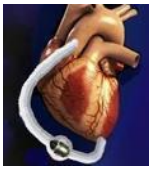

The VAD Journal: *The journal of mechanical assisted circulation and heart failure*

Invited Review

What Did We Learn about VADs in 2015?

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Key words: Left ventricular assist device; heart failure

Introduction

The field of mechanical circulatory support is rapidly evolving and new data are published at a rate that can be overwhelming. Last year, we published a review paper entitled “What Did We Learn about VADs in 2014?” That paper was well received – the full text was downloaded over 350 times by the readers around the globe. Encouraged by this, we wrote the present review, where, like before, we summarized some of the publications from 2015 that we think are particularly important.

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

HeartMate III

Perhaps the biggest news this year was the first clinical information on Heartmate III (HMIII) (St. Jude Medical, Pleasanton, California) which already received the Conformité Européene (CE) Mark approval in Europe for advanced heart failure patients, both as bridge to transplantation or as destination therapy.

The HMIII is an intrapericardial centrifugal-flow pump with a magnetically levitated rotor. This design eliminates the need for mechanical bearings. Because the rotor is “floating”, the gaps through which the blood flows are wide (0.5-1 mm), to minimize both blood stasis and shear stress to the blood. The new features are addressing all the adverse effects of currently used devices, including lack of pulsatility resulting in gastrointestinal bleeding (GIB) and aortic insufficiency, high shear stress leading to hemolysis and acquired von Willebrand syndrome, heat generation prompting pump thrombosis, and the driveline design precluding its replacement in case of damage (Figure 1).

In summary, major novel features of HMIII are (1):

- Intrapericardial position
- Fully magnetically levitated rotor

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- Rotor speed range of 3, 000 to 9,000 revolutions per minute (rpms)
- Maximum flow rate of 10 L/min
- No friction, heat generation, wear and tear
- Wide gaps for the blood flow (blood flow paths) through the device (10-20 times wider than in currently used pumps)
- Pump speed change 30 times per minute to create pulsatility
- External portion of the driveline can be changed without pump exchange
- Texturing of the internal surface with titanium microspheres

These features are designed to achieve following effects:

- Minimization of blood stasis
- Minimization of shear stress to blood
- Development of a pseudo-intima on the inside of the pump to prevent pump thrombosis
- Maximizing of the aortic valve opening

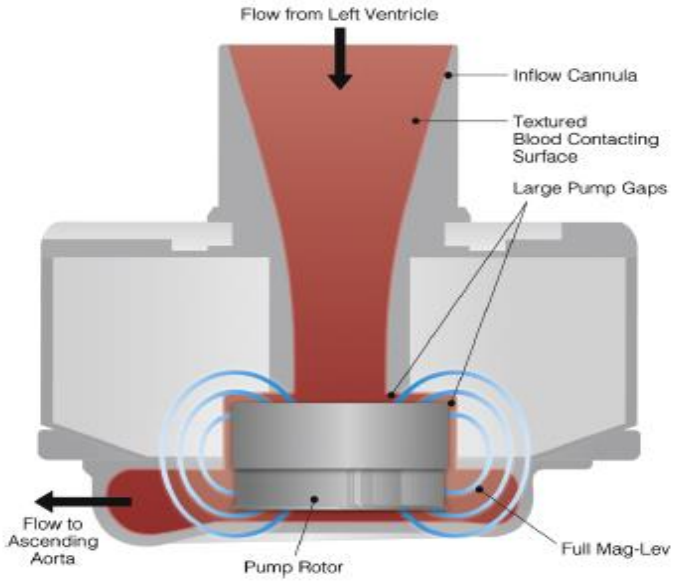


Figure 1 The Heart Mate III left ventricular assist device blood pump with the full magnetically levitated rotor allows large pump gaps. Blood flow is received from the left ventricle and is pumped through a graft attached to the ascending aorta.

Figure 1. HeartMate III

Reproduced from Scmitto et al. (2), with permission

The chest radiograph with HMIII is shown on Figure 2.

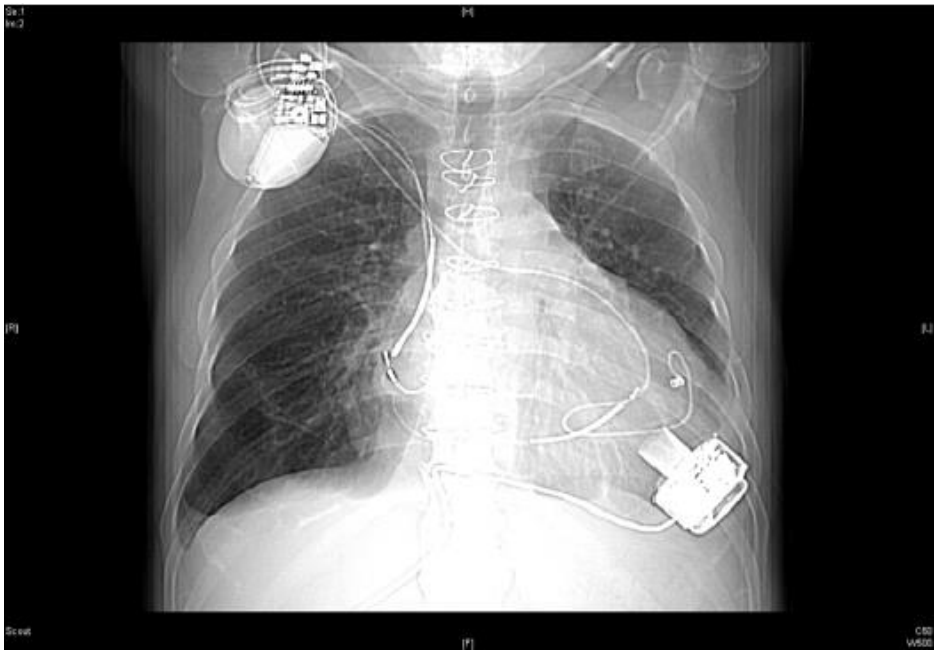


Figure 2. Chest radiograph with HMIII

Reproduced from Scmitto et al. (2), with permission

The single-arm, prospective, multicenter study, designed to evaluate the performance and safety of the HMIII, enrolled 50 patients who received the LVAD as a bridge to transplant or as destination therapy. The primary endpoint was 6-month survival compared with Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).

