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Early Signatures of Bleeding and Mortality in Patients on Left Ventricular Assist Device Support: Novel Methods for Personalized Risk-Stratification

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Abstract

Background—Left ventricular assist devices (LVAD) provide support for patients with end-stage heart failure. Aims of this study were to determine whether baseline analysis and early trends in routine laboratory data, platelet activity, and thromboinflammatory biomarkers following LVAD implantation reveal trends that predict personalized risks of one-year gastrointestinal (GI) bleeding, stroke, pump thrombosis, drive-line infections, and mortality in patients on LVAD support.

Methods—We performed an observational study at the University of Kentucky with 61 participants who underwent first-time LVAD implantation. Blood was collected at baseline and post-op days 0, 1, 3, and 6 as well as clinical follow-up. Demographics, clinical characteristics, one-year adverse events, and routine laboratory data were collected from electronic medical records. Platelet function and plasma biomarkers were profiled.

Results—Evaluation of routine laboratory results revealed that sustained thrombocytopenia and increased mean platelet volume (MPV) were associated with development of GI bleeding and mortality. Platelet function at follow-up visit predicted one-year bleeding events. Thrombotic biomarker sCD40L strongly predicted one-year GI bleeding at baseline before implantation and within the first week following LVAD implant.

Conclusions—Early trends in routine bloodwork and platelet function may serve as novel signatures of patients at risk to experience adverse events.

Keywords

Platelet; Inflammation; VAD; Thrombocytopenia; Heart Failure; MPV

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Introduction

Left ventricular assist devices (LVADs) serve a crucial role in severe heart failure. Currently, more than 5.7 million Americans have heart failure, with projections of 400,000 to 700,000 new cases yearly, and an average 5-year survival rate of only 50% (Levy et al., 2002, Writing Group et al., 2016). Although pharmacologic and resynchronization therapies have improved chronic management, definitive treatment now often requires mechanical circulatory support or heart transplantation (Puehler et al., 2014). Due to the supply-demand mismatch for donor hearts, LVADs are increasingly employed. By some estimates, more than 250,000 patients are eligible yearly (Miller et al., 2013, Slaughter et al., 2009).

Survival and quality of life are significantly improved in patients on LVAD support (Allen et al., 2010); however unique complications frequently develop due to the simultaneous risk of thromboembolic and bleeding events (Blitz, 2014). Pump thrombosis rates have decreased with better anticoagulation protocols and improved biomechanical engineering of devices (Krabatsch et al., 2017, Mehra et al., 2017, Schroder and Milano, 2017). Yet gastrointestinal (GI) bleeding and stroke remain highly problematic sources of extended hospital readmissions, patient duress, and mortality (Tchantchaleishvili et al., 2014). In particular, GI bleeding occurs in 30 to 75% of patients during the first year on LVAD support and a develops early with a median time to event of only 1.6 months following implantation (Crow et al., 2010b, Harvey et al., 2014, Meyer et al., 2010).

Mechanistically, LVADs introduce supraphysiologic shear stress and significantly disrupt normal laminar blood flow (Bartoli et al., 2015, Shah et al., 2017), leading in part to platelet destruction, increased platelet activation, and the formation of platelet-mediated thrombi (Tarzia et al., 2014). Shear can unfold von Willebrand factor (vWF) (Bartoli et al., 2015, Crow et al., 2010a), a multimeric adhesion glycoprotein crucial for hemostasis, thereby exposing sites for the metalloprotease enzyme ADAMTS13 that cleaves vWF into smaller non-active multimers (Bartoli et al., 2015, Geisen et al., 2008, Jilma-Stohlawetz et al., 2016). An acquired vWF deficiency results that reverses upon device removal with cardiac transplantation or successful bridge to recovery (Bartoli et al., 2015, Geisen et al., 2008, Heilmann et al., 2010, Patel et al., 2018, Slaughter et al., 2009, Uriel et al., 2010, Yuan et al., 2012). While acquired vWF deficiency inherently increases risks of bleeding and hemorrhagic stroke, studies show that vWF levels are laborious to quantify and not predictive of bleeding or stroke events (Boyle et al., 2009, Crow et al., 2010a).

Following the results of the HeartMate II Pivotal and PREVENTion of HeartMate II Pump Thrombosis Trials, anticoagulation, e.g. with warfarin and aspirin, is employed to prevent thrombosis in the setting of device foreign surfaces and heat production (Maltais et al., 2017). While such anticoagulation use alone increases the risk of bleeding, patients on LVAD support have higher bleeding risks compared to matched patients receiving analogous anticoagulation therapy but without a LVAD (Adatya and Bennett, 2015). Currently, no anticoagulation standard has reached national consensus and the suitability of automatic chronic anticoagulation in all patients has recently been questioned (Kilic A KM, 2017). This reflects an opportunity for the evaluation of personalized risk analysis to assist with the evolving clinical management of patients on LVAD support.

