



Review

What Did We Learn About VADs in 2014?

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The field of mechanical circulatory support is evolving rapidly and new data are published at a rate that can be overwhelming. In this review, we summarized some of the publications from 2014 that we think are particularly important. We have also included a few selected papers from the end of 2013 and the very beginning of 2015. Some of this overlap reflects the inevitable delay between online and paper publications.

Readers who wish to supplement this review or argue with the author's statements are encouraged to do so on our Facebook page at <https://www.facebook.com/TheVADJournal>.

Outcomes

The sixth annual report of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) presented data for 10,000 patients on long term ventricular assist devices (VADs). Actuarial survival on continuous-flow pumps is 80% at 1 year and 70% at 2 years. A total of 141 centers are approved for destination therapy implants (1).

McIlvennan et al. (2) reviewed the data systematically and summarized the data from clinical trials and registries that relate to outcomes on continuous flow LVADs (Figure 1).



Table 1. Estimated Actuarial Survival of CF Left Ventricular Assist Device: All Trial and Registry Data With >100 Patients With CF*

Study	First Author	Year	Total CF	BTT	DT	1 mo	6 mo	12 mo	24 mo	36 mo	48 mo
Industry-Funded Trials and Related Registries											
HMII BTT Trial ¹⁰	Miller	2007	133	133	0	89%	75%	68%
HMII BTT Trial Registry ¹¹	Pagani	2009	281	281	0	92%	82%	73%
HMII DT Trial ¹²	Slaughter	2009	133	0	133	68%	58%
ADVANCE: HVAD BTT Trial ¹³	Aaronson	2012	140	140	0	99%	94%	86%
ADVANCE: HVAD BTT Trial CAP ¹⁴	Slaughter	2013	332	332	0	97%	91%	...	84%
Multicenter Registries											
INCOR Analysis ¹⁵	Schmid	2008	216	56%	43%
64 European Institutions ^{16†}	Lahpor	2010	411	300	86	...	74%	72%
University of Minnesota, Pittsburgh, and Columbia ¹⁷	Boyle	2011	101	86	15	77%
John INTERMACS ¹⁸	John	2011	1496	1496	0	...	89%	85%
INTERMACS 2013 ¹⁹	Kirklin	2013	5436	3742	1694	95%	...	80%	70%	59%	47%
INTERMACS Thrombosis ⁷	Kirklin	2014	6910	95%	87%	80%	69%	58%	46%

BTT indicates bridge to transplant; CAP, continued access protocol; CF, continuous-flow; DT, destination therapy; HMII, HeartMate II; HVAD, HeartWare ventricular assist device; INCOR, INCOR left ventricular assist device; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; and LVAD, left ventricular assist device.

*See Data Supplement for all single-center studies or those with <100 continuous-flow patients.

†Study includes alternative indications for implant (eg, bridge to decision, bridge to candidacy).

Fig 1. Estimated Actuarial Survival of continuous flow LVAD; reproduced from McIlvennan et al. (2), with permission

Interestingly, mortality in LVAD patients is improving but morbidity remains approximately the same. Khazanie et al. (3) analyzed outcomes between 2006 and 2011 for patients who received LVADs and who were Medicare beneficiaries. They concluded that short and long term mortality decreased while the admission rate remained stable at about 80%. Unlike mortality, admission rate did not depend on the number of implants performed by the center. We look forward to seeing the data from 2011 onwards as we predict that morbidity will drop as centers gain experience in post-LVAD care.

Good outcomes with LVAD implantation in uninsured patients in the USA were reported by Rajagopalan et al.(4). This study analyzed patients from our institution. Almost all of them benefited from a device.

Outcomes for specific devices were also reported in 2014. Data from the post-market Registry to Evaluate the HeartWare Left Ventricular Assist System (ReVOLVE) confirmed excellent outcomes in 254 commercial implants with a mean duration of support of 363 ± 280 days (median 299.5 days). The survival was 87% at 6 months, 85% at 1 year, 79% at 2 years and 73% at 3 years (5).

Bernhardt et al. (6) shared European experience with HeartWare (HeartWare Inc., Framingham, MA) for isolated right ventricular (RV) dysfunction with preserved left ventricular (LV) function. There were a total of 8 such patients in the EUROMACS registry, all with acute RV failure due to acute myocardial



infarction, failure to wean from cardiopulmonary bypass, or post-cardiotomy syndrome. Although only 3 patients survived to either heart transplant or recovery, most programs lack experience with these types of patients, so the data are very valuable.

