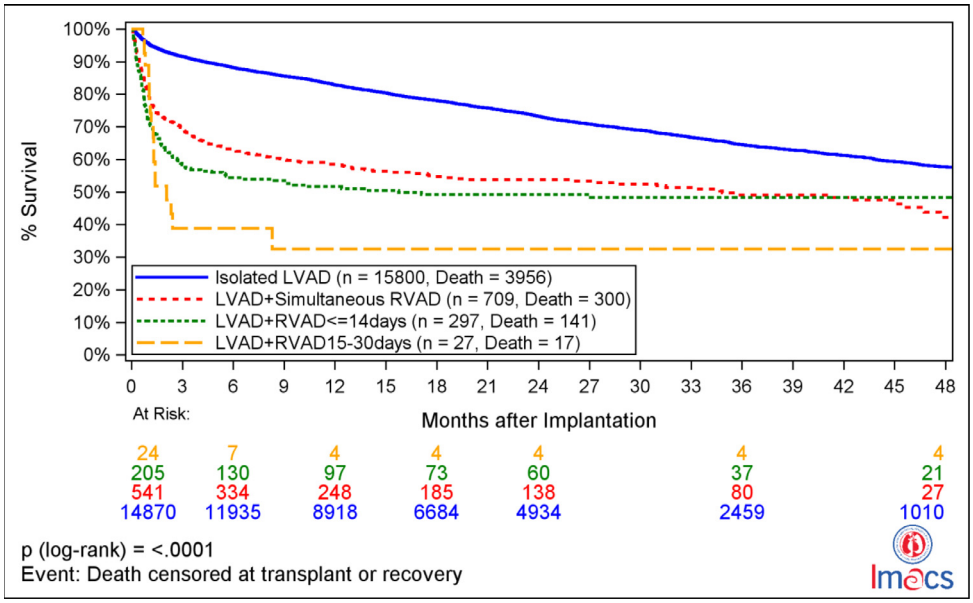


Months after Implant	Intermacs Level 1	Intermacs Level 2	Intermacs Level 3	Intermacs Level 4 to 7
1	89.3%	94.6%	96.5%	96.0%
6	78.8%	86.9%	90.0%	89.7%
12	73.3%	81.7%	84.5%	84.7%
24	65.2%	71.6%	74.8%	75.7%
36	57.3%	63.0%	65.8%	67.8%
48	51.4%	55.6%	58.6%	61.5%

Figure 6 Survival in isolated CF-LVADs by INTERMACS patient profile.

Several important differences exist in the baseline profile of axial and centrifugal pump recipients (Table 1), and thus the following findings must be interpreted with caution:

1. Centrifugal-flow pump implants are now outpacing axial-flow devices. This change is likely to magnify as outcomes from recent trials,[3,6] and growing interest in less invasive approaches favor the former.[7]
2. Nearly 85% of implants are in patients who are IM1–3. This observation suggests that the move to implant these devices in ambulatory heart failure patients still lacks sufficient endorsement by clinicians concerned with the existing burden of adverse events.
3. Survival is similar between axial- and centrifugal-flow device recipients, although, after 2.5 years of support, there is a trend favoring centrifugal devices.
4. The survival gap seen in destination therapy patients compared with BTT patients becomes even more marked over time. This is likely due to the competing risks of a younger population, with less comorbidity and an opportunity for life prolongation through transplantation in the BTT cohort.
5. The lower survival for IM1 patients when compared with less-sick patients is due to early death rates. Beyond 3 months, the curves for all profiles become parallel. Among IM1 patients, those requiring preimplant ECMO support have the worst prognosis.
6. Need and delay for institution of RVAD support markedly compromises survival. The effect is more pronounced with greater delays in institution of support.
7. No significant difference in the actuarial freedom from all strokes or either stroke subtype (hemorrhagic or ischemic) is seen among the 2 types of pumps, although a higher event rate could be seen in the first 3 months among centrifugal pump recipients.
8. Two hemocompatibility-related adverse events, GI bleeding and pump thrombosis, develop more frequently in axial-flow recipients, particularly during the first 3 months of support.
9. Stroke and multisystem organ failure are the most common causes of death, irrespective of pump type.
10. New composite end-points can be used to further characterize patient outcomes and may aid in the decision-making process facing prospective LVAD recipients.