At present, little data is available to identify patients at risk of develop adverse events while on LVAD support. Such tools would personalize clinical care, patient education, and guide management as well as long-term surveillance for complications (Maltais et al., 2017). To investigate further, our studied aimed to determine whether baseline analysis and early trends in routine laboratory data, platelet activity, and thromboinflammatory biomarkers following LVAD implantation may reveal: 1—pathophysiologic responses to LVAD hemodynamics and 2—signature trends that help predict personalized risks of one-year gastrointestinal (GI) bleeding, stroke, pump thrombosis, drive-line infections, and mortality in patients on LVAD support.

Methods and Materials

Study Population

We performed a single-center observational study of enrolled 61 patients undergoing first-time implantation of a continuous-flow LVAD between March 2014 and August 2016. Eligibility criteria included age over 18 and selection to undergo implantation of a HeartMate II (ThoratecCorp, Pleasanton, CA) or HeartWare (HeartWare International Inc., Framingham, MA) device. Standard operating and clinical procedures were employed for implantation. Post-operative care was per institutional standards. Baseline patient demographics were obtained from the electronic medical records (EMR). The Institutional Review Board at the University of Kentucky approved the study and all patients gave written informed consent for study participation.

Sample collection

Venous blood was collected 1 day before surgery for baseline analysis. Following VAD implant, venous blood samples were collected on post-op days 0, 1, 3, and 6. In 42 of the 64 patients, platelet function and thromboinflammatory biomarkers were profiled. In a smaller cohort ($n = 22$), a follow-up sample was collected between 3 and 12 months of VAD implant. A total of 172 samples were collected for an average of 4 samples per patient.

Platelet Activity Analysis

Multiple electrode aggregometry (MEA) was performed using the Multiplate device (Roche, Basel, Switzerland) as previously described (Sexton et al., 2016) using hirudin-anticoagulated blood diluted with saline solution (0.9%) at a 1:1 ratio. Aggregation was continuously recorded for 6 minutes and reported as area under the curve (AUC), an integrated measure of velocity and maximal aggregation and expressed in arbitrary units (U) (Sexton et al., 2016).

Biomarker Analysis

For biomarker analysis, blood was collected into CTAD (citrate-adenosine-theophylline-dextrose) supplemented with EDTA (to a concentration of 10mM). Samples were centrifuged at 3000g for 10 minutes and plasma was immediately harvested, flash frozen, and stored at -80°C . Plasma sCD40L concentrations were measured using multiplex kits (Millipore) and detected using a MAGPIX multiplex reader. Healthy plasma was obtained

and pooled from 5 healthy volunteer donors and included as internal reference standards in assays with LVAD patient samples.

Clinical Data and Adverse Clinical Events

Clinical data were collected via the EMR for inpatient and outpatient visits at the University of Kentucky and entered into a de-identified and protected database (REDCap). Platelet concentration and mean platelet volume (MPV) during the first seven days following implantation were obtained from each patient's EMR. Additionally, MPV was recorded from EMR at each patient's 30 day follow-up visit. Clinical outcomes were captured within one year following LVAD implantation and included GI bleeding, hemorrhagic stroke, embolic stroke, pump thrombosis, driveline infection, readmission, and all-cause mortality. GI bleeding was defined by endoscopic diagnosis or documented guaiac-positive stool, melena, or hematochezia. Hemorrhagic and embolic stroke events were diagnosed by CT or MRI. Pump thrombosis was defined by documented diagnosis with resultant medical or surgical intervention. Driveline infection was defined by documented clinical diagnosis and treatment.

Statistics

Statistical summaries are reported as mean $\pm$ standard deviation (SD) for normally distributed variables or medians and range for skewed data. Graphical display of data distribution includes boxplots with the typical five-number summaries (i.e., minimum, first quartile, median, third quartile, and maximum). Significance between two categorical variables was assessed via Fisher's exact test. Repeated measurements among the individual time points were analyzed with linear mixed-effects models to compare baseline trends over time among the sub-groups within the cohort, with random effects accounting for within-subject correlation. In general, unstructured correlation matrix with unequal variances was assumed to account for dependence among observations over time and within a subject. For limited sample sizes, compound symmetric correlation structure was adopted to ensure model convergence. In cases of skewed distribution of clinical marker measurements (e.g., the distribution of platelet count), analysis was completed on the natural logarithm scale. For all tests, $\alpha=0.05$ level was used to conclude statistical significance. The analysis and graph generation were performed using R (version 3.2.0) statistical software and SigmaPlot (version 13).