The 6 month survival was 92%, with 88% of patients continuing on support and 4% transplanted, which exceeded the 88% performance goal. Major adverse events included re-operation for bleeding (14%), driveline infection (10%), gastrointestinal bleeding (8%), and debilitating stroke (8%). There were no pump exchanges, pump malfunctions, pump thrombosis, or hemolysis events. Overall stroke rate was 12% which was higher than expected (3), and infection rate 36% (1).

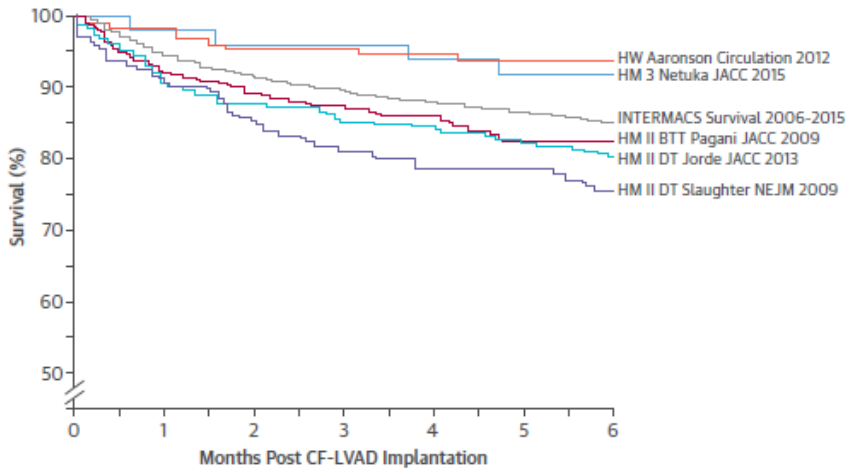
Outcomes

The seventh annual report of the INTERMACS summarized the data on 15,000 patients, up from 10,000 last year, from 158 participating hospitals, and the number of implants of nearly 2,500 a year, roughly half of that as destination therapy. Noteworthy, the freedom from the adverse events is not improving (4). This may mean that the peak benefit that can be obtained from the current

technology, is already achieved, and further improvement should occur with major technological breakthroughs. Hopefully, HMIII is one of them.

Putting the first outcomes with HMIII in the context of other continuous flow devices and the INTERMACS survival rates, the current survival is shown on Figure 3.

FIGURE 1 **Progressive Improvement in Outcomes of Patients Supported With CF-LVADs for Advanced Heart Failure**



Study	Patients	Device	Indication	1 Month Survival	6 Month Survival
Netuka et al. 2015	50	HM 3	BTT + DT	98%	92%
Aaronson et al. 2012	140	HW	BTT	99%	94%
INTERMACS 2006-2015	14,037	HW + HM II	BTT + DT	94%	85%
Pagani et al. 2009	281	HM II	BTT	92%	82%
Jorde et al 2013	247	HM II	DT	90%	80%
Slaughter et al. 2009	133	HM II	DT	91%	75.5%

Figure 3. Progressive improvement in outcomes with LVADs

Reproduced from Uriel et al.(3), with permission

Important information about the outcomes of less sick LVAD candidates on mechanical circulatory support versus medical management was obtained from the ROADMAP (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management). This was a prospective, multicenter observational study of 200 patients (97 LVAD, 103 medical management) who had at least one hospitalization for HF in the last year and walked less than 300 m on 6-min walk, i.e. were functionally limited but not inotrope-dependent. Currently, such patients can be managed medically, but are also eligible for LVAD, depending largely on their own and their doctor's

preferences. According to these preferences, they either underwent an LVAD implant, or continued on medical management. Although LVAD patients were sicker at baseline, the primary endpoint - survival with improvement in 6 minute walk distance by more than 75 m at 12 months – was achieved by 39% patients on LVADs versus 21% on medical management (OR 2.4 p = 0.012). Survival per se was also greater for LVAD versus medical management (80 ± 4% vs. 63 ± 5%; p = 0.022). Even despite more hospitalizations on LVADs, mostly for GI bleedings, quality of life improved greater than in the medical arm. (5).

Basically, this study means, that many INTERMACS class IV patients, or the first class of patients which are not inotrope dependent, can benefit from the LVAD.

In terms of ventricular recovery, there was even less enthusiasm in 2015 than before. The query of the UNOS registry of patients on long-term continuous-flow LVADs, explant due to recovery was done in 5% of patients (34 out of 594), mostly young and non-ischemic. In the first year, one third of these patients either died or had heart transplant, therefore bringing the rate of true recovery down to slightly over 3% (6). In fact, this still represents an overestimation, because some patients will need re-implant of the LVAD, or cardiac transplantation, more than one year after the explant.

LVAD-related physiology

In 2015, several important contributions were made in terms of changes in the body that occur on LVAD support.