Months after Implant	Isolated LVAD	LVAD+ Simultaneous RVAD	LVAD+RVAD<=14 days	LVAD+RVAD15-30days
1	95.5%	79.9%	71.4%	88.9%
6	88.2%	63.3%	54.4%	38.9%
12	82.9%	58.5%	51.6%	32.4%
24	73.2%	53.7%	49.2%	32.4%
36	64.5%	49.0%	48.3%	32.4%
48	57.7%	42.2%	48.3%	32.4%

Figure 7 Post–30-day survival in CF-LVADs/BiVADs by timing of RVAD implantation.

Table 3 Distribution of primary cause of death among continuous flow LVAD recipients

Primary cause of death	Axial flow	Centrifugal flow	Overall
Neurologic dysfunction	547 (20%)	274 (19%)	821 (19%)
Multisystem organ failure	470 (17%)	249 (18%)	719 (17%)
Right heart failure	304 (11%)	140 (10%)	444 (11%)
Infection	185 (7%)	161 (11%)	346 (8%)
Circulatory other	186 (7%)	84 (6%)	270 (6%)
Bleeding	70 (3%)	52 (4%)	122 (3%)
Device malfunction	56 (2%)	40 (3%)	96 (2%)
Arrhythmia	67 (2%)	18 (1%)	85 (2%)
Gastrintestinal disorder	37 (1%)	15 (1%)	52 (1%)
Other	711 (25%)	345 (24%)	1056 (25%)
Total	2,797 (100%)	1,431 (100%)	4,228 (100%)

In conclusion, in this Third Annual Report of the IMACS Registry, we have demonstrated a transition from axial to centrifugal flow with 4-year survival that approximates 60% (about 10% lower than transplant survival at 4 years; see https://ishltregistries.org/registries/slides.asp/.). A high frequency of adverse events remains an impediment to the wider adoption of these technologies. In the future, composite study end-points, as introduced here, examining life quality and adverse events beyond survival, may help in shared decisionmaking before MCS implantation, and may provide the requisite data to support extension of MCS therapy into the less-sick heart failure population.

Disclosure statement

D.G. is the national primary investigator for the MOMENTUM 3 clinical trial, and has received travel expenses to PI meetings. He has also served as a surgical proctor and educator for Abbott, Inc., and aa a consultant for Terumo, Inc. J.C. has served as a consultant and has

Table 4 Baseline risk factors identified by multivariate hazard modelling as predictive of death

	Early		Constant	
Variable	Hazard ratio	*p*-value	Hazard ratio	*p*-value
Demographics				
Age (by 10-year increase)	1.5	<0.0001	1.23	<0.0001
Female	1.37	0.0001		
BMI (increase by 5 units)	1.11	0.0008	1.05	0.0053
Not blood Type O			1.15	0.0007
Europe	2.3	<0.0001		
Americas			1.71	<0.0001
Active smoking			1.21	0.017
Peripheral vascular disease			1.28	0.002
Ischemic etiology			1.15	0.0011
Concomitant surgery	1.39	<0.0001		
Clinical status				
Ventilator support	1.42	0.0003		
ECMO	1.83	<0.0001		
IABP			1.18	0.0002
Dialysis	2.27	<0.0001		
INTERMACS 1 to 3			1.17	0.0026
Destination therapy	1.29	0.0009	1.14	0.0032
Laboratory values				
Creatinine (per 1-mg/dl increase)	3.67	0.0034	1.13	0.0009
BUN (per 25-mg/dl increase)			1.16	<0.0001
AST (per 10-U/L increase)	1.08	<0.0001		
Sodium (per 10-mEq/liter increase)	0.77	0.0002		
White blood cell count (per 100-μl increase)	1.32	<0.0001		
Total bilirubin (per 1-mg/dl increase)	3.27	<0.0001		
Hemodynamics				
Central venous pressure (per 10-mm Hg increase)	1.59	<0.0001		
Pulmonary diastolic pressure (per 10-mm Hg increase)	0.82	<0.0001		
Echocardiographic parameters				
Tricuspid regurgitation moderate/severe	1.41	<0.0001		

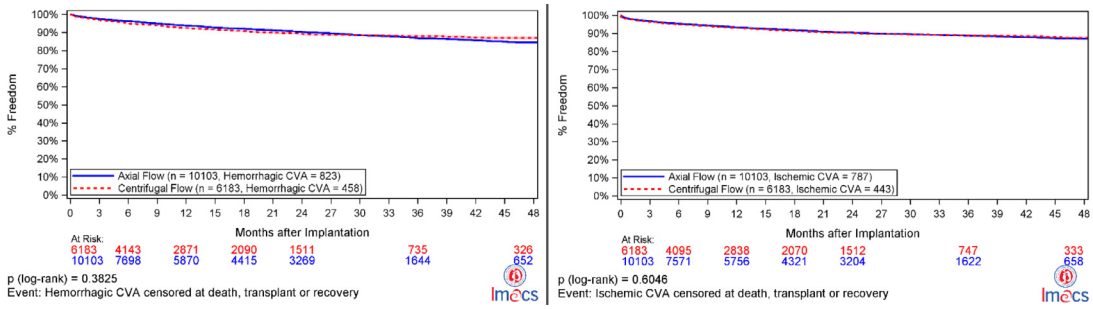
AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