Results

Study Cohort Characteristics

Between March 2014 and August 2016, 61 patients undergoing first time LVAD implantation at the University of Kentucky were prospectively enrolled for this study. Baseline demographics are presented in Table 1. The mean age at time of implant was 55.7 years old (range 33–77). Nine (15%) were female; 52 (85%) were Caucasian and 9 (15%) were African-American. Forty six (75%) received the HeartMate II® and 15 (25%) received the HeartWare®. The only statistically significant difference in demographics and clinical baseline characteristics between device groups was that the HeartMate II cohort was

associated with destination therapy (98%) while the HeartWare cohort was associated with bridge therapy (87%) ($p < 0.001$).

Within the first year on LVAD support, 13 participants (21%) received a heart transplant with a median time from LVAD implantation to transplantation of 7 months. In these participants, no adverse clinical events of GI bleeding, stroke or mortality occurred during the period following transplantation to one year from LVAD implantation. No data were removed from statistical analysis to adjust for participants bridged to transplant.

There were no differences in the initiation of anticoagulation. The INR goal was between 2.0 and 3.0. The median time to goal after surgery was 8 days (range 6 – 18 days) in bleeders and in 7 days (range 2 – 19 days) for non-bleeders. After two bleeding episodes, the INR goal was lowered to a range of 1.8 to 2.5. At follow-up, the INR was 1.9 ± 0.9 (mean $\pm$ SD) in bleeders and 2.5 ± 0.8 in non-bleeders (data not shown).

Adverse Clinical Events of Cohort, Device Groups, and Gender

One-year clinical outcomes are listed in Table 2. Following LVAD implantation, the average length of hospital stay following implantation was 21 days. Three patients (5%) were never discharged. Of those discharged, readmission rates were 21% by 3-months post-discharge, 66% by 6-months post-discharge, and 83% by 12-months post-discharge. Of the 61 enrolled patients, 55 survived 6-months (90%) and 51 survived one year (84%). Within the first year following LVAD implantation, 13 patients (21%) had at least one episode of gastrointestinal (GI) bleeding, while 9 (15%) had multiple episodes of GI bleeding. 13 patients (21%) had stroke (all-types), and further analysis revealed that hemorrhagic stroke occurred in 6 (10%) while ischemic stroke occurred in 7 (11%). Pump thrombosis occurred in 8 patients (13%). Drive-line infections were diagnosed in 18 (30%). There were no statistical differences in one-year outcomes between the two devices (Table 2).

All patients received blood product during the implant surgery. Forty-two (69%) of the patients received blood products in the week following implant. Sixteen (26%) received a single unit of blood product in the week following implant while 26 (43%) patients received 2 or more units. There was no correlation between post-procedure blood transfusion and one-year outcomes.

Interestingly, no females in the study population had any episodes of GI bleeding. However, among enrolled patients, only 9 were female (15%), so there is no appreciable association between gender and risk of GI bleeding ($p = 0.184$). However, only 5 out of 9 females (56%) survived twelve months, while 44 out of 52 males (85%) survived this benchmark ($p = 0.065$). Nonetheless, this association between gender and mortality did not reach statistical significance and the trend is most likely due to a small number of females receiving an LVAD during the study period. There were no further statistically significant associations discovered between gender and adverse clinical outcomes.

Platelet Count in Response to VAD Implantation

Prior to implantation, baseline median platelet counts were $200 \times 10^3/\mu\text{L}$ (interquartile range (IQR): $150 - 247 \times 10^3/\mu\text{L}$) (Table 3). Median values with IQRs are reported due to the

skewed distribution nature of data. Median platelet count decreased by 46% between baseline and post-op day 3. During this time, 87% of patients were thrombocytopenic, as defined by a platelet count $<150 \times 10^3/\mu\text{L}$. Platelet counts reached a nadir between post-op day 2 and 3 and began to recover in a non-linear fashion by post-op day 4. By the end of the first week, median platelet counts reached $221 \times 10^3/\mu\text{L}$ (IQR: $149 - 256 \times 10^3/\mu\text{L}$), and returned to the baseline levels ($p = 0.969$). No statistically significant differences in platelet count were observed between HeartMate II and HeartWare devices at any time point (all $p > 0.05$; Figure 1A).