Cognitive function improves after LVAD (7). On the contrary, sexual activity is reduced, as well as satisfaction with sex. Surprisingly, pulmonary function tests, including forced expiratory volume in one second, forced vital capacity, and diffusing capacity for carbon monoxide deteriorated after LVAD implant (8).

All the above studies were done on relatively small number of patients and should not discourage other group from re-addressing the same questions.

Exercise physiology on LVAD

The exercise physiology in LVAD recipients is not well known. Several studies in 2015 were dedicated to this topic.

In one study, patients with a swan-ganz catheter exercised on a supine bicycle, either at a fixed pump speed, or with progressive pump speed increase

It appeared, that while at rest, increase in pump speed resulted in 18.8% increase in the blood flow, and decrease in pulmonary capillary wedge pressure, roughly from 14 to 9 mmHg. With exercise, the flow also increased, but so did the filling pressures, bringing the wedge pressure up to 25 mmHg, and right atrial pressure to 17 mmHg. Concomitant increase in pump speed did not alleviate this effect. The concentration of lactate and B type natriuretic peptide increased as well (9).

For comparison, healthy people usually experience some increase in pulmonary capillary wedge pressure after the beginning of the exercise, but the wedge

decreases, although not to the baseline, and typically stays around 15 mmHg (10).

Also, the cardiopulmonary stress test, performed in 6 months after the LVAD implantation, showed that peak oxygen consumption improves somewhat from pre-LVAD level (11.6 ± 5.0 to 15.4 ± 3.9 ml/kg/min, P=0.009)., but never reaches normal values (11).

The findings explain why LVAD patients almost always have some limitation of the activity. An extensive review on exercise physiology in LVAD recipients was published by Jung et al. (12)

Candidate selection

Obesity

Over and over, obesity (body mass index ≥30 kg/m^2) is proven not to be a contraindication for LVAD implant (13). Obese patients had similar survival to non-obese, although they had more HF readmissions after the LVAD (OR 2.47, 95% CI 1.15-5.32; P =0.02). The difference lost significance after adjustment for covariates (14).

There is also a growing acceptance of surgical options for obesity treatment in LVADs. Last year, there was a report of successful sleeve gastrectomy in patients with LVAD. The surgery allowed them to lose weight and become transplant candidates (15). This year, Shah et al. (16) reported same procedure performed simultaneously with LVAD implant.

Adult Congenital Disease

One of the most challenging tasks in cardiology is caring for adults with complex congenital heart defects. A case series of 5 patients (17) and a separate case report (18) last year described successful use of LVAD on systemic right ventricle in adult patients with d-transposition of great arteries after an atrial switch procedure. The time on support was over a year in one case and a mean of 284 ± 177 days in the series. In total, 4 out of 6 patients underwent heart transplant.

Management of patients on LVAD support

Blood pressure measurement

The group from Columbia University addressed a very practical and very important question about blood pressure measurement in patients with continuous flow LVADs. Because elevated blood pressure is associated with stroke (19), it is very important to know whether you are dealing with systolic or mean blood pressure.

Obtaining blood pressure measurements via arterial line, Doppler, or standard automated cuff, the authors observed that if at least two out of three measurements by automated cuff were achieved (meaning that some pulsatility

was present), the blood pressure was measured more accurately than with the Doppler which tended to overestimate mean pressure (20).

Ramp study

In 2015, Uriel et al. (21) demonstrated that the ramp test guided by invasive hemodynamic measurement, results in better optimization of the LVAD function, than traditional echo-guided approach. They found that only 42.9% of patients had normal central venous and pulmonary capillary wedge pressure at their original settings. With the pump going from low to high speed in HMII recipients, cardiac output improved by 0.16 ± 0.19 L/min/step (total change 1.28 ± 1.41 L/min) and pulmonary capillary wedge pressure decreased by 1.23 ± 0.85 mm Hg/step (total change 9.9 ± 6.5 mm Hg). Each step was 400 rpms. Central venous pressure and systolic blood pressure did not change. In over half of the patients (56%), they managed to approach near normal filling pressures. Increases in device speed were associated with increases in pulmonary artery oxygen saturations indicative of improved cardiac output.

In patients with Heartware (HeartWare Corp., Framingham, Massachusetts), cardiac output increased by an average 0.09 L/min for each 100 rpm. In HMII, there was an increment of 0.2 L/min for each 400 rpms., with a trend to decrease in central venous pressure. Overall, increases in the pump speed were made in one third of the patients.

Another important contribution was made by Adatya et al. (22). They showed that blunted response of the left ventricular size to aggressive unloading with increasingly high pump speed may result not only from pump thrombosis but from increased afterload: aortic regurgitation or systemic hypertension with mean arterial pressure over 85 mmHg. Both conditions would make it difficult to unload the LV. Practically, it means that positive ramp study should be used for confirmation of pump thrombosis only in the presence of elevated lactatedehydrogenase (LDH), as a sign of hemolysis.

Pulmonary hypertension

It is generally thought that pulmonary hypertension resolves after LVAD, but the timing is not established. Studying patients who had serial right heart catheterizations before and after LVAD implant, Houston et al. (23) found that patients with reactive pulmonary hypertension (>3.5 Wood units) may still have high pulmonary vascular resistance even after 6 months of being on LVAD, and if transplant is considered, repeat right heart catheterization is justified. However, if reactive pulmonary hypertension was not present before the LVAD, there is no need to repeat right heart catheterization while the patients are on LVAD support, even if they need to be listed for heart transplant.