Table 5 Early and late event rates for key averse events following LVAD implant

	Early (≤3 months) event rate (per 100 patient-months)				Late (>3 months) event rate (per 100 patient-months)			
Adverse event	Overall	Axial	Centrifugal	*p*-value	Overall	Axial	Centrifugal	*p*-value
All strokes	2.6	2.45	2.83	0.01	0.75	0.73	0.79	0.1
Device-related infection	2.1	2.27	1.8	<0.01	1.41	1.45	1.33	0.01
GI bleeding	6.18	7.35	4.12	<0.0001	1.95	2.32	1.19	<0.0001
Pump thrombosis	1.99	2.37	1.35	<0.0001	0.69	0.78	0.5	<0.0001

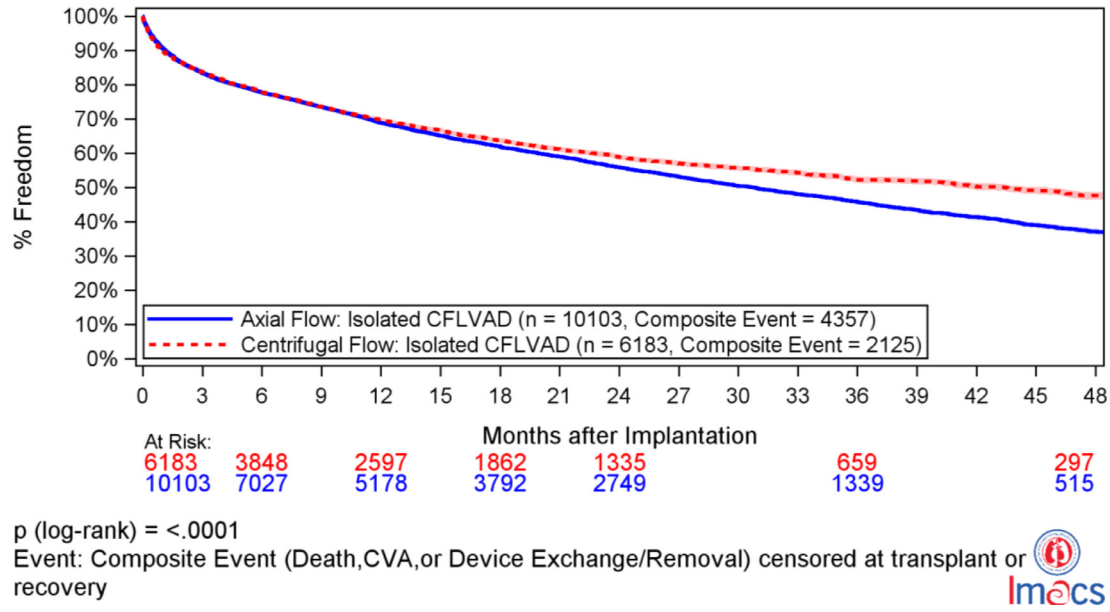
GI, gastrointestinal.

received institutional clinical trial support and paid speaker fees for Abbott and Medtronic, Inc. She has also served on the steering committee for Procyrion, Inc. (unpaid). S.P. has received support for educational activities from Abbott. I.N. has served as a consultant for



Months after Implant	Hemorrhagic CVA		Ischemic CVA	
	Axial Flow	Centrifugal Flow	Axial Flow	Centrifugal Flow
1	98.8%	98.5%	97.9%	97.8%
6	96.2%	95.1%	95.4%	94.9%
12	93.8%	92.5%	93.2%	93.0%
24	90.3%	89.2%	90.4%	90.2%
36	86.9%	87.9%	88.7%	88.9%
48	84.5%	86.9%	87.0%	87.4%