Short term hemodynamic support

To our knowledge, Stretch et al. (7) presented the first data quantifying the impact on outcomes of short-term hemodynamic support. In adult patients, who received receiving short-term mechanical circulatory support (MCS) in the United States from 2004 to 2011, use of percutaneous devices (Tandem-Heart and Impella) for short-term MCS increased by 1,511% compared with a 101% increase in non-percutaneous devices (Centrimag and some older devices). Intra-aortic balloon pump and ECMO were excluded from the analyses. The most rapid growth started in 2008. Mortality rates in patients on short-term support declined from 41.1% in 2004 to 2007 to 33.4% in 2008 to 2011 (p for trend = 0.027). Mortality in cardiogenic shock decreased from 51.6% to 43.1% (p for trend = 0.012). Hospital costs also declined (p for trend = 0.011).

Candidate Selection

Several papers in 2014 focused on candidate selection and presented valuable data relating to indications and contraindications/precautions.

RV failure

An analysis of INTERMACS data showed that more than 70% of patients with chemotherapy (anthracycline) induced cardiomyopathy are female. These individuals required more right ventricular assist device support than patients with non-ischemic and ischemic cardiomyopathy (19% vs. 11% versus 6%, $p=0.006$) (8).

Obesity

An article by Chaudhry et al. (9) showed that LVADs can be implanted in very obese patients, who can subsequently undergo a weight reduction surgery. Six morbidly obese patients (body mass index 47.6 ± 3.0 kg m⁻²), half of them already on LVAD support, underwent laparoscopic sleeve gastrectomy. One of the three LVAD patients developed pump thrombosis and required pump exchange. Surgery in the other two patients was uneventful. At median follow-up of 22 months, mean body mass index decreased to 34.3 ± 2.4 kg m⁻². All six patients became transplant candidates.

Frailty

Handgrip strength was reported as an easy to measure variable that predicts outcomes in patients with LVADs. When measured in 72 patients before and after LVAD implantation, grip strength increased by $18.2 \pm 5.6\%$ at 3 months and



by $45.5 \pm 23.9\%$ at 6 months. Patients with a handgrip strength $<25\%$ of body weight had an increased risk of mortality and increased postoperative complications (10). Frailty before destination LVAD implantation was also associated with increased risk of death (11).

Adult congenital disease

One of the most challenging tasks in cardiology is caring for adults with single ventricle physiology. Failure of the systemic morphologic right ventricle is frequently encountered in congenitally corrected transposition of the great arteries or after atrial switch for transposition of the great arteries. Peng et al. (12) reported their experience with 7 such patients (mean age 36 years) who received HeartWare devices.

There were no early deaths within 30 days. The rate of stroke was high at 43% (hemorrhagic and ischemic combined). Overall, 6 of the 7 patients (86%) returned home. More specifically, 3 patients (44%) received a cardiac transplant, 2 patients (28%) died of non-cardiac causes, and the remaining 2 individuals (28%) continued on VAD support for a median length of 232 days. The three patients that received transplants showed an improvement in median transpulmonary gradient (18.5 mm Hg to 8.0 mm Hg) in repeat catheterizations. The authors conclude that LVAD is a reasonable strategy for such patients.

New data from experiments with pigs may also help to advance the treatment of congenital heart defects. A porcine model of Fontan physiology was created by surgically placing catheters from the inferior and superior cava veins to the pulmonary artery. A VAD was then implanted into the common graft to facilitate pulmonary circulation. Arterial pressure and aortic flow, which both decreased dramatically with Fontan physiology, returned to baseline after the VAD implant. Similarly favorable changes occurred within the systemic venous circulation (13). This raises the hope of using VADs as a bridge to transplant in failing Fontans.

LVADs and Co-Morbid Conditions

Arrhythmias

There are still no clear results showing how to manage arrhythmia in patients with LVADs.

Atrial arrhythmia

A particularly interesting study was published by Sean Pinney's group from Mount Sinai, New York. In retrospective review, paroxysmal or persistent atrial fibrillation was present in 51.9% of patients. While paroxysmal atrial fibrillation did not adversely affect outcomes, the persistent form of fibrillation was associated with an increased composite endpoint of death or HF hospitalization (HR: 3.54; 95% CI 1.52 to 8.25; $p < 0.01$). The difference was mainly driven by HF



hospitalizations. These patients also had thromboembolic events at higher international normalized ratios (INRs) (14).

Brisco et al.(15) also showed that atrial arrhythmias in HeartMate trials were associated with lower quality of life and slower functional recovery but did not influence mortality. Unfortunately, the authors did not define atrial arrhythmias in their report and, moreover, analyzed supraventricular arrhythmias separately. We presume that the majority of the patients had atrial fibrillation but there may be alternative explanations.

Ventricular arrhythmia

It is well known that ventricular tachycardia/fibrillation is generally well tolerated in patients with LVADs. To underscore this, a case report published by Naito et al.(16), describes a patient who was supported by an LVAD through incessant ventricular fibrillation, resistant to all anti-arrhythmics, for 18 months.