Arrhythmias

There are still no clear results showing how to manage arrhythmias in patients with LVADs. Lee et al. (24) found only marginal benefit of automated implantable

cardioverters-defibrillators for survival. In their experience with a small (100 patients) sample there were no deaths attributable to ventricular tachycardia, directly (sudden arrhythmic death) or indirectly (right ventricular failure induced by frequent arrhythmic episodes), but 43% of patients experienced defibrillator shocks, sometimes inappropriate.

Ablation for VT in patients with LVADs is not such a rare procedure. A series of 39 ablations in 34 patients with good success rate indicated that about two thirds of tachycardias were related to intrinsic myocardial scar, and only one third to the inflow cannula (25)

A meta-analysis of observational studies confirmed that post-LVAD ventricular arrhythmias were associated with increased risk of all-cause mortality after adjusting for competing risk factors at 60 days (OR 1.91, 95% CI 1.18 to 3.11, p = 0.001), 120 days (OR 1.97, 95% CI 1.01 to 3.85, p = 0.05), and 180 days (adjusted OR 2.04, 95% CI 1.01 to 4.15, p = 0.05) (26). Because almost all individual studies, selected for this meta-analysis, report worse outcomes in patients with ventricular arrhythmias, such results were quite predictable.

LVAD and valves

Tricuspid valve

The issue of concomitant tricuspid valve repair during the LVAD implant in patients with more than mild tricuspid regurgitation is still controversial. This year, a propensity-matched group comparison indicated that such repair did not make difference in one year survival, need for re-thoracotomy, or early and late right heart failure and hepatic or renal failure.(33)

Aortic valve

Severe aortic insufficiency carries substantial morbidity and mortality in LVAD patients. Treatment options include transcatheter closure using an Amplatzer Multi-Fenestrated Septal Occluder "Cribriform" device. In a series of 10 patients, technical success was achieved in all patients, but only three (30%) survived six months (34).

LVAD and kidneys

Several good reviews were published this year. The first of them (27) is dedicated to kidney issues and LVADs in general. Importantly, it analyzes in detail the dynamic changes in renal function after LVAD implant depending on the baseline (pre-LVAD) glomerular filtration rate. Originally, this was reported by Brisco et al. (28). Although renal function, after initial improvement, deteriorates on LVAD support in patients with lower baseline glomerular filtration rate, the function is still better than before the implant (Figure 4)

Three other reviews specifically discuss the issues of hemodialysis in patients on LVAD support, including access, blood pressure management, infection risks, etc.(29-32) .

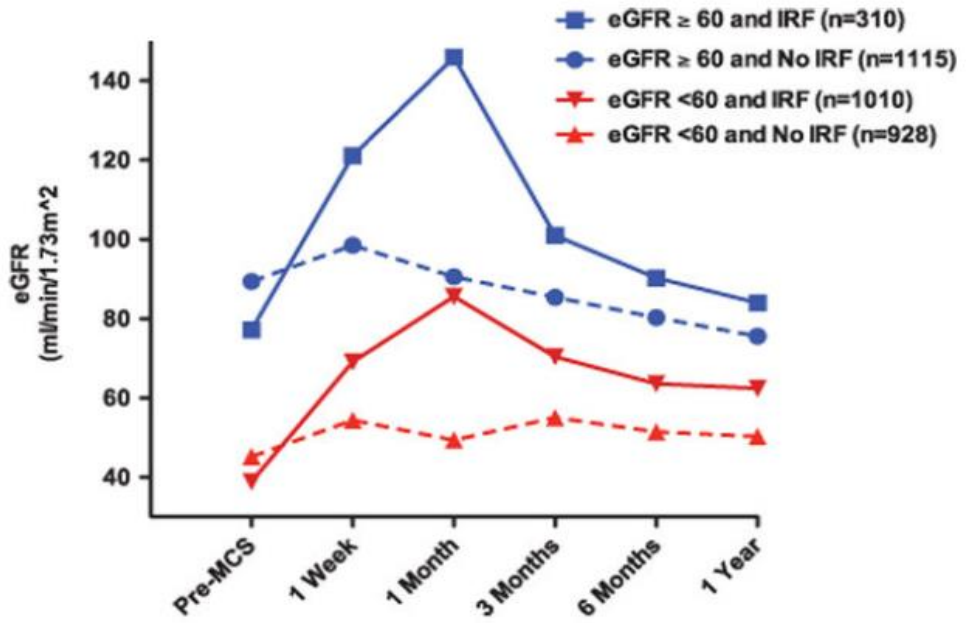


Figure 4. Dynamic changes in kidney function after LVAD implant, stratified by the pre-implant glomerular filtration rate.

Reproduced from Brisco et al.(28), with permission

Anticoagulation in VADs

Like in 2014, the topics of anticoagulation and pump thrombosis were in the spotlight last year. While the management of these aspects are still mostly empiric, number of studies added some evidence. The initiation of anticoagulation in the post-operative period after LVAD implant was studied in the non-interventional, retrospective, matched historical control cohort study. All patients were started on aspirin 325 mg after the hemostasis was achieved. Patients bridged to warfarin with intravenous heparin, intravenous bivalirudin, or not bridged were compared in terms of thromboembolic and bleeding complications up to 30 days post implant. Thromboembolism was significantly lower on heparin versus no bridging (4.9% vs. 27.0%, p = 0.008). Heparin was also associated with increased risk of bleeding in a multivariate analysis (OR 2.93, 95% CI 1.15-7.43). Bivalirudin was no different from no bridging. It appears that bridging with heparin was the most effective regimen to prevent

thromboembolic events, but at the cost of higher bleeding risk. The median time to starting parenteral bridge therapy was 2 days post-LVAD implantation (35).