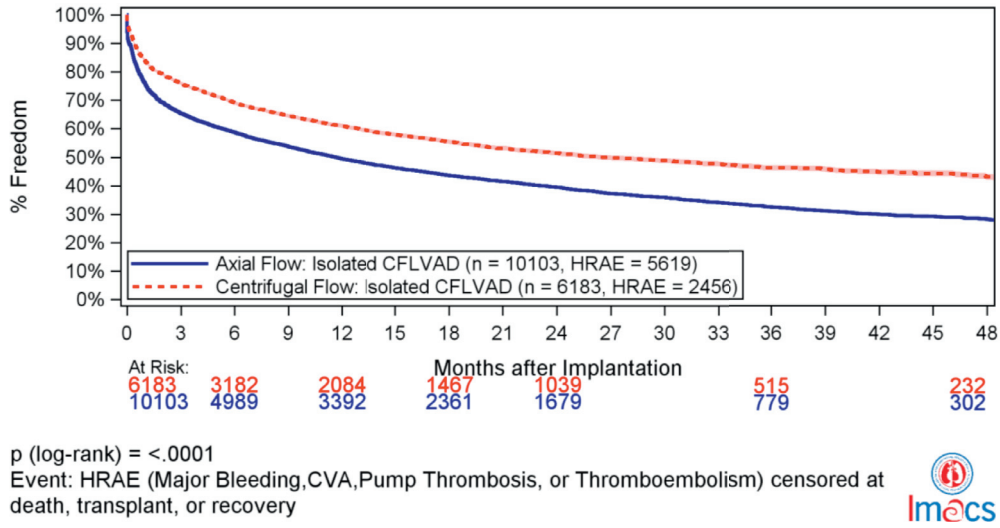
Figure 8 Freedom from first hemorrhagic cerebrovascular accident (CVA) (a) or first ischemic CVA (b) in isolated CF-VADs by pump type.



Months after Implant	Axial Flow: Isolated CFLVAD	Centrifugal Flow: Isolated CFLVAD
1	90.7%	89.9%
6	77.8%	77.9%
12	68.8%	69.7%
24	55.9%	58.9%
36	45.9%	52.3%
48	37.1%	47.6%

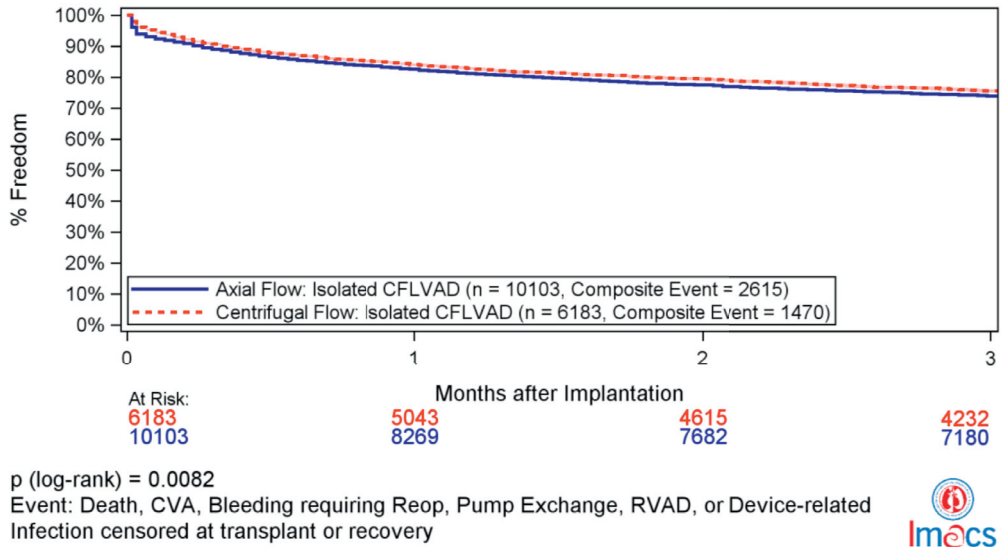
Figure 9 Freedom from first composite event (death, CVA, or device exchange/removal) in isolated CF-VADs by pump type.

Abbott and has received institutional grant funding and served on the advisory board for Carmat SA. He is the principal investigator for the CE Mark Study. In addition, he is a board member for LeviticusCardio, Ltd., and is also a stockholder of the company. S.S. has served as a consultant and paid speaker for Abbott. J.K.K. is director of the IMACS Data Coordinating Center. The remaining authors have no conflicts of interest to disclose.