On the other hand, a study from the Cleveland Clinic demonstrated that cardiac output in patients on LVAD support drops by about 30% during ventricular fibrillation. These tests were performed in the electrophysiology laboratory during defibrillation threshold testing. Cardiac output returns to baseline seconds after successful defibrillation (17). This finding explains why many LVAD patients are symptomatic during ventricular arrhythmias even though they don't die.

Ablation for ventricular tachycardia remains a topic of interest. Garan et al. (18) reported successful ablation of ventricular tachycardia in 6 out of 7 patients with LVADs. In almost half of the patients, the source of tachycardia was located in the apex.

Cardiac resynchronization devices, when compared to implantable defibrillators, did not significantly improve mortality, all-cause hospitalization, LV dimensions, or incidence of arrhythmias in LVAD recipients (19).

LVAD and diabetes

Several reports in 2014 confirmed Uriel et al.'s 2011 discovery (20) that diabetes improves after LVAD. Our own group reported that HbA1C, which was 7.6 ± 1.6 % before LVAD, decreased to 5.7 ± 0.9 % within 3 months of the implant and remained below the pre-LVAD level for at least 12 months. (21). Choudhary et al.(22) also found that fasting blood glucose improved from 136 ± 35 to 108 ± 29 mg dl⁻¹ post-LVAD ($p < 0.001$), and daily insulin dose decreased from 43 ± 37 to 29 ± 24 units ($p = 0.02$). Mohamedali et al.(23) presented similar findings and added that some patients were able to completely discontinue oral hypoglycemics. Subauste et al. also published related data (24).

The mechanisms underlying this phenomenon remain unclear. Koerner et al. measured cortisol and plasma catecholamine levels and found that both decreased after the LVAD implant. (25). This may implicate systemic inflammatory and stress responses. Another possibility is that improved



hemodynamics in the pancreas and/or peripheral tissues increase glucose metabolism. Irrespective of the mechanism, diabetes should not be considered a contraindication to LVAD.

LVAD and valves

An excellent review of valvular problems in LVAD patients was published by the group from Duke (26). The summary table is reproduced below (Figure 2).

Table 2. Current Approaches for Valvular Heart Disease in Patients Supported With LVADs

Pathology	Current Approach
Aortic insufficiency	Correct moderate or greater AI at time of LVAD implantation (if patient deemed appropriate to receive LVAD)* Consider surgical intervention for mild AI Suture closure is preferred method
Aortic valve prostheses	Prefer bioprosthetic valve if replacement undertaken* Cohn sandwich plug technique for previously implanted mechanical prostheses
Mitral insufficiency	Not contraindication to LVAD implantation*† May require surgical repair if anticipation of ventricular recovery†
Mitral stenosis	Mean pressure gradient ≥ 10 mm Hg should be corrected at time of implantation
Mitral valve prostheses	May require higher level of anticoagulation* No need for routine replacement of a properly functioning mechanical valve†
Tricuspid regurgitation	Moderate or greater lesion should prompt consideration for concomitant repair†

AI indicates aortic insufficiency; and LVAD, left ventricular assist device.

*In accordance with *Recommendations for the Use of Mechanical Circulatory Support* from American Heart Association.²⁴

†In accordance with *The 2013 International Society of Heart Lung Transplantation Guidelines for Mechanical Circulatory Support: Executive Summary* (Level C recommendations).¹⁶

Fig 2. Approach to valvular problems in LVADs; reproduced from Wang et al. (26), with permission

Detailed analysis of the clinical data for 382 patients supported by HeartWare devices in the ADVANCE trial demonstrated that concurrent valve surgery during the device implantation resulted in higher postoperative early RV failure but similar one year survival compared with implantation only (27). Valve surgeries were performed in ~20% of patients (56 tricuspid, 13 aortic, and 6 mitral valve procedures). Unoperated severe tricuspid regurgitation was associated with higher odds of late postoperative RV failure.



Analysis of the much larger cohort of 1106 patients who received HeartMate II devices in clinical trials showed similar results. About 20% of patients had concomitant valve procedures and their survival was impacted.

Patients undergoing both LVAD implantation and valvular surgery were older, had higher blood urea nitrogen levels, higher central venous pressure, and decreased right ventricular stroke work index. Their 30-day mortality was higher (10.3% versus 4.8% for LVAD alone, $P = 0.005$). These patients also had higher rates of right heart failure and received more right ventricular assist devices (28).

Tricuspid valve

Extra caution may be appropriate when considering concomitant tricuspid valve repair in tricuspid regurgitation. Robertson et al. (29) analyzed the outcomes for 588 patients from 115 institutions who had moderate to severe tricuspid regurgitation and who underwent tricuspid valve repair when they received their LVAD. The most common procedure was annuloplasty. The authors concluded that tricuspid valve repair was associated with an increased risk of post-operative renal failure, dialysis, reoperation, greater transfusion requirement, longer times on a ventilator and in the intensive care unit, and longer hospital stay. There was no effect on operative mortality or post-operative RVAD requirement. Long term outcomes were not reported in this paper.