Regarding antithrombotic management, Jorde's group from Montefiore retrospectively compared three regimens, concomitantly with warfarin, in patients on HMII:

- ASA 81 mg+dipyridamole 75 mg, target INR 2 to 3
- ASA 81 mg, target INR 1.5 to 2
- ASA 325 mg, target INR 2 to 3

With similar rates of thrombotic events, bleeding episodes almost tripled on high dose aspirin. From this study, the 81 mg a day dose of ASA is sufficient for HMII recipients, and the dose of 325 mg/day increases the bleeding risk without adding the antithrombotic benefit.(36)

Safety of reduced anti-thrombotic therapy in HMII recipients, most of which had a bleeding event on LVAD support, was explored in the TRACE U.S. (STudy of Reduced Anti-Coagulation/Anti-plateIEt Therapy in Patients with the HeartMate II LVAS). This was a multicenter, prospective and retrospective, observational study.

The enrolled 100 participants were outpatients on a regimen of reduced anti-thrombotic therapy, defined as warfarin only (38%), aspirin only (28%), or no anti-thrombotic agent (34%). Freedom from ischemic stroke at 1 year was 93.8% ± 2.5%, and freedom from device thrombosis was 92.7% ± 2.7%. Despite reduced anticoagulation and antithrombotics, a subsequent bleeding event occurred in 52%, although there were no intracerebral bleeds. There was no comparison of strategies against each other (51).

Another open question in the area of anticoagulation in LVADs is optimal monitoring when patients are on intravenous heparin, for bridging to therapeutic INR or for pump thrombosis. Adatya et al. (37) compared anti-Xa factor and activated thrombin time (aPTT) and found disturbingly high discordance in paired blood samples. The results of the two assays were considered concordant if they both indicated that anticoagulation was within therapeutic, subtherapeutic, or supratherapeutic range. The discordance was 63.8% in the bridging cohort and 84.2% in the pump thrombosis cohort, where therapeutic level of anticoagulation is critically important. The most common pattern of discordance was a supratherapeutic aPTT value and a therapeutic anti-Xa level (49.1% for bridging vs. 75.8% for device obstruction; $p < 0.001$), likely because hemolysis per se, as well as elevated INR, which was frequent in these patients, can prolong aPTT. Anti-Xa assay may therefore give a more accurate guidance on heparin concentration in this population (37).

Complications of the VADs

HeartMate II versus Heartware

In a single institution experience with these two devices, mortality was similar, as well as GI bleeding or pump thrombosis. The time-related cumulative risk of any infection was significantly higher with the HVAD, but the rate of driveline infection was similar. The risk of stroke was higher with Heartware (HR: 1.8,(1.25, 2.5), P = 0.003), with the difference being driven by hemorrhagic stroke (39).

Pump thrombosis

Histologic analysis of clots in explanted axial continuous-flow LVADs revealed 2 distinct clot varieties. The young clot, found in acute pump failure, was primarily seen around the inlet and outlet stators. It was composed of serum proteins mixed with fibrin and red blood cells breakdown products. The more chronic clot variety had more fibrin layering with more erythrocyte breakdown products and small amount of cellular infiltrate, and it was found mostly on the rotor. This kind of clot is likely originates from the heat due to friction on the bearings. Such clot may cause partial obstruction of the device with subsequent increase of hemolysis/shear stress and propagating of the clot via platelet activation. (40)

The summary of data on pump thrombosis in different cohorts was published by Stewart et al. (41) (Figure 5)

Table 1 Estimates of Left Ventricular Assist Device Pump Thrombosis Incidence

Device	Source	Setting	No.	Implant year	6 months (%)	12 months (%)	24 months (%)
HeartMate II	Kirklin et al[12]	INTERMACS registry	9,808	2008–2014	Overall: 5	Overall: 7	Overall: 11
					2012: 7	2012: 10	2012: N/A
					2013: 8	2013: 11	2013: N/A
					2014: 5	2014: N/A	2014: N/A
	Smedira et al[13]	INTERMACS registry	11,123	2008–2014	2012: 7	2012: 10	2012: 13
					2013: 8	2013: 11	2013: 14
					2014: 9	2014: 12	2014: 14
	Starling et al[6]	Multicenter study	837	2004–2013	7	11	18
	Pagani et al[15]	ENDURANCE trial	149	2010–2012	N/A	N/A	13
	Estep et al[4]	ROADMAP study	94	2011–2013	N/A	6	N/A
HVAD	Slaughter et al[2]	ADVANCE trial and CAP	332	2008–2011	N/A	5	N/A
	Pagani et al[15]	ENDURANCE trial	200	2011–2012	N/A	n/a	11
	Stulak et al[16]	Multicenter study	175	2009–2014	8	13	24

ADVANCE, HeartWare Left Ventricular Assist Device for the Treatment of Advanced Heart Failure; CAP, continued access protocol; ENDURANCE, A Clinical Trial to Evaluate the HeartWare® Ventricular Assist System; HVAD, HeartWare ventricular assist device; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; N/A, not available; ROADMAP, Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients.

Figure 5. Incidence of pump thrombosis. Reproduced from Stewart et al, (41), with permission.

According to the INTERMACS data, the growing rate of pump thrombosis began in 2010, reached a maximum in 2012, and then plateaued at a level that was 3.3-times higher than pre-2010 (42). There was some decrease during the first half of 2014. It appears from the graph on Figure 6, the peak of pump thrombosis occurs within first three months after the LVAD implant, underscoring the importance of early anticoagulation.

Risk factors for pump thrombosis included younger age ($p < 0.001$), higher body mass index ($p = 0.02$), history of non-compliance ($p = 0.004$), severe right heart failure ($p = 0.02$), later date of implant ($p < 0.0001$), and elevated LDH during the first month post-implant ($p < 0.0001$). Subsequent pump thrombosis was more likely if the initial pump exchange indication was pump thrombosis ($p < 0.0001$). After the pump exchange for thrombosis, the 1 year mortality was high at 30% (43). Also, erythropoietin in LVAD patients was clearly associated with higher rate of pump thrombosis (52).

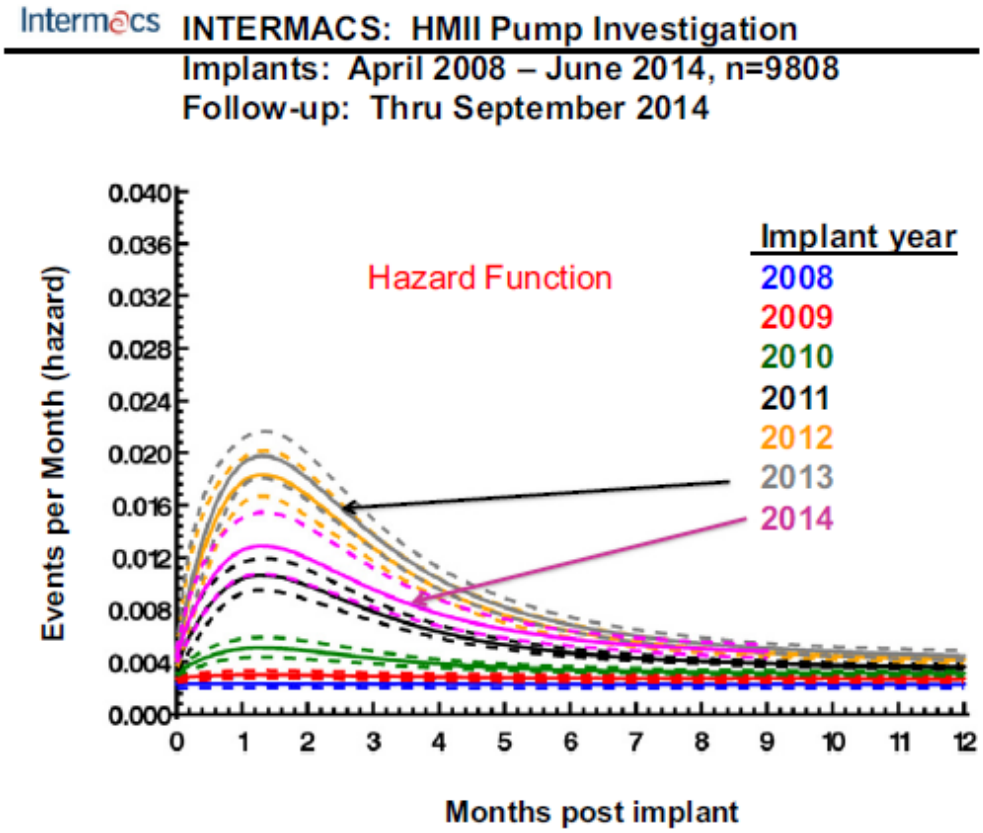


Figure 6. Rate of pump thrombosis up to 1 year post implant, by the year of implant. Reproduced from Kirklin et al. (43), with permission.

While there is no further increase in the rate of pump thrombosis, some centers report this complication in up to 20% of patients (44). Last year, several publications discouraged medical treatment of this complication, favoring early pump exchange (45,46). In 2015, once again, there were several papers comparing different strategies in treatment of pump thrombosis.

In one of the studies, medical therapy with intravenous heparin, antiplatelet agents, antithrombotic agents, or thrombolytics led to resolution of hemolysis, and discharge to home, in 15 of 25 (60%) cases; however, this strategy was

associated with intracranial hemorrhage in 4 patients and readmission with recurrent thrombosis in 10 patients.

Specifically, neither unfractionated heparin nor bivalirudin reliably resolved thrombosis in the patients where these agents were used as a first line therapy. Primary therapy with eptifibatide, was successful in one of four patients (25%). Alteplase, added on top of one or more agents, resulted in 50% success, one recurrence, and one intracerebral bleeding. LVAD exchange, predictably, provided better results (44).

In patients with Heartware, initial medical treatment was successful in 48% ofcases, while surgery was successful in all cases (47). Pump exchange still appears the safest option when dealing with pump thrombosis.

In the 2014 review, we included the innovative report from the Berlin group (48) about the use of acoustic characteristics of the working pump for diagnostics of pump thrombosis (Heartware). In 2015, there was a further development of this topic. An electronic stethoscope was used to record sounds from HMII. The data were then uploaded to a computer and analyzed. Device thrombosis was found to be associated with reduced LVAD acoustic amplitude in two patients who underwent surgical device exchange (49).

A novel method of diagnosis of pump thrombosis and of successful treatment with thrombolytics using the log files of the Heartware pump was suggested by Jorde et al. (50). The growth rate and percent of expected power were the log file parameters associated with successful treatments

Gastrointestinal Bleeding

In 2015, the nature of LVAD-related coagulopathy was further investigated. Exposure of blood from healthy people to LVAD resulted in rapid decrease of the level of von Willebrand factor in general, and high molecular weight multimers in particularly. This demonstrated the role of the cleavage protein ADAMTS-13 in the process, because no similar depletion occurred when the blood was taken from patients with congenital deficiency of ADMTS-13. Additionally, when platelets were removed from normal blood, no depletion occurred despite same shear stress. Hence, sheer stress, ADAMTS-13, and dysfunctional platelets with abnormal aggregation are all essential in the development of LVAD related coagulopathy (53).

Inhibition of ADAMTS-13 may be therefore considered a therapeutic target to reduce degradation of von Willebrand factor resulting from shear stress. One of the drugs inhibiting ADAMTS 13 is doxycycline. In vitro, doxycycline (5 mg/dl) decreased ADAMTS-13 activity and protected multimers of von Willebrand factor. Because usual therapeutic dose of doxycycline normally produces plasma levels of 0.3 to 0.5 mg/dl, or 10 times lower than in the study, clinical application of this finding is so far uncertain (54).

In one retrospective study, severe RV dysfunction was identified as a risk factor for GI bleeding (HR 1.799, 95% CI: 1.089 to 2.973, p = 0.022). Because coagulation parameters, antithrombotic regimens, and flow pulsatility/aortic valve opening were no different in patients with and without RV dysfunction, liver congestion or decreased pulsatility due to severe RV dysfunction did not explain the difference. Congestion in mesenteric circulation was proposed by the author as a hypothesis explaining this phenomenon.(55)

Infections in LVADs

Once again, there was strong evidence to support leaving the entire velour portion of the driveline below the skin – this technique was associated with 50% reduction in driveline infection compared with results from the HMII destination therapy trial.(57) Also, there were reports from individual centers about their strategies to curb the driveline infection (58).

Early post-operation ileus

Ileus can be a problem early after the surgery. In order to decrease postoperative ileus, an aggressive bowel regimen was used with good results: clear liquids until first bowel movement, then full liquids until the second bowel movement, then advancing the diet. Docusate was given on postoperative day 1 and bisacodyl rectally on the second day, and the enema was added if ileus developed. The goal was a bowel movement every 2 days, with enemas and polyethylene glycol given daily as needed. The incidence of ileus was 4%, a dramatic decrease comparing with less aggressive protocol (38).

Various pumps

Several interesting new pumps were introduced or further developed in 2015.

Impella

Although this pump is not new, the data about it, published in 2015, were quite interesting. Many of us empirically know that hemolysis is a frequent complication on Impella support, but for the first time as high rate as 62.3% (60) reported when the device was in use for more than 6 hours, which is typical when it is inserted for treatment of cardiogenic shock rather than protection during high risk percutaneous coronary intervention. Such a high rate raises concern of utility of this pump for the purpose of hemodynamic support. The average time of support was 86.63 hours. After 24 hours of support, the hemoglobin decreased significantly despite 17% of patients receiving blood transfusion (p = 0.0001). By the time of removal, 65% of patients were transfused to maintain a hemoglobin of 10 mg/dL (p = 0.0014). The LDH increased to 5,201 U/L (n = 22; p = 0.0096), the bilirubin to 5.6 mg/dL (p = 0.008), and the haptoglobin level was 15.4 mg/dL (n = 25).

Impella for RV support

Last year, we mentioned the study The RECOVER RIGHT, unpublished at that time, as a basis for the FDA approval of right sided Impella. 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 in our review "What did we learn about LVADs in 2014?"). Now this prospective, open label, single arm, non-randomized, multicenter study is published.

This study included two cohorts in several American centers: 18 patients with RVF after left LVAD) implantation and 12 patients with RVF after cardiotomy or myocardial infarction. The primary end point was survival to 30 days or hospital discharge (whichever was longer). Implantation of the device resulted in immediate increase in cardiac index from 1.8 ± 0.2 to 3.3 ± 0.23 liters/min/m^2 ($p < 0.001$) and a decrease in central venous pressure from 19.2 ± 4 to 12.6 ± 1 mm Hg ($p < 0.001$). Average time on support was 3.0 ± 1.5 days (range, 0.5-7.8 days). The overall survival at 30 days was 73.3%. All patients discharged were alive at 180 days (61).

Historically, survival in similar patient population is less than 50% (62)

A HeartWare MVAD (HeartWare, Inc., Miami Lakes, FL USA), is shown on Figure 7, 8

This minipump weighs only 78 g compare with MMII -290 g, and Heartware – 160 g).

It can deliver up to 7L/min of flow. Implanted in 4 sheep, it demonstrated good performance.

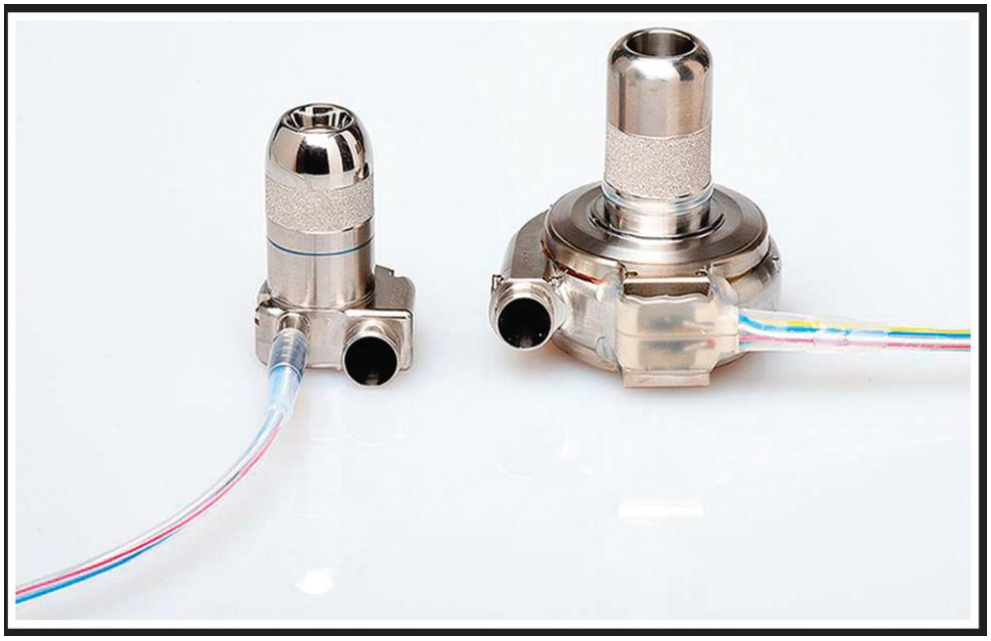


Figure 7. The Heartware Minituarized LVAD (left) and Heartware device (right). Reproduced rom Cheung et al. (59), with permission

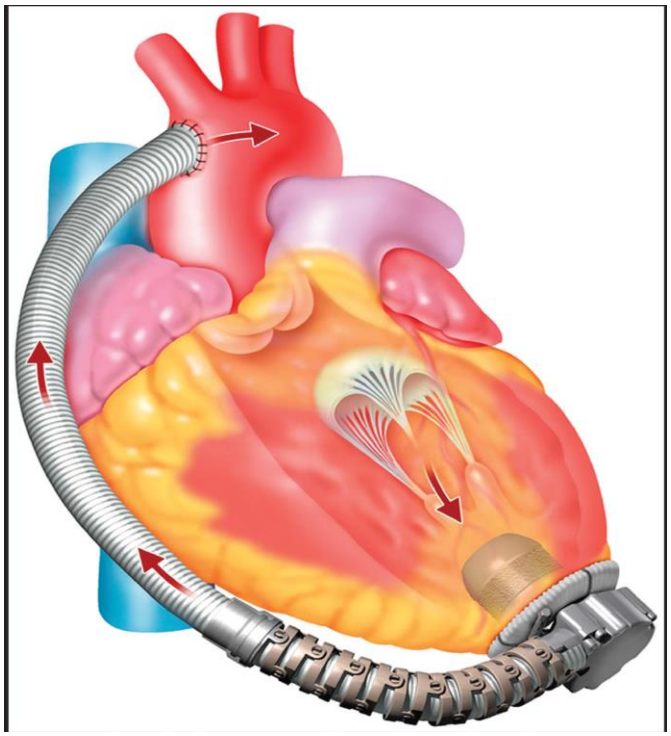


Figure 8. Heartware MVAD. Reproduced from Cheung et al. (59), with permission

The Synergy Micro-pump

The Synergy Micro-pump (The Synergy System, HeartWare Inc, Framingham, MA) is the smallest implantable LVAD that is currently available and can produce flows of up to 4.25 L/min. In a simulation theoretical model, Burkoff et al. (64) tested this device in HF with preserved LVEF. In this condition, regardless of the etiology, LV is usually not dilated and therefore not very suitable for implantation of an LVAD. However, the LV end diastolic pressure is elevated, as well as left atrial pressure, and left atrium is typically enlarged. Decompressing the left atrium with the Synergy pump was hemodynamically beneficial.

Symphony device

A new partial support device was implanted with good outcome. The Symphony device (Abiomed, Danvers, MA) is a 30-mL stroke volume pump that is placed in the infraclavicular fossa (Figure 9). The pump is attached to the subclavian artery through a single short graft that functions as a bidirectional flow conduit. Pump filling occurs during ventricular systole, which provides afterload reduction.

During ventricular diastole, the pump ejects blood, which increases coronary and systemic blood flow (63)

.

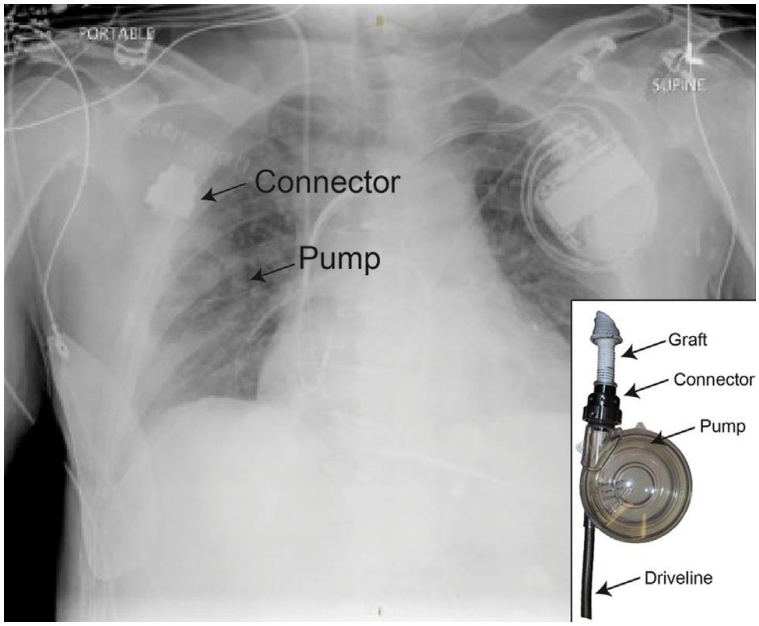


Figure 9. The Symphony device for partial support. Reproduced from Cecere et al. (63), with permission.

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