LVAD Thrombus and the need to service rather than replace an LVAD

The Problem

Literature Review along with a survey of LVAD clinicians conducted March 2015 reveal that nearly 10% of a combination of Thoratec and HeartWare LVADs occlude with life-threatening thrombus blockage.

Current Solution

Two and only two approaches are currently available to alleviate thrombus lodged in an LVAD:

- Inject a known thrombolytic solution, such as tPA at the inflow of the LVAD. The tPA is delivered via a catheter, but it is not confined to the LVAD and passes through the LVAD. More often than not, tPA causes catastrophic brain bleeds and any freed thrombus particles could cause stroke.

- Exchange the patient’s pump. Pump exchanges are linked to high mortality rates in the short and long term, and are very costly.

Literature Review

The articles that follow are valuable representations of the frequency of LVAD thrombosis and the shortcomings with the current treatments. The articles also emphasize the urgent need for improved methods for eliminating LVAD thrombus.

Clinician Survey March 2015

The survey launched March 16th, 2015 and tallied March 24th, 2015 collected responses from 117 individuals, representing 792 LVAD implants performed in 2014. These results revealed that alleviating thrombus in the Thoratec HeartMate II and the HeartWare HVAD is not easy and often has poor clinical outcomes. The clinicians that responded have expressed that there is a desperate need for a better and safer solution.

The Survey corroborates the Literature review

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**Question:** What are the most common outcomes following administration of tPA?

In a survey of late 2014, one hundred and four worldwide centers responded indicating that 43% of their 3,040 implants were HeartWare HVAD and 53% were Thoratec HMII. As illustrated below 64% of the centers indicated that thrombus build up on the bearings of the Thoratec HMII was a reason for replacement. Two hundred and fifty one LVADs were replaced representing a replacement rate of slightly greater than 8%.

The respondents to the March 2015 survey indicated that out of 792 LVADs that were implanted, 80 (10%) were exchanged due to thrombus, keeping with the earlier reported replacement rate of approximately 8%.

**Reasons for Replacement**

Percentage of All Centers

The respondents to the March 2015 survey indicated that out of 792 LVADs that were implanted, 80 (10%) were exchanged due to thrombus, keeping with the earlier reported replacement rate of approximately 8%.

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**Question:** If an LVAD must be exchanged due to occlusion, what are the most common patient outcomes?

The detail below indicates that 63% of the LVAD exchanges led to unsatisfactory results: death, stroke or recurrence of the occlusion.

![Graph indicating patient outcomes](image)

**Solution - VAD Maintenance System**

The VAD Maintenance System is designed to antiquate existing dangerous and often unsatisfactory treatment methods.

The VAD Maintenance System includes two co-axial balloon catheters consisting of large inner lumens to aid in evacuating debris. The catheters are introduced through the left and right femoral artery. One catheter will inflate in the inflow side of the LVAD, while the other will inflate in the outflow side. Once the balloons have been properly placed and inflated the LVAD is successfully isolated from the patient’s body.

Once isolation occurs, clinicians have the option of introducing thrombolytic therapies and/or tools that they believe will aid in thrombus removal, all while the LVAD is sequestered from the patient. A final wash out of the LVAD using saline is the last step in restoring the LVAD.
Conclusion

The current methods of treatment for patients who experience LVAD thrombosis pose very high and dangerous risks to their survival and well-being.

The VAD Maintenance System isolates the LVAD from the patient’s body to allow cleaning and may be a superior alternative for thrombus removal.

Literature Review

The articles that follow are valuable representations of the frequency of LVAD thrombosis and the shortcomings with the current treatments. The articles also emphasize the urgent need for improved methods for eliminating LVAD thrombus.
ReliantHeart Literature Review of Articles Referring to the VAD Maintenance System

A literature review was conducted in order to determine if sufficient clinical data existed in literature to demonstrate the significant need for a left ventricular assist device maintenance program, in this case the ReliantHeart VAD Maintenance System.

A plan was developed to guide the document selection and set the rules for evaluation of the articles. Articles were gathered through the information retrieval company PubMed®. Search criteria for the articles included the words LVAD Thrombus, LVADs and TPA, Thrombolytic Therapy, LVAD exchange, LVAD isolation and LVAD adverse effects and publication dates after 2012. Of the articles obtained, those selected for review were limited to those that described the current issues with the diagnosis and management of thrombus. No articles meeting these selection criteria were excluded from the review. All articles that met these search criteria were carefully reviewed and summarized; those that did not were not summarized and labeled “NR”. Each article was indexed according to its order of receipt.

Assessment of articles was by relevance; those deemed “Highly Relevant” discussed the large impact of LVAD thrombus and the lack of ways to mitigate it, those in the “Relevant” group discussed LVAD thrombus and the strategies used for anticoagulation, “Somewhat Relevant” group discussed LVAD adverse effects.

For this review, thirty seven (37) articles were found according to the search criteria, thirty one (31) of these were applicable when the selection criteria were applied to the title or abstract of the articles. Each of the thirty one (31) articles were assigned a number one through thirty one (1-31) and complete texts were ordered. Of these thirty one (31), two (2) was not obtainable due to incomplete information. Thirty (30) articles were summarized in this review.

The literature review was conducted in accordance with NB-MED/2.7/Rec 3 and is comprised of the following:

Attachment A – LVAD Maintenance System Literature Review Plan
Attachment B – List of LVAD Maintenance System Articles Reviewed
Attachment C – Individual LVAD Maintenance System Article Reviews
Attachment D – LVAD Maintenance System Literature Review Summary and Conclusion
Attachment E – Articles Received and Reviewed

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Attachment A –

VAD Maintenance System Literature Review Plan
VAD MAINTENANCE SYSTEM LITERATURE REVIEW PLAN

OBJECTIVE

To determine if there is sufficient relevant clinical data available to demonstrate the need for a VAD Maintenance System.

DOCUMENT SELECTION CRITERIA

A PubMed search of the published scientific literature will be conducted to identify publications discussing LVAD thrombus, LVAD thrombus treatment, LVAD exchanges, LVAD isolation, LVAD adverse events, balloon catheters and thrombolytic therapy. PubMed provides an avenue for searching a broad range of databases. The search will cover published literature from 2012 to date.

Articles selected for review will be limited to those involving LVAD thrombus, current ways to eliminate thrombus and other thrombolytic therapies used. Such articles are relevant because they define the importance and need for a tool that allows LVADs to be cleaned safely.

No articles meeting the selection criteria shall be excluded from review.

DOCUMENT ASSESSMENT

Published articles and unpublished documents which meet the assessment criteria will be grouped into highly relevant, relevant, and somewhat relevant. The grouping will be based upon the relevance to LVAD thrombus.

A) Highly Relevant - Articles discussing the issues with thrombus in LVADs and the lack of ability to mitigate them.
B) Relevant - Articles discussing anticoagulation and explants
C) Somewhat Relevant - Articles discussing ventricular recovery and LVAD adverse effects
D) Not relevant – Articles that are not relevant to the search criteria

REPORT

A report covering all literature meeting the document selection criteria shall be prepared without regard for whether or not it is favorable or unfavorable for the VAD Maintenance System. If any documents are excluded from the report their exclusion must be justified.

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The report shall contain:

a) A short description of the VAD Maintenance System and the products indication for use
b) A brief discussion of each article reviewed grouped by category (highly relevant, relevant, somewhat relevant) addressing, where the article discusses use of a product
c) A brief discussion of the product (when appropriate)
d) A brief discussion of patient population where successful use appeared to vary dependent upon the patient population
e) A brief discussion of the experience reported (positive and negative)
f) A conclusion with a
   1) Justification of any probable benefit to health from the use of the VAD Maintenance System
   2) Discussion of the probable benefit as compared to any risk that the literature review revealed
   3) Determination that the objectives of the literature review have been satisfied with an identification of any gaps necessary to cover all relevant aspects of safety and performance
h) A list of publications reviewed which are appropriately cross-referenced in the survey
i) Signatures of the authors and date
Attachment B –

List of VAD Maintenance System Articles Reviewed
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<td>A MULTICENTER ANALYSIS OF CLINICAL HEMOLYSIS IN PATIENTS SUPPORTED WITH DURABLE, LONG-TERM LEFT VENTRICULAR ASSIST DEVICE THERAPY Katz, Jason N. et. al. “A multicenter analysis of clinical hemolysis in patients supported with durable, long-term left ventricular assist device therapy.” <em>The Journal of Heart and Lung Transplantation</em>, 2015</td>
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<td>LATE BLEEDING AND NEUROLOGICAL SEQUELAE AFTER HEARTMATE II LEFT VENTRICULAR ASSIST DEVICE: RISK FACTORS FROM THE PREQUEL Najjar, Samer S. “Late Bleeding and Neurological Sequelae After HeartMate II Left Ventricular Assist Device.” Journal of the American College of Cardiology: Vol. 63, No. 9, 2014</td>
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<td>VENTRICULAR RECONDITIONING AND PUMP EXPLANTATION IN PATIENTS SUPPORTED BY CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES Frazier, O.H., et. al. “Ventricular reconditioning and pump explantation in patients supported by continuous-flow left ventricular assist devices” The Journal of Heart and Lung Transplantation, 2014</td>
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<td>LEFT VENTRICULAR ASSIST DEVICE THROMBOSIS IN THE SETTING OF LEFT VENTRICULAR RECOVERY Hurst, Thomas E., et. al. “Left ventricular assist device thrombosis in the setting of left ventricular recovery” The Journal of Heart and Lung Transplantation, 2015</td>
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<td>PRIOR HEMATOLOGIC CONDITIONS CARRY A HIGH MORBIDITY AND MORTALITY IN PATIENTS SUPPORTED WITH CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES Fried, Justin, et. al. “Prior hematologic conditions carry a high morbidity and mortality in patients supported with continuous-flow left ventricular assist devices” The Journal of Heart</td>
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Attachment C –

Individual VAD Maintenance System Article Reviews
Article 1

RELEVANT

TREATMENT OF LEFT VENTRICULAR ASSIST DEVICE THROMBOSIS WITH EXTENDED CATHETER-DIRECTED INTRAVENTRICULAR THROMBOLYTIC THERAPY


Although anticoagulants, such as Warfarin are highly used in patients with LVADs, device thrombosis may still occur, which require LVAD exchange. In this study authors were able to treat thrombosis found in two patients using a catheter-directed intraventricular administration of a single bolus dose of fibrinolytic therapy. The first patient was a 45 year old male with a HeartMate II, who has developed thrombus. Clinicians were able to perform a trial of intraventricular fibrinolytics in the cardiac catheterization laboratory. After 30 hours of alteplase infusion, the patient LDH levels were normalized. The second patient was a 46 year old man with a HeartMate II implant, after the clinicians were sure that thrombus was present they performed the same procedure as described above and found that after 96 hours all LDH and bilirubin levels had normalized. Although clinicians were successful in treating thrombus in these 2 patients, this procedure involves high risk. It is associated with serious bleeding complications, especially given the inherent bleeding risks associated with LVAD’s. Another concern when performing this procedure is the dislodgement of the pigtail catheter into the LVAD inflow cannula. Further studies are required to determine the safety, and efficacy of this procedure.

Article 2

HIGHLY RELEVANT

DIAGNOSIS AND MANAGEMENT OF LVAD THROMBOSIS


VAD thrombus has been one of the most devastating complications, leading to increases of morbidity and mortality. Since 2011, there has been more and more incidences of Heartmate II device thrombosis, from 2.2% to 8.4%. The reasons for device thrombosis remain unclear but the magnitude of the issue will continue to increase if development of new strategies fails to happen. VAD thrombosis is the formation of a blood clot within one of the VAD components. Diagnosis of VAD thrombosis can be very challenging. There are some diagnostic approaches, such as lactate dehydrogenase levels, free plasma
hemoglobin and echocardiographic RAMP studies can increase a patient’s chance of survival. There are two theories that could describe why thrombus occurs. The first is flow-induced. There could be a geometric device characteristic, such as heat, that is causing elevated shear stress. The second is hypersensitivity and inflammatory response, which occurs in patients that have titanium hypersensitivity, causing an allergic response from the body. The signs and symptoms that most clinicians pay mind too are symptoms of heart failure, change in functional capacity, VAD parameters, elevated LDH, elevated BNP and new right ventricular dysfunction. Nevertheless, diagnosis continues to pose great difficulties. When thrombosis does occur, the ways of treating it most often than not has fatal outcomes. Rates of morbidity and mortality rise after pump exchanges, anticoagulation techniques, and urgent transplantation. There is not enough data that dictates that VAD replacement is the best therapy in all VAD patients, it has become an essential need to find new strategies in how to eliminate thrombus.