On the other hand, some single center studies, such as the one from Henry Ford Hospital, Detroit, MI, saw survival benefit in concomitant tricuspid valve repair (30).

Aortic valve

The Columbia university program summarized their experience with aortic regurgitation in 232 LVAD patients. They repaired the aortic valve in 43 of these individuals at the time of implant. After three years on support, about 40% of patients developed at least moderate aortic regurgitation. This was particularly common if the aortic valve remained closed during LVAD support. Seven of the patients with moderate or severe aortic insufficiency developed symptoms of heart failure, requiring surgical intervention (31).

Interestingly, British investigators found that the incidence of aortic regurgitation was lower in HeartMate II than in HeartWare recipients (43.1% versus 65.7%, $p = 0.035$) (32). Overall, de novo aortic regurgitation after LVAD implant did not affect survival (33).

For the first time, based on the INTERMACS data, it was shown that closure of aortic valve during LVAD implant compromises survival (34).



Innovative approaches to valvular problems, published in 2014, include transcatheter aortic valve replacement for severe aortic regurgitation (35), and transcatheter aortic valve replacement via left ventricular assist device inflow cannula (36).

Resuscitation in LVADs

In a small case series, chest compressions during cardiac arrest in 8 LVAD patients did not result in dislodgement of the cannulae or other device complications (37).

Another group of authors searched existing literature and found 10 other cases of chest compression (longest duration of chest compression was 150 minutes), also without complications. In some cases, neurological function was regained. However, assessment of the efficacy of the compressions was not the objective of either study (38).

Complications of the VADs

Pump thrombosis

Pump thrombosis was, perhaps, the leading topic of the year, with many excellent papers. The discussion was launched in late 2013 when the *New England Journal of Medicine* published the paper by Starling et al. (39) reporting abrupt growth in pump thrombosis (2.2% to 8.4%) between 2011 and 2013. This was observed at the Cleveland Clinic, Duke, and Barnes-Jewish. At the same time, the time from implant to pump thrombosis shortened from 18.6 to 2.7 months. This increase was also apparent in an analysis of data from INTERMACS (40).

Data suggest that increased lactate dehydrogenase (>600 U/mL for HeartMate II and >400 U/mL for Heartware) is the most reliable predictor of pump thrombosis (41), and some centers have adopted the policy of immediate hospitalization based on elevated LDH alone. The best way to treat patients who have elevated LDH but no clinical signs of pump thrombosis is still unclear.

An echocardiographic method of the diagnosis of pump thrombosis was proposed by Estep et al. (42). These authors leveraged the principle that in a normally functioning LVAD, higher pump speed results in reduced LV dimensions, less opening of the aortic valve, and longer filling times (longer mitral E wave deceleration time). Specifically, the authors measured LV end diastolic dimension, aortic valve opening duration, and E wave deceleration time as they increased the revolutions per minute (rpm) from 8000 to 12000 in HeartMate II devices (2 minutes per stage, 1000 rpm increments). Thrombosis was indicated if patients had a less than a 0.6 cm reduction in LV end-diastolic dimension, less than an 86 ms shortening of aortic valve opening, and less than a 73 ms increase mitral E wave deceleration time. Matching one of these criteria predicted pump malfunction (normally due to thrombosis) with 100% sensitivity and 89%



specificity. Matching two parameters increased these values to 100% sensitivity and 95% specificity.

A very innovative method of detecting pump thrombosis was proposed by the Berlin group. They recorded the sound produced by HeartWare devices and noticed that the acoustic spectrum was different if the pump contained a thrombus. Eight pumps were exchanged because of their acoustic signature and thrombi were confirmed in each case (43).

In terms of treatment of pump thrombosis, eptifibatid, once again, appeared to cause more harm than good, with many bleeding events and very modest therapeutic benefits reported (44). A case series with bivalirudin also reported high recurrency rate, with most patients eventually receiving a transplant or pump exchange (45). There was an anecdotal report of good experience with argatroban (46).

Complications were reported when investigators tried to facilitate intermittent opening of the aortic valve by decreasing the LVAD speed. Such practice increased the rate of thromboembolic events (47). This may be because high flow rates dissipate heat from the LVAD more effectively than low flow conditions.

Karimi et al.(48) tested using thrombelastography to adjust antiplatelet therapy in 57 HeartMate II recipients. These patients were followed for about a year. Specifically, the authors adjusted aspirin and dipyridamole to maintain maximum amplitude (a measure of clot strength) between 60 and 70 mm. This allowed aspirin and dipyridamole to be used in lower doses in some patients. The rate of bleeding events was 0.21 per patient-year, which was lower than historic controls collected from the literature. Specifically, in 7 other studies where no tests were used to adjustment of antiplatelet therapy, the rate of bleeding events was 0.49 events per patient-year.