In order to determine if platelet count predicted one-year outcomes, values were correlated with GI bleeding, stroke, driveline infections, pump thrombosis, and mortality. Baseline platelet count and the initial decline were similar between bleeders and non-bleeders. A statistically significant trend emerged overtime after implantation. Platelet count was on average 25% lower in bleeders than non-bleeders on post-op day four (Tukey-adjusted $p = 0.023$), 24% lower at day five ($p = 0.055$), and 29% lower by post-op day 7 ($p = 0.031$) (Figure 1B). Thus, in patients who went on to bleed, thrombocytopenia following LVAD implantation was more significant and sustained as compared to non-bleeders. Further, patients that survived within 1 year of VAD implant had statistically higher platelet count levels post-operatively than those who died. Specifically, future survivors had 30% higher platelet counts than non-survivors at day five (Tukey-adjusted $p = 0.041$), 40% higher at day 6 ($p = 0.012$), and 50% higher at day seven ($p = 0.002$) (Figure 2A). No statistically significant correlations were found between platelet count and stroke, pump thrombosis, or drive-line infections (Supplemental Figure 1).

Sustained Increase in Mean Platelet Volume May Predict Long-Term Bleeding and Mortality

To investigate if the decline in platelet count could be attributable to a decline in platelet production, mean platelet volume (MPV) was analyzed. Median MPV was found to slightly increase following LVAD implantation, reaching a peak between post-op day two and three (Table 3). Similar MPV patterns were observed between the two VAD device types (Figure 1C). Similar to the evaluation of platelet count, a multivariate analysis of early post-implant MPV patterns and each one-year adverse clinical outcome of interest was performed. Future bleeders had statistically significant higher MPV levels over the first week as compared to those who did not go on to develop GI bleeding during the first year (non-bleeders) (Figure 1D). Specifically, during the early post-implantation period, MPV in future bleeders was 8% higher on post-op day five (Tukey-adjusted $p = 0.005$), 11% higher on post-op day six ($p < 0.001$) and 12% higher on post-op day seven ($p < 0.001$). In addition, early MPV levels were also strongly predictive of one-year mortality (Figure 2B). Patients that survived 1 year after VAD implant had statistically lower MPV levels post-operatively than those who survived. By post-op day 6, survivor MPV levels were 8% lower than non-survivor ones (Tukey-adjusted $p = 0.011$) and 7% lower by post-op day 7 ($p = 0.028$) (Figure 2B). There were no statistically significant associations with early MPV levels following implantation in those who developed stroke, pump thrombosis, or drive-line infections within one year (Supplemental Figure 2). Furthermore, there were no significant differences in MPV at 30 day follow-up for any of the recorded outcomes (data not shown).

Platelet Dysfunction as a Response to VAD Implantation

Platelet aggregation in response to PAR-1 activating peptide (TRAP), adenosine diphosphate (ADP), collagen, or ristocetin was measured by Multiplate impedance aggregometry in samples of whole blood. Average Area Under Curve (AUC) values along with the standard deviations of these platelet dysfunction measurements are presented in Table 4. In general, platelet activity declined immediately upon LVAD implantation. TRAP-induced aggregation decreased 27% ($p = 0.007$) right after operation and remained below the baseline level till post-op day 7 (23% lower on day 7; $p = 0.041$). ADP-induced aggregation significantly decreased by 37% ($p < 0.001$) immediately upon LVAD implantation and remained significantly lower than baseline level through post-op day three ($p = 0.001$). A similar pattern was observed with high-dose ristocetin-induced aggregation, which was reduced by 66% ($p < 0.001$) immediately upon LVAD implantation and remained 31% lower than baseline levels through post-op day three ($p = 0.029$). Collagen-induced aggregation was not consistently altered. Platelet aggregation in HeartMate II and HeartWare patients did not differ significantly between the two devices (Supplemental Figure 3).

None of the platelet dysfunction measurements (TRAP-, ADP-, collagen- or ristocetin-induced aggregation) within a week after VAD implantation was predictive of one-year bleeding events (Figure 3A–D). However, at the follow-up visit, future bleeders demonstrated a significantly higher ristocetin-induced aggregation (103%) than those of non-bleeders (Tukey-adjusted $p = 0.006$). (Figure 3D).

sCD40L as a Baseline Biomarker of Platelet Dysfunction and Long-Term Bleeding Risk

Soluble CD40 Ligand (sCD40L), a biomarker released into circulation by activated platelets, was measured at baseline, immediately after implant, on post-op days 1, 3, and 7, as well as during a follow-up visit. Although no statistically significant changes in aggregate sCD40L levels occurred following LVAD implantation between the two device types (Figure 4A), baseline, post-op, and post-op day 3 sCD40L measurements were associated with one-year bleeding events (Figure 4B). Indeed, at baseline, future bleeders had sCD40L levels that were 328% higher than those of