**Article 3**

**HIGHLY RELEVANT**

**HEMORRHAGE AND THROMBOSIS WITH DIFFERENT LVAD TECHNOLOGIES: A MATTER OF FLOW?**


"Hemorrhage and thrombosis with different LVAD technologies: a matter of flow?" *Ann Cardiothac Surg* (2014); 3(6):582-524

The high risks of morbidity and mortality that are associated with VADs are due to thrombotic complications. A lot is to be said regarding the geometry of LVADs, such as comparisons between axial flow and centrifugal flow pumps. In this study patients with the Jarvik 2000, which is an axial flow pump was compared to patients with the Heartware HVAD, which is centrifugal flow pump. The results were that patients with the Jarvik 2000 experienced a significant reduction in platelet count after implantation and the patients with the HVAD observed levels of platelet activation and activation of the coagulation system were significantly greater. The issues in managing anticoagulation are that the geometry of VADs have not been well studied and although life-long treatment of anticoagulants and antiplatelet therapies are vital, they often lead to hemorrhage. A well-established example of this is the blood thinning drug, Clopidogrel. It is used often as an antithrombotic therapy but recent studies showed that 5 out of 9 patients demonstrate insufficient platelet inhibition. It is believed that the best way to reduce thromboembolic and hemorrhagic complications in VAD patients is using thromboelastometry, but further studies are still required to better understand individual responses to antiplatelet therapy in patients undergoing VAD therapy.
**Article 4**

**HIGHLY RELEVANT**

EVALUATION AND TREATMENT OF PUMP THROMBOSIS AND HEMOLYSIS

Ventricular assist devices are not fully hemocompatible, which makes them predisposed to developing thrombosis and subsequent pump dysfunction. The evaluation and management of VAD thrombosis and hemolysis is vital to the survival and success of a VAD patient. The three major factors that impact thrombosis of continuous flow LVADs, are the pump, the patient and the clinician. Most institutions struggle between over-anticoagulation and under-anticoagulation. Both methods have devastating adverse effects. Over-anticoagulating includes gastrointestinal bleeding and intracranial hemorrhage, which under-anticoagulating includes hemolysis, pump thrombosis and stroke. Clinicians are left without any safe-zone, and are forced to pick the less bad method. Factors causing thrombosis are not clear and concise, many factors include the geometry of the pump, patient’s age and gender and the clinician’s anticoagulation protocol or at what speed the pump is run. VAD thrombosis presents itself in many different ways. The most important laboratory test to perform is the measurement of LDH levels. The most important diagnostic imaging method to see VAD thrombosis is through an echocardiogram. Once the presence of thrombus has been established, there certain steps that clinicians will take. These steps include anticoagulation protocols, where the patient is intravenously infused with heparin, and soon after that begins the patient is medically optimized in anticipation for pump exchange. Pump exchanges vary in severity. The primary approach for pump exchange is an isolated subxiphoid approach, which allows for VADoscopy. The most severe of operative approaches is a full redo sternotomy.

**Article 5**

**HIGHLY RELEVANT**

ANTICOAGULATION STRATEGIES FOR LEFT-VENTRICULAR ASSIST DEVICES
Pump thrombus is a devastating complication that requires immediate attention. Treatments for thrombus are also very lacking, and anticoagulation can lead to further complications. There has been a significant increase in pump thrombosis in HeartMate II at 3 months after LVAD implantation starting in March 2011. Recent changes in perioperative anticoagulation, accepting lower target INR, and the lack of heparin bridging may play a substantial role in the increase. International Society for Heart and Lung Transplantation has put together minimum criteria for perioperative anticoagulation. It is vital that clinicians need to have the flexibility to treat different patients differently in regards to anticoagulation following implantation. It is important to find the right balance between thromboprophylaxis while still minimizing bleeding.

**Article 6**

**HIGHLY RELEVANT**

**AROUND AND AROUND THE MERRY-GO-ROUND: MULTIPLE IMPLANTATIONS OF SHORT-AND LONG-TERM VENTRICULAR ASSIST DEVICES IN A PATIENT WITH SEVERE HEART FAILURE**


A study where multiple implantations of left ventricular assist devices showed to be crucial to the survival of a 17-year old gentleman with non-ischemic dilated cardiomyopathy and congestive cardiac failure. The patient's first implant was a HeartMate II. After 2 years, the device was taken out. The 17-year old began to show signs of health deterioration and clinicians decided to put a partial support device. Due to the development of thrombus clinicians explanted the partial support device and implanted a short-term LVAD. The authors describe that thrombus can migrate into the VAD from the left ventricle and mostly occlude the inflow tract. The probability of a VAD patient developing thrombus is 8%/year. Thrombolytic therapy is minimally invasive but requires a relatively stable patient from a hematological perspective.
**Article 7**

**HIGHLY RELEVANT**

**MANAGEMENT OF PUMP THROMBOSIS IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES**


Although LVAD devices have been used for a considerable amount of time, there continues to be unintended consequences, including the most common, infection, bleeding, and thrombosis. The authors have reviewed the current status of the field of mechanical circulatory support in its approach to diagnosis, management and prevention of LVAD pump thrombosis. Authors found that the majority of pump thrombus occurred in patients with sub-therapeutic warfarin anticoagulation and taking low-dose or no antiplatelet therapy. No society guidelines or consensus statements exist regarding the diagnosis of management of LVAD thrombosis, despite the potential morbidity and mortality conferred by this clinical entity. The choice of initial therapy for patients that have diagnosed with LVAD thrombus depend on several factors, which include the health of the patient, surgical candidacy and institutional philosophy. The field is still learning how to appreciate the differences in etiology and mechanism, and subsequent implications on the most appropriate clinical approach for each device.

**Article 8**

**HIGHLY RELEVANT**

**MANAGEMENT OF ANTICOAGULATION AND ANTIPLATELET THERAPY IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES**


Despite the advances that have been made to LVADs, hemorrhage requiring surgical intervention has been reported in up to 30% of adults and 50% of children after having LVADs implanted. The high occurrences and reoccurrence of thrombosis and embolic stroke have played a significant role in the long-term morbidity of LVAD patients. Heart failure is a devastating economic burden, with an estimation report of 39.2 billion dollars in 2010 to care for heart failure patients. There are many variables as to what causes these issues in LVADs, an important question is, does blood passing through an LVAD cause platelet activation? Authors report that nearly 20% of LVAD patients experience gastrointestinal bleeding. Ischemic stroke has been reported in 7-8% patients and arterial
embolism in 4-7% of patients. Antithrombotic therapies are continuously trying to be improved, yet the percentages of patients having to undergo reoperation are significant. Future studies are highly needed to determine the correct antithrombotic regimen that patients should undergo and that the regimen is able to effectively balance bleeding and thrombosis in LVAD patients.

**Article 9**

**RELEVANT**

**SHOULD DEVICE REPLACEMENT BE THE FIRST CHOICE STRATEGY IN CONTINUOUS-FLOW LEFT VENTRICLE ASSIST DEVICE THROMBOSIS? ANALYSIS OF 9 EVENTS AND RESULTS AFTER ENDOVENTRICULAR THROMBOLYSIS.**


The incidence of thrombosis occurring in HeartWare ranges from 4.2%-8%. Pump thrombosis can result in stroke, peripheral embolism, heart failure, pump exchange and death. The definitive treatments for pump thrombosis are pump replacements and cardiac transplantation. Authors report an annual rate of 0.06% for LVAD replacement due to pump thrombus. Authors performed a study on 4 patients that had developed clinical signs of pump thrombus that were associated with device malfunction. These patients were successfully treated with thrombolytic therapy in a total of nine procedures. The patients were treated with endoventricular thrombolytic therapy consisted on tPA, a recombinant tissue plasminogen activator. Clinicians infused tPA through the left ventricle using a pigtail catheter at a rate of 1mg/min for a total of 30 or 50 mg. All patients survived thrombolysis and no major bleeding events occurred. Authors report that pump thrombosis can successfully be treated in HeartWare by thrombolytic therapy. Success of this treatment has also been reported with the MicroMed DeBakey LVAD. Authors also report that the economic burden is much less when patients are treated with thrombolytic therapy instead of pump exchange. The quality of life of these patients seemed to not be impaired when readmissions for thrombolytic therapy are required.
Article 10

SOMEWHAT RELEVANT

GASTROINTESTINAL BLEED AFTER LEFT VENTRICULAR ASSIST DEVICE IMPLANTATION: INCIDENCE, MANAGEMENT, AND PREVENTION.


LVADs have improved much durability in comparison to earlier devices but the complications that develop after implantation still remain. Such complications include gastrointestinal bleeding, pump thrombosis and hemolysis. Authors have reported that 18-40% of patients acquire gastrointestinal bleeding after continuous flow LVAD implantation. Out of 233 patients who were implanted with the HeartMate II, 51 patients acquired GIB. The event rate of GIB is reported as 0.17. When managing an LVAD patient who has GIB, a multi-disciplinary approach is needed. One proposed mechanism for GIB after LVAD implantation is through acquiring von Willebrand Syndrome. It is a protein expressed that plays an essential role in preventing pathological coagulopathy or bleeding. More research is needed on the etiology of GIB as well as the establishment of proper management of anti-coagulation that will not lead to other complications, such as stroke.

Article 11

RELEVANT

THE ROLE OF MEDICAL MANAGEMENT FOR ACUTE INTRAVASCULAR HEMOLYSIS IN PATIENTS SUPPORTED ON AXIAL FLOW LVAD


The authors report that acute intravascular hemolysis due to the LVAD pump remains a clinical challenge. A single center retrospective review of 115 consecutive HeartMateII patients were screened for the role of medical therapy in treating hemolysis that occurred in 8 (7%) of the patients. A rise of >6X of baseline LDH was the indicator. Hemolysis occurred as early as 2 months and as late as 2.2years after implant. Use of heparin and enhanced anti-platelet therapy reduced the LDH to near baseline within 2 weeks. One patient required additional treatment of tPA. Complications included cerebrovascular attack (stroke) after tPA. Recurrence of the hemolysis was common in 6 of the 8

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patients. Thrombus was identified in the LVAD in all four patients who had signs of hemolysis at the time of LVAD removal.

**Article 12**

**HIGHLY RELEVANT**

DIRECT THROMBOLYTIC THERAPY FOR INTRAVENTRICULAR THROMBOSIS IN PATIENTS WITH THE JARVIK 2000 LEFT VENTRICULAR ASSIST DEVICE


The authors describe two cases where they performed a catheter insertion into the left ventricle across the aortic valve via femoral access to directly infuse recombinant tissue plasminogen activator (tPA) to lyse a thrombus within the ventricle and restore the function of the pump. High LVAD power consumption was the indicator of a thrombus in the pump or ventricle. Twenty milligrams of tPA was infused over a 20-minute period. Reduction in motor power and sound indicated success. This method greatly reduced the amount of tPA required for the therapy. The authors indicated that the risks associated with this procedure include embolization of a partially lysed thrombus and complication related to catheterization.

**Article 13**

**RELEVANT**

A MULTICENTER ANALYSIS OF CLINICAL HEMOLYSIS IN PATIENTS SUPPORTED WITH DURABLE, LONG-TERM LEFT VENTRICULAR ASSIST DEVICE THERAPY


The majority of LVAD patients will ultimately have an adverse event. The incidence and clinical significance of hemolysis in LVAD therapy is largely unknown. These authors review the INTERMACS data of all adults implanted with an LVAD between June 2006 and March 2012 to quantify the incidence of hemolysis. Hemolytic event defined as plasma-free hemoglobin >40 mg/dl. Out of 6,094 patients, a total of 4,850 patients were analyzed. 340 hemolytic events occurred in 260 patients. 44 of the 260 ultimately required pump explant or exchange. The authors’ review of data suggests that “like mortality and thrombotic device malfunction, the need for urgent operative intervention was greatest early after hemolysis.” In the discussion they point out that after a...
hemolytic event, device malfunction (thrombus in the pump) and the need for exchange occurred frequently and survival decreased. They found a 20% chance of requiring a device replacement within 6 months of hemolysis and the risk of death is not negligible. The authors found that the number of device exchanges after a hemolytic event exceeded the number of device malfunctions indicating that some clinicians choose to replace an LVAD after hemolysis but before a device problem. At 2 years after implant hemolysis occurred in nearly 10% of patients. Hemolysis events occur in 3 to 5% of all patients 3 months post implant.

Article 14

SOMEWHAT RELEVANT

LEFT VENTRICULAR ASSIST DEVICE PUMP THROMBOSIS: IS THERE A ROLE FOR GLYCOPROTEIN IIb/IIIa INHIBITORS?

These authors report on their experience using a glycoprotein IIb/IIIa inhibitor (epitifbatide) which has anti-thrombolytic and anti-platelet properties in LVADs to combat pump thrombosis. Their experience involved treating four HeartMateII patients (out of 20 implanted between 2009 and 2013) with epitifbatide after they presented with the “classic triad of LVAD thrombosis: elevated pump power, elevated lactate dehydrogenase (LDH), and symptoms of embolic phenomena.” They administered epitifbatide infusion at 1µg/kg/min after a bolus of 180µg/Kg for 2 to 4 days. Only one of the four patients responded as hoped with an LDH level dropping to baseline. The second patient experienced a massive cerebrovascular accident and later died. The third and fourth patients each endured a device exchange and both pumps revealed thrombus on the rotor. They conclude that use of epitifbatide may offer only limited value as a treatment for pump thrombosis.

Article 15

SOMEWHAT RELEVANT

DURABILITY OF CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES: A SYSTEMATIC REVIEW
A systematic review and screening of six electronic databases for original LVAD studies through August 2014 revealed twelve such studies that included 5,471 patients supported by continuous flow LVADs. Durability data indicated, on average, pump thrombosis was the most common mode of failure (50.5%) followed by cable damage (21.7%), mechanical failure (11.6%), infection (11.1%) and surgical complications (2.5%). Average incidence of device failure in the population was 3.9%. Long term failure rates by month: 0.5% at 2 months, 1.8% at 6 months, 2.9% at 12 months, 4.5% at 18 months and 6.5% at 24 months. Patients requiring device replacement had significantly reduced survival. The authors conclude that CF-LVAD durability has improved as designs, anticoagulation and infection control have improved. However thrombosis remains poorly understood.

Article 16

SOMEWAT RELEVANT

MECHANICAL CIRCULATORY SUPPORT DEVICES AS DESTINATION THERAPY-CURRENT EVIDENCE


This report summarizes worldwide experience with mechanical circulatory support for destination therapy gathered from 70 documents and published registries. Also included was data and experience specific to the authors’ institutions in Germany. Shortages of donor organs and improving clinical results are driving the increased use of MCS devices especially LVADs. Better results are the results of improved device design, therapy and earlier and better patient selections. Right heart failure is discussed as the biggest non-device failure mode of the therapy among all devices. Concerning device related problems cited are acquired von Willebrand Syndrome, gastrointestinal bleeding, driveline fractures and infection, thromboembolic events and pump thrombosis leading to pump exchange. Pump thrombosis is revealed by a rise in LDH. Suspected or confirmed thrombosis was the most common cause of device exchange with 72 exchanges out of 1,128 patients between 2005 and 2010. One year survival after pump exchange was reported at approximately 80%, about 65% after the second replacement and only 50% after the third exchange. They conclude that prevention of pump malfunction and pump thrombosis is critical. The HMII thrombosis rate was reported to increase from 2.2% at three months after implant to 8.4% by January 2013. The authors suggest that further improvements in survival will be associated with smaller, easier to implant devices, improved surface coatings and better design. Transcutaneous energy transfer (TET) should help to reduce infection.
Article 17

HIGHLY RELEVANT

SAFETY OF ANTICOAGULATION REVERSAL IN PATIENTS SUPPORTED WITH CONTINUOUS-FLOW LEFT-VENTRICULAR ASSIST DEVICES

Jennings, Douglas L., Minu Jacob, Anuvrat Chopra, Carrie W. Nemerovski, Jeffrey A. Morgan, and David E Lanfear. “Safety of anticoagulation reversal in patients supported with continuous-flow left ventricular assist devices”. ASIO Journal. (2014); 60:381-384

The purpose of the study was to expose the threats that thromboembolism poses to LVAD patients who have experienced warfarin-based anticoagulation. The study reported on all patients that had continuous flow implants between the dates of January 1, 2008 and August 1, 2012. Authors reported on the incidence of thrombotic events that the patients underwent, which included stroke, device thrombosis, and venous thromboembolism. This data was recorded within the first 30 days of anticoagulation reversal. The study included 122 screened patients, and 25 out of these 122 patients experienced 38 anticoagulation reversal events. The mortality rate within the first 30 days of reversal was 20%, and out of these mortalities, 3 of the patients died due to acute intracranial hemorrhage. Authors make clear that these results should be viewed in the context of this single center. They concluded that warfarin reversal can be safely attempted in patients with continuous flow LVADs and has a low risk of acute thrombosis. However, clinicians have the responsibility to carefully assess each individual patient. Once clinicians make the decision of reversal, a vitamin K regimen should be given.

Article 18

HIGHLY RELEVANT

STROKE WHILE ON LONG-TERM VENTRICULAR ASSIST DEVICE SUPPORT: INCIDENCE, OUTCOME AND PREDICTORS


This study began in March 2006 and continued through November 2011. 100 patients were included into this study, which all suffered from chronic heart failure and underwent HeartMate II implantations. 65 of these patients were bridge-to-transplant and 35 were destination therapy. Strokes occurred in 12 patients, in which were 4 embolic and 8 hemorrhagic. The purpose of the study was to see the prevalence of stroke in these patients. The mortality rate of these patients within 30 days was 25%, with 3 patients expiring at 8, 14, and 18 days after the stroke had occurred. Authors concluded that a higher incidence of stroke occurs in patients who suffer with diabetes. They also found
that aortic clamping was associated with the incidence of stoke. Aortic clamping was compared to sub-biting clamp and it is unclear why, but stroke occurred at a median duration of 131 days in patients who had aortic clamping. These finding lead authors to conclude that it is imperative to further improve the outcomes and reduce the incidence of postoperative stroke.

**Article 19**

**HIGHLY RELEVANT**

**HEMOLYSIS: A HARBINGER OF ADVERSE OUTCOME AFTER LEFT VENTRICULAR ASSIST DEVICE IMPLANT**

This study was conducted to examine the importance of elevated serum markers of hemolysis in patients who have LVADs. 182 patients with HeartMate II implants were closely managed for elevations in their LDH and serum-free hemoglobin levels. Two definitions were used for hemolysis on these patients, the first was defined by INTERMACS and the other was defined by LDH. The results were that hemolysis occurred in 32 patients by INTERMACS criteria and in 68 patients by LDH criteria. This was recorded over 427 days. Authors conclude that serum hemolysis marker elevations are associated with an increase in LVAD events. LDH monitoring provides an earlier diagnosis of adverse events that monitoring serum-free hemoglobin, which means that there is a need for a new INTERMACS definition of hemolysis in LVADs.

**Article 20**

**HIGHLY RELEVANT**

**THROMBOLYTIC THERAPY FOR THROMBOSIS OF CONTINUOUS FLOW VENTRICULAR ASSIST DEVICES**

Patients implanted with LVADs remain at high risk for developing thrombus and very limited data exists for the management of pump thrombus. In this study authors present a series of 8 patients with LVAD implants who showed signs of intravascular hemolysis secondary to pump thrombus. These patients were treated with inteventricular thrombolytic therapy. These patients were studied from September 2011 to May 2012. The results of the study were that only 3 patients were treated with tPA, which resulted in
recovery of hemolysis and dissolution of thrombus. In the remaining 5 patients the thrombolytic therapy failed. Thrombus and hemolysis could not be eliminated in these patients. One patient required an emergency pump exchange. Two patients progressed to cardio shock and died. Another patient suffered from a debilitating stroke, which led to having care withdrawn, and the last patient underwent cardiac implantation. Before offering a patient thrombolytic therapy, the patient’s health needs to be carefully assessed. Often tPA, as shown in this study will not rid thrombus or the presence of hemolysis, and pump exchange becomes the second mode of action but pump exchange is no less complicated. There is no guarantee that the newly implanted pump won’t develop recurrent thrombosis, as shown in the 2 patients in this study. Authors conclude that in the event that thrombosis is present, thrombolytic therapy is an alternate treatment in only a subset of patients. Candidacy for patients needs to be carefully weighed, due to running the risks of hemorrhage and thromboembolism.

**Article 21**

**HIGHLY RELEVANT**

**LATE BLEEDING AND NEUROLOGICAL SEQUELAE AFTER HEARTMATE II LEFT VENTRICULAR ASSIST DEVICE: RISK FACTORS FROM THE PREQUEL**

Najjar, Samer S. “Late Bleeding and Neurological Sequelae After HeartMate II Left Ventricular Assist Device.” *Journal of the American College of Cardiology*: Vol. 63, No. 9, 2014

The article discusses the study by Boyle et al.(Reference Number 6 in the article), which is a retrospective analysis included 956 patients (220 women, 23%) who were being implanted with the HeartMate II device and who survived to hospital discharge. During a median follow-up of 1.5 years, 38% of patients suffered a bleeding event (nearly one half of them due to gastrointestinal bleeding), 8% had a hemorrhagic stroke, 6% had an ischemic stroke, and 4% had a pump thrombosis. The striking finding is that female sex was a risk factor for all 4 events (late bleeding, hemorrhagic stroke, ischemic stroke, and pump thrombosis). In this study, women with LVADs had a 67% higher incidence of post-discharge bleeding than men. Of particular concern, women also had a nearly two-fold higher rate of both hemorrhagic and ischemic strokes than men, a finding that could not be attributed to differences in body size. Importantly, women enrolled in the HeartMate II BTT clinical trial and in other LVAD studies have a survival similar to men. Thus, a higher neurological event rate in women than men, even if confirmed in future studies, should not dissuade centers from considering mechanical circulatory support in women. The article further outlines that integrating all this information should allow to tailor anticoagulation and antiplatelet strategies to balance the bleeding and thrombotic profiles of a given patient.
Article 22

HIGHLY RELEVANT

OUTCOMES AFTER IMPLANTABLE LEFT VENTRICULAR ASSIST DEVICE REPLACEMENT PROCEDURES

The article discusses the outcomes of LVAD replacements/exchanges at a reputed center, the Duke University Medical Center. From 2003 to 2012, over 342 LVADs were implanted and out of which 30 patients underwent 35 LVAD replacements/exchanges. The three major indications for LVAD replacement were mechanical/electrical failure about 57%, hemolysis/thrombosis about 29% and infection about 14%. The survival outcomes were worse for patients undergoing device replacement compared to the primary patient cohort. Given the findings discussed in the article, earlier timing for pump replacement and therapeutic strategies, which address monitoring and treating patients who develop early signs of device failure, infection or thrombosis, will significantly improve outcomes.

Article 23

RELEVANT

DRIP AND SHIP THROMBOLYTIC THERAPY FOR ACUTE ISCHEMIC STROKE

The article reports on data analyzed for patients with ischemic stroke treated with tPA. The data was analyzed using the US national Get With The Guidelines (GWTG)-Stroke registry, where in 44,667 patients administered with tPA were analyzed. There were two methods compared, the Drip and Ship method, whereby tPA is administered locally in an emergency department followed by transfer to a stroke center, the Front-Door method, where tPA is administered to directly admitted patients at a stroke center. The drip and ship method accounts for 1 in 4 of the patients with acute ischemic stroke treated with tPA. Outcomes in patients treated by the drip and ship method showed modest differences in mortality and symptomatic intracranial hemorrhage, compared with those of directly admitted Front-door patients treated with tPA. Ship and drip method evolved to be important from a standpoint of timely administration of tPA as a critical determinant of efficacy.
Article 24

SOMETHING RELEVANT

VENTRICULAR RECONDITIONING AND PUMP EXPLANTATION IN PATIENTS SUPPORTED BY CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES
Frazier, O.H., et. al. “Ventricular reconditioning and pump explantation in patients supported by continuous-flow left ventricular assist devices” The Journal of Heart and Lung Transplantation, 2014

This article reports on ventricular reconditioning and subsequent device explantation after long-term LVAD support. Between August 2006 and January 2014, 30 patients out of the 657 patients supported with continuous-flow LVADs, at Texas Heart Institute, were evaluated and assessed for device explantation. Each patient underwent an individualized process of weaning. After varying reconditioning periods, 27 patients (ranging from 27 to 61 years, 16 men and 11 women) underwent LVAD explantation and 3 patients could not be weaned eventually underwent heart transplantation. Out of the 27 patients explanted, there were two deaths despite satisfactory native cardiac function. One patient required resumption of LVAD support almost 2.7 years after device removal and the remaining 25 patients were transitioned to medical therapy with most of them in NYHA class I to II. The article suggests an aggressive approach to ventricular reconditioning with LVAD support with the goal of device explantation and return to medical therapy particularly in young patients with dilated cardiomyopathy.

Article 25

HIGHLY RELEVANT

LEFT VENTRICULAR ASSIST DEVICE THROMBOSIS IN THE SETTING OF LEFT VENTRICULAR RECOVERY
Hurst, Thomas E., et. al. “Left ventricular assist device thrombosis in the setting of left ventricular recovery” The Journal of Heart and Lung Transplantation, 2015

This article presents an outline of a 51 year old patient implanted with HMII as bridge-to-recovery and enrolled in RESTAGE clinical trial. Approximately 9 months after LVAD placement, the patient presented to the emergency department following 3 firings of her implantable cardiac defibrillator for ventricular tachycardia. The patient was admitted for suspected LVAD thrombosis. Low-flow alarms were present on LVAD interrogation, and subsequently the LVAD was explanted. Visual inspection revealed a ring of thrombus formed at pump bearing near the inflow cannula of HMII. Typically for bridge-to-recovery patients it is very challenging to identify early diagnosis of LVAD thrombosis because of the effective recovery of myocardial function. In conclusion, the article outlines that the use of LVADs for bridge-to-recovery continues to increase, monitoring...
for pump thrombosis in this population is essential using biomarkers or more advanced technological solutions.

**Article 26**

**HIGHLY RELEVANT**

**FAILED REPEATED THROMBOLYSIS REQUIRING LEFT VENTRICULAR ASSIST DEVICE PUMP EXCHANGE**


The article presents a case study of a 51 year old male with a HMII LVAD (5 months after implant) with multiple complications, including right heart failure and cardiogenic shock, an INR of 7, hemolysis and renal failure. Acute LVAD thrombosis was suspected. In spite of the patient condition, HMII console reported LVAD parameters within prescribed ranges of 9,200 rpm and flow of approximately 6 L, without excessive pump power and all readings compatible with normal pump function. Multiple interventions of alteplase (tPA) did not restore an adequate pump output, eventually resulting in an emergent pump exchange. The patient had an uncomplicated postoperative recovery and was discharged uneventfully. Inspection of the HMII, identified a thrombus wedged between the spines of the impeller. The case highlights the challenges managing pump thrombosis, were both interventions of intra-ventricular and intravascular thrombolysis failed necessitating a pump exchange. A multidisciplinary approach is recommended in managing these patients.

**Article 27**

**HIGHLY RELEVANT**

**PRIOR HEMATOLOGIC CONDITIONS CARRY A HIGH MORBIDITY AND MORTALITY IN PATIENTS SUPPORTED WITH CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICES**

Fried, Justin, et. al. “Prior hematologic conditions carry a high morbidity and mortality in patients supported with continuous-flow left ventricular assist devices” *The Journal of Heart*

This article presents and examines a study of patients with history or prior hematologic conditions who underwent continuous flow LVAD implantation. The retrospective study highlights selection of 12 patients with baseline hematologic conditions out of the 286 patients implanted with an LVAD between April 2008 and December 2013 at Columbia University Medical Center. The 12 patients were considered to have a significant hematologic condition predisposing them to either bleeding or thrombotic events. There was a high frequency of thrombotic (0.57 event per patient-year), neurologic (0.36 event per patient-year) and bleeding (0.64 event per patient-year). The survival rates decreased over the 2 year period, the 12 month was 81.8% fell to 49% at 24 months. The article
questions the benefit of the LVAD therapy with patients with preexisting hematologic conditions and the appropriate management with regard to anticoagulation. The article recommends that further studies are warranted in such patients.

**Article 28**

HIGHLY RELEVANT

AN ANALYSIS OF PUMP THROMBUS EVENTS IN THE HEARTWARE ADVANCE BRIDGE TO TRANSPLANT AND CONTINUED ACCESS PROTOCOL TRIAL


The article presents a study of patients who underwent HVAD implantation as part of the HeartWare BTT trial and subsequent Continued Access Protocol (CAP). Out of the 382 patients who were part of the BTT trial and CAP, 31 patients were studied with 34 pump thrombotic events, which is 8.1% of the cohort at a rate of 0.08 events per patient per year. Out of the 31 patients, 15 patients (50%) were treated successfully with Medical therapy which consisted of heparin, glycoprotein (GP)2b/3a antagonists (e.g., eptifibatide), and tPA, used individually or in combination. The remaining 15 patients, 8 patients underwent pump exchange after failed medical therapy, 2 patients underwent heart transplantation and 5 died after failed medical therapy and pump exchanges. The interesting statistics is the survival rates with and without thrombus at 1 year was 69.4% and 85.5% respectively. The article suggests that pump thrombosis event rates could be reduced through careful adherence to patient management guidelines like monitoring of blood pressure and instituting anti-coagulation therapies.

**Article 29**

HIGHLY RELEVANT

PUMP THROMBOSIS- A RIDDLE WRAPPED IN A MYSTERY INSIDE AN ENIGMA


This article is part of a keynote lecture series which reviews the state of the art regarding the subject of pump thrombosis. The historical context of pump thrombosis and the clinical data are described in detail. The article further clarifies the origination factors of
pump thrombosis and discusses some of the preventive strategies like monitoring of INR and patient coagulation. The article further reviews the diagnostic approaches along with patient management principles and treatment options are discussed. The article concludes and recommends further studies to unravel mysteries of pump thrombosis.

**Article 30**

**SOMEWHAT RELEVANT**

**EFFECTS OF LEFT VENTRICULAR ASSIST DEVICE SUPPORT ON BIOMARKERS OF CARDIOVASCULAR STRESS, FIBROSIS, FLUID HOMEOSTASIS, INFLAMMATION AND RENAL INJURY**


The article outlines the study carried out at Duke University Medical Center, to examine changes in a broad panel of biomarkers following LVAD implantation. The study enrolled 37 patients, 17 patients received the HVAD LVAD and 20 patients received the HMII LVAD. A broad panel of biomarker levels were measured in frozen plasma collected from 37 individuals prior to continuous flow LVAD implantation and repeated again after a median of 136 days after implantation. Despite improvement over time, the comparison of the absolute values of cardiovascular biomarkers of myocardial stretch, fibrosis, fluid homeostasis, and inflammation improved with long-term LVAD use but remained higher than previously noted in patients with chronic heart failure patients. The results suggest the need for targeted therapeutic interventions to mitigate such abnormalities and potentially increase rates of myocardial recovery.

A successful technique for surface immobilization of heparin with preserved anticoagulation activity is covalent end-point immobilization. This avoids compromising the functional activity of the molecule and allows the molecule to extend from the surface into the fluid phase where it is free to interact with coagulation factors and inhibitors in the blood. The catalytic nature of heparin is a critical property because the immobilized heparin is not functionally exhausted during exposure to blood, but remains a stable catalytic activity on the surface.
Attachment D –

VAD Maintenance System Literature Review
Summary and Conclusion

VAD MAINTENANCE SYSTEM LITERATURE REVIEW SUMMARY

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Literature Review Summary:

A thorough review of literature, specifically peer reviewed articles gathered from PubMed, revealed and confirmed the prevalence and hazard of thrombus forming within approximately 6.4-8%\(^{1234}\) of all implanted LVAD devices currently approved for human use. The bulk of the articles indicated that even though the currently approved LVADs are offering good results they occasionally continue to be subject to the formation of thrombus that causes hemolysis signaled by a rise in plasma free hemoglobin a \(>6X\) rise from baseline of LDH\(^{56}\), activated platelets and finally a pump-stopping thrombus. These results persist for several reasons including neglect of therapeutic levels of systemic anticoagulation while being supported by an LVAD and imperfect LVAD design. The most prevalent resolution for a thrombosed LVAD appears to be an exchange of the device for a new one. This exchange is hazardous to the patient even if successful and certainly is expensive. The one year survival after pump exchange was reported as about 80%, about 65% after the second replacement, and only 50% after the third exchange\(^{7}\). These authors conclude that prevention of pump malfunction and pump thrombosis is crucial if this therapy is to continue to grow and be considered effective. One alternative to replacing or exchanging a thrombosed LVAD includes aggressive systemic anticoagulation including heparin and enhanced anti-platelet therapy to reduce a formed thrombus and return the device to its normal operating parameters.\(^{8}\)

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aggressive approach is to use systemic tPA (a recombinant tissue plasminogen activator) however complications can be severe and include cerebrovascular attack (stroke).  

Another approach described and used with limited success was to deliver tPA into the pump with a catheter, guided through the femoral artery around the aortic arch through the aortic valve directly into the inflow of the LVAD. Clinicians infused tPA at a rate of 1 mg/min for a total of 30 or 50 mg. This method appeared to work when the thrombus was treated very early in its formation but again the systemic exposure of the body to tPA risked stroke and other forms of bleeding. This method did have the benefit of greatly reducing the volume of tPA used compared to the systemic approach.


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In conclusion, these articles and their authors point to a need for LVAD pumps and anticoagulation systems that work together to eliminate the adverse event of thrombus and subsequent pump failure because the treatment for this failure is ultimately risky and increases mortality and morbidity. The hazards associated with aggressive use of system thrombolytic drugs or exchanging the pump for a new device will ultimately limit the usefulness of this heart failure therapy. An alternative that was not mentioned in any article or found in the larger search was to use minimally invasive methods to rehabilitate the LVAD or removed thrombosis within the pump without exposing the patient to the potentially dangerous systemic thrombolytic drugs. The lack of reference to safer alternatives to treat an LVAD thrombus indicates there is an opportunity for innovation and satisfies the goal of this literature review to determine if there is sufficient relevant clinical data available to demonstrate the need for a VAD Maintenance System.

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March 18, 2002


Survey #2
Launched Mid December 2014 and closed mid-January 2015

It is estimated that approximately 6,500 LVADs were implanted in the year 2014. It is expected that the worldwide 2014 LVAD sales will approach ¾ of a million dollars.

Without revealing any privileged detail, one hundred and four centers responded to the VAD Maintenance Survey representing 3,040 LVAD implants year to date or 47% of the estimated 2014 implants.

Responding German centers implanting 519 LVADs indicated that 70% were HeartWare HVAD and 19% Thoratec HeartMate II (HMII). Fifty six LVADs were replaced representing a replacement rate of 10.76%. As illustrated below 64% of the German Centers indicated that build up under the HVAD impeller was a reason for replacement. Use this example to interpret the chart below.

Forty seven USA centers responding implanted 1,731 LVADs. They indicated the ratio was 65% Thoratec HMII, 3% Thoratec HMIII and 32% HeartWare HVAD. One hundred and seventy one LVADs were replaced representing a replacement rate of 9.9%. Thirty six of the 47 US Centers (77%) indicated that build-up on the bearings of the Thoratec HMII had necessitated the replacement.
One hundred and four worldwide centers that responded indicated that 43% of the implants were HeartWare HVAD and 53% were Thoratec HMII. As illustrated below 64% of the centers indicated that build up on bearings of the Thoratec HMII was a reason for replacement. Two hundred and fifty one LVADs were replaced representing a replacement rate of 9%.
The remote monitoring survey conducted in September produced a large response and dependable data with a 2% standard deviation.

Since we at ReliantHeart are intimately familiar with the value of True Flow Measurement and the display of the Amplitude of Flow, it was surprising to us that power consumption by the pump was considered by the clinicians to be the most important indicator of pump performance and thus on the top of the Remote Tracking list. True Flow Measurement along with Blood Pressure and Pump Speed achieved a 70% importance and INR Tracking a 75% importance.

![Remote Monitoring Features - % of Importance](image)

It is clear that clinicians are now solidly focused on reducing adverse events associated with LVADs. The generous and liberal response of the clinicians to the surveys and the results of both surveys have led us to the following conclusions and actions:

We will accelerate the VAD Maintenance System to regulatory review.
Survey #3
March 16 – 24, 2015

Survey results have been compiled and tallied as to LVAD Maintenance, Driveline Complications and TET. This survey was launched March 16th, and tallied March 24th.

The findings below have been excerpted from the survey summary and pertain only to LVAD service.

Adverse events due to administering tPA to alleviate pump occlusions in 117 out of 792 LVADs resulted in unsatisfactory outcomes 83% of the time.

As seen below 53% of pump occlusions were treated with tPA.

**Question:** Do you attempt to alleviate LVAD occlusions with tPA?

![Bar Chart]

And 52% of the pumps treated with tPA experienced recurrence of occlusion, 34% of the patients experience stroke and 15% died.
**Question:** What are the most common outcomes following administration of tPA?

In a survey compiled in December 2014, one hundred and four worldwide centers responded indicating that 43% of their 3,040 implants were HeartWare HVAD and 53% were Thoratec HMII. As illustrated below 64% of the centers indicated that thrombus build up on the bearings of the Thoratec HMII was a reason for replacement. Two hundred and fifty one LVADs were replaced representing a replacement rate of slightly greater than 8%.

The respondents to the current survey indicated that out of 792 LVADs, 80 (10%) were exchanged in keeping with the earlier reported replacement rate of a bit over 8%.
The detail below indicates that 63% of the LVAD exchanges led to unsatisfactory results; death, stroke or recurrence of the occlusion.

**Question:** If an LVAD must be exchanged due to occlusion, what are the most common patient outcomes?