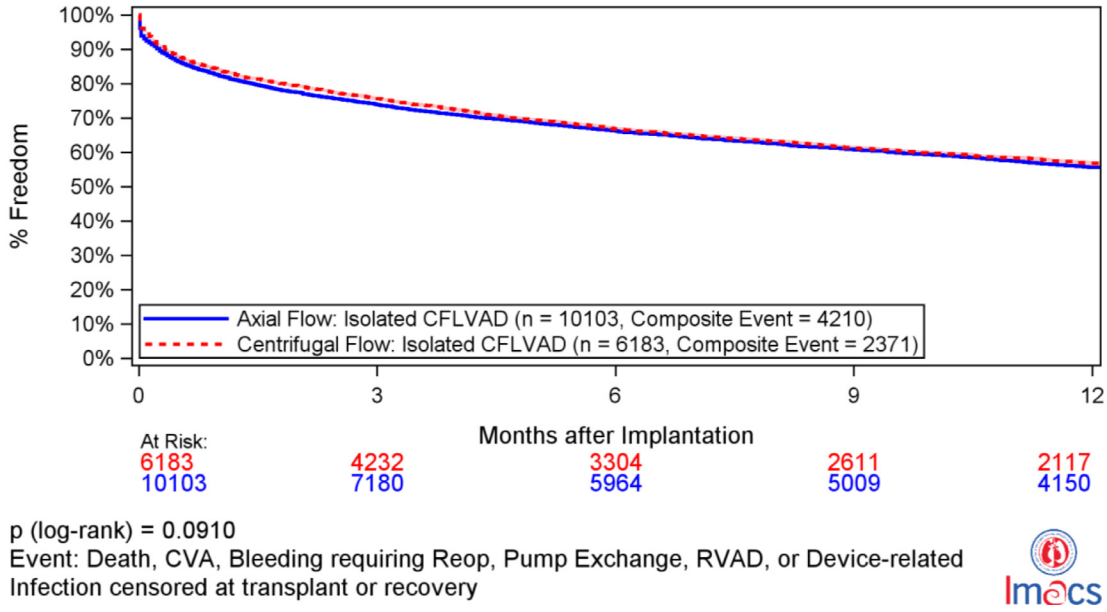
Months after Implant	Axial Flow: Isolated CFLVAD	Centrifugal Flow: Isolated CFLVAD
1	75.9%	83.8%
6	58.7%	69.1%
12	49.4%	61.0%
24	39.4%	51.4%
36	32.5%	46.3%
48	28.2%	43.0%

Figure 10 Freedom from first hemocompatibility-related adverse event (HRAE: major bleeding, CVA, pump thrombosis, or thromboembolism) in isolated CF-LVADs by pump type.



Months after Implant	Axial Flow: Isolated CFLVAD	Centrifugal Flow: Isolated CFLVAD
1	82.6%	84.0%
3	73.9%	75.6%

Figure 11 "Uneventful implant": Freedom from first composite event (death, CVA, bleeding requiring reoperation, pump exchange, RVAD, or device-related infection) within first 3 months in isolated CF-LVADs by pump type.



Months after Implant	Axial Flow: Isolated CFLVAD	Centrifugal Flow: Isolated CFLVAD
1	82.6%	84.0%
3	73.9%	75.6%
6	66.2%	66.8%
9	60.8%	61.2%
12	55.7%	56.8%

Figure 12 "Living well at 1 year": Freedom from first composite event (death, CVA, bleeding requiring reoperation, pump exchange, RVAD, or device-related infection) within first year in isolated CF-LVADs by pump type.

Supplementary data

Supplementary data associated with this article can be found in the online version at www.jhltonline.org/.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.healun.2019.02.004.

References

1. Kirklin JK, Pagani FD, Kormos RL, et al. Eighth annual INTERMACS report: special focus on framing the impact of adverse events. J Heart Lung Transplant 2017;36:1080-6.
2. Kirklin JK, Xie R, Cowger J, et al. Second annual report from the ISHLT mechanically Assisted Circulatory Support Registry. J Heart Lung Transplant 2018;37:685-91.
3. Mehra M, Naka Y, Uriel N, et al. A fully magnetically levitated circulatory pump for advanced heart failure. N Engl J Med 2017;376:440-50.
4. Mehra M, Goldstein DJ, Uriel N, et al. Two-year outcomes with a magnetically levitated cardiac pump in heart failure. N Engl J Med 2018;378:1386-95.
5. Uriel N, Colombo PC, Cleveland JC, et al. Hemocompatibility-related outcomes in the MOMENTUM 3 trial at 6 months: a randomized controlled study of a fully magnetically levitated pump in advanced heart failure. Circulation 2017;135:2003-12.
6. Milano CA, Rogers JG, Tatooles AJ, et al. HVAD: the ENDURANCE Supplemental Trial. JACC Heart Fail 2018;6:792-802.
7. Maltais S, Anwer LA, Tchantchaleishvili V, et al. Left lateral thoracotomy for centrifugal continuous flow left ventricular assist device placement: an analysis from the mechanical circulatory support research network. ASAIO J 2018;64:715-20.