Gastrointestinal bleeding

Much attention was paid in 2014 to the nature of acquired von Willebrand syndrome. It is now widely accepted that the sheer stress produced by a continuous flow pump destroys multimers of von Willebrand factor. The larger multimers capture more platelets and facilitate their adhesion and aggregation. The destruction of the multimers impairs hemostasis and causes bleeding. This year, several papers elucidated on the role of metalloprotease ADAMTS-13, which apparently plays an important role in destruction of this coagulation factor.

In particular, Bartoli et al. (49) used a laboratory vortexer to mimic the effects of an LVAD on von Willebrand factor. Their control experiments showed that the vortexer modestly reduced the concentration of large von Willebrand factor multimers. Adding ADAMTS-13, the von Willebrand factor protease, substantially enhanced the degradation of the large multimers and also increased the concentration of degradation fragments. These effects are similar to those induced by LVADs. Bartoli et al. concluded that sheer stress alone is not enough



to destroy the von Willebrand factor. They also suggested that targeting ADAMTS-13 may preserve the multimers, prevent their cleavage into fragments, and reduce gastrointestinal (GI) bleeding in patients with LVADs.

One potential strategy described by Bartoli et al. is to use tetracycline antibiotics. These drugs inhibit matrix metalloproteinases (such as the ADAMTS protease) and might therefore impact von Willebrand factor degradation. Doxycycline is an example of a tetracycline antibiotic that has been used safely for years (for example, for acne) and that could be tested relatively easily in patients who have LVADs. As an additional benefit, tetracycline might help to prevent driveline infections caused by methicillin-resistant *Staphylococcus aureus*.

Additional manuscripts presented anecdotal evidence that GI bleeding could be controlled with the following medications:

- Danazol (200 mg BID) (50)
- Octreotide (100 mcg SC BID in the hospital and then 20 mg depot IM monthly) (51). Other authors report 50 mcg SQ BID (52).
- Thalidamide (50 mg BID with potential increase to maximum daily dose of 200 mg, reduce to 50 mg QOD if toxicity develops), monitor blood count while up-titrating, try decreasing the dose when therapeutic effect achieved (53,54).

Additional strategies described in 2014 include double balloon enteroscopy. This was reported to provide a high diagnostic yield of 69%, and an even more impressive therapeutic effect of 89 %. These results were achieved using argon plasma coagulation, epinephrine injection, and/or hemoclip placement (55). Hirose et al. (56) suggested initiating work-up for GI bleeding with deep bowel enteroscopy and omitting the usual upper and lower endoscopy and capsule endoscopy because they are low-yield procedures. This approach appeared to reduce the number of procedures and transfusions and also to reduce costs. Unfortunately, not every hospital has the equipment for deep bowel enteroscopy.

Several papers reported that anticoagulation in LVAD patients can be safely reversed. Data from the Henry Ford Hospital program described 38 reversals of anticoagulation in 25 patients using vitamin K at a mean dose of 10 ± 8 mg or fresh frozen plasma. Only one patient had a thromboembolic event within 30 days of reversal (57).

14 of 213 (6.5%) patients at the University of Minnesota had discontinuation of anticoagulation: 10 patients had warfarin discontinued and 4 had both aspirin and warfarin discontinued. Most of these interventions were for GI bleeding. The mean duration off warfarin was 392 days. There was only one pump thrombosis episode, and this occurred in the patient with surgical malpositioning of the LVAD cannula (58).



Infections in LVADs

Several excellent papers were published in 2014 relating to infections. The importance of burying the velour portion of the HeartMate II driveline well under the skin was underscored by Singh et al (59). This technique improved driveline infection-free survival. 44.4% of patients had driveline infections when velour was exposed but the infection rate was only 8.8% when the exposed region was silicone.

Yarboro et al. (60) shared experience from the University of Virginia where the driveline infection rate dropped from 20% to zero. They described, step by step, their approach to driveline care at every stage of LVAD implantation and follow-up.

Kretlow et al.(61) reported the use of antibiotic beads for salvage of LVADs with deep infection in the pocket. 17 of 26 patients with LVAD-related infections were cleared of their infection and many survived. Plastic surgery was often required to cover the device with a flap.

A strong association between LVADs and blood stream infection was described by Trachtenberg et al.(62). Out of 149 patients who received an HMII device, 19 patients (13%) had strokes (7 hemorrhagic and 12 ischemic). During the same period, there were 28 patients (19%) with persistently positive blood cultures and 17 patients (11%) with intermittently positive blood cultures. Only persistently positive blood cultures were associated with an increased risk of mortality and with all cause cerebrovascular accident on multivariate analysis (OR 5.97, P=0.003).

Recovery

Diakos et al. (63) discovered, that, unlike animal models, human hearts do not develop cardiomyocyte atrophy as a result of prolonged mechanical circulatory support. Cardiomyocyte size (cross-sectional area) decreased after LVAD unloading but not beyond that of normal donor hearts. Other approaches that did not show evidence of myocardial atrophy included evaluation of ultrastructure using electron microscopy, analysis of cardiomyocyte glycogen content, and echocardiographic assessment of myocardial mass and left ventricular function. We note that patients were only followed for 6 months in this study and, in our opinion, atrophy could still occur after longer period of support.

Some genetic predisposition to myocardial recovery while on LVAD support was demonstrated by Posch et al.(64). They studied a connective tissue growth factor that is associated with adaptive cardiomyocyte hypertrophy. Homozygosity of the promoter-activating G allele was overrepresented in patients with cardiac recovery (50%) relative to patients who did not recover (17%).



Non-Cardiac Surgery

An interesting survey of current practices was published by Sheu et al. (65). 72% of inpatient endoscopic procedures were performed in the endoscopy suite. Most (59%) procedures were also completed by a solo practitioner with a 1:1 staffing ratio. LVAD coordinators were present for more than 80% of all procedures. Both endoscopy and surgical patients used recovery units and intensive care units for recovery. Patients who had non-cardiac surgery recovered in the intensive care beds more often than those who had endoscopy (45.5% versus 29.1%, $p < 0.001$). 18% of endoscopy patients recovered on site. An arterial line for blood pressure monitoring was inserted in ~50% of the endoscopy patients and in 71% of surgical patients. Institutions with high LVAD volumes used less invasive monitoring.

Imaging in LVADs

Two papers that focus on echocardiographic evaluation of LVAD patients and which we judge to be particularly important were published by Jerry Estep and co-authors. One of the manuscripts discussed using echocardiography to diagnose pump thrombosis (42) and was discussed earlier in this article.

The second article compared invasive and echocardiographic hemodynamic data and found that hemodynamic echo measurements are valid in patients supported by continuous flow LVADs. Good correlations were obtained between invasively measured and non-invasively estimated values for mean right atrial pressure ($r = 0.863$; $p < 0.0001$), systolic pulmonary artery pressure ($r = 0.880$; $p < 0.0001$), right ventricular outflow tract stroke volume ($r = 0.660$; $p < 0.0001$), and pulmonary vascular resistance ($r = 0.643$; $p = 0.001$). Furthermore, the authors proposed an algorithm that was able to distinguish between patients with normal and elevated left ventricular end diastolic pressure with 90% accuracy (Figure 3) (66).

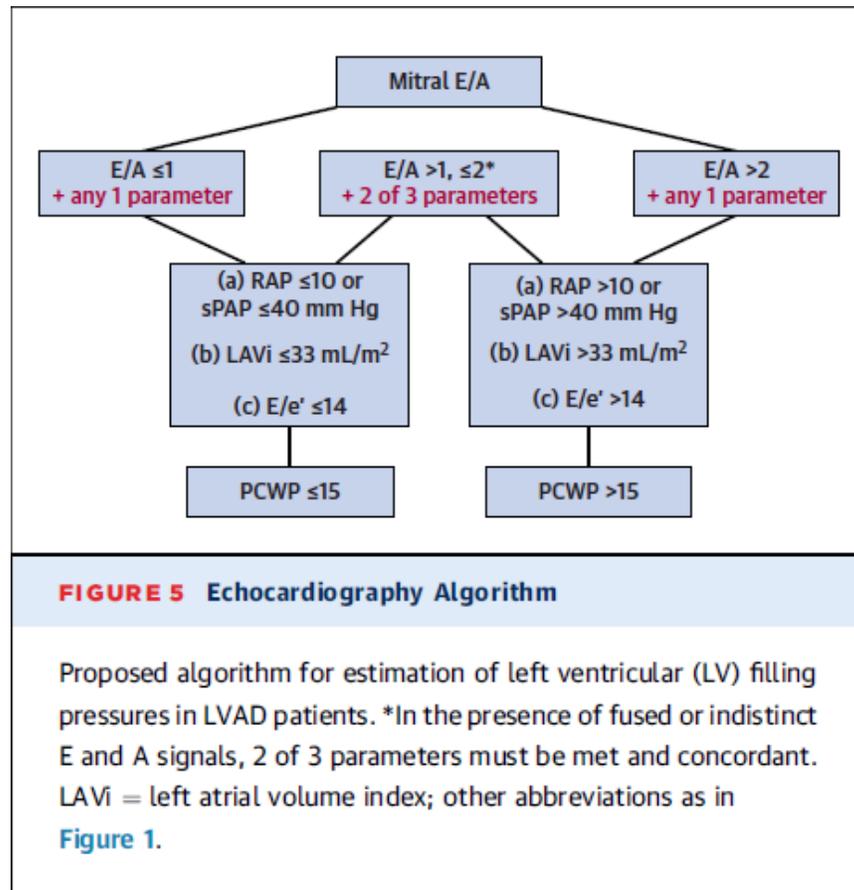


Fig 3. Echocardiography algorithm for estimation of left ventricular filling pressure in LVAD patients; reproduced from Estep et al. (66), with permission

A comprehensive review of echocardiographic assessment of patients who are being considered for LVAD treatment as well as patients who are already on LVAD support was published by Todaro et al (67). We found the following algorithm of assessment of the right ventricle prior to implant very helpful (Figure 4).

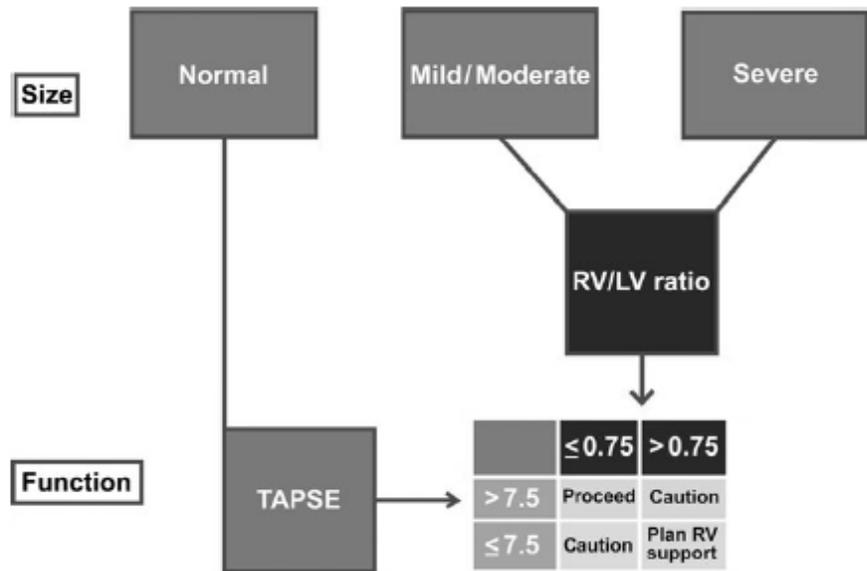


Fig 4. Echocardiographic assessment of the right ventricle before LVAD implantation; reproduced from Todaro et al. (67), with permission

Finally, a nice series of images showing how PET/CT can be used to find the exact location and the extent of LVAD-related infections was published by Kim et al (68).

New Pumps

Several interesting new pumps were introduced or developed further in 2014.

A HeartWare MVAD

A HeartWare MVAD (HeartWare, Miami Lakes, FL) pump (length 50mm, diameter 21 mm; maximum flow 7–8 liters/min) was combined with a novel inflow cannula and tested in sheep with good results (69) (Figure 5).

Impella for RV support

In January of 2015, the FDA approved a percutaneous right-sided Impella PR (right peripheral; Abiomed, Danvers, MA) for 14 days of support for right ventricular failure under a humanitarian device exemption (Figure 6). The approval was based on the results of the RECOVER-RIGHT study which is still, to the best of our knowledge, unpublished. According to clinicaltrials.gov, the goal of this study is to show that using the Impella RP is safe and feasible and that the device provides a hemodynamic benefit in patients with right ventricular failure (<https://clinicaltrials.gov/ct2/show/record/NCT01777607>).

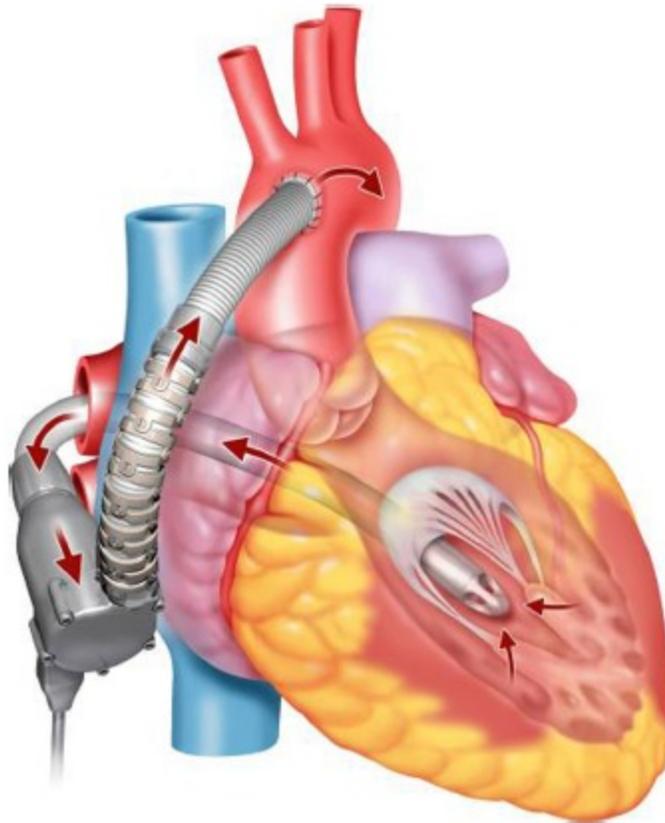


Fig 5. Miniaturized HeartWare LVAD; reproduced from Schima et al. (69), with permission

Data from the trial were presented by William O'Neill at the TCT meeting in 2014. A total of 30 patients were supported with a right-sided Impella, with a 30 day survival of 73%. Patients who developed right ventricular failure after receiving an LVAD had a mean survival of 83.3% while patients with right ventricular failure due to acute myocardial infarction or postcardiotomy syndrome had a mean survival of 58.3% (Abiomed press release at <http://investors.abiomed.com/releasedetail.cfm?ReleaseID=871213>).

Additional positive data were published by Cheung et al.(70) from Vancouver, British Columbia, Canada. They presented a retrospective analysis of 18 patients. All of these individuals were on intravenous inotropes, 39% on inhaled nitric oxide, 39% on intra-aortic balloon counterpulsation, and 11% survived cardiac arrest. Device implantation increased the mean cardiac index from 2.1 to 2.6 L min⁻¹ m² (p=0.04) and reduced central venous pressure from 22 to 15 mm Hg (p < 0.01). 14 of the 18 patients had their Impella device explanted due to recovery. The other 4 patients died on support. Survival to 30 days was 72% and to 1 year was 50%.



Neither of the above studies compared outcomes with Impella support to outcomes without an Impella.

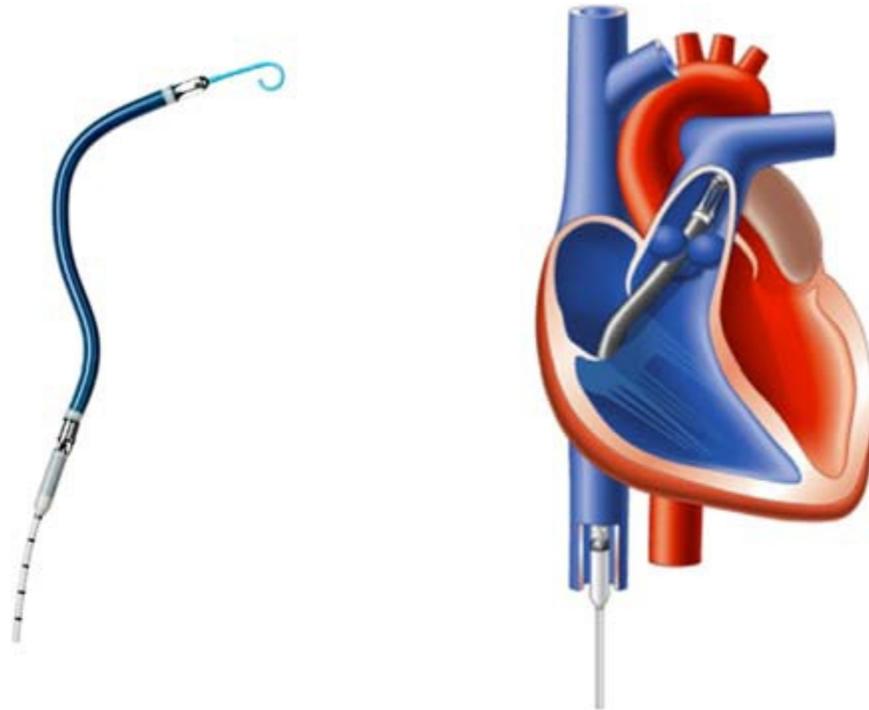


Fig 6. Impella RP (right peripheral); reproduced from Cheung et al. (70), with permission

The Synergy CircuLite for partial support

The Synergy Micro-pump (HeartWare Inc, Framingham, MA) is the smallest implantable LVAD that is currently available and can produce flows of up to 4.25 L min^{-1} . This device was tested in 7 INTERMACS class 1–2 patients and 6 INTERMACS class 3–4 patients. The mean support times for the two groups were 108 ± 114 days and 238 ± 198 days respectively. The overall survival was comparable for the two groups, with one late death in each group, log-rank $p = 0.608$). Two patients from the high-risk group were upgraded to a full-support LVAD after 65 ± 85 days of support with the Synergy Micro-pump. The authors concluded that the pump is a feasible approach even in very high risk patients (71).

Mohite et al. (72) described an algorithm to check for pump thrombosis. Apparently, the Synergy speed fluctuates periodically at 10-second intervals to reduce the probability of thrombosis. If the pulse oximeter waveform was recorded from the index fingers of the left and right hand, patients with normal device function had a more pronounced variation (giant wave) in the trace from the right hand than from the left. These giant waves coincided with the variation in sound detected by auscultation using a stethoscope positioned over the right infra-clavicular pocket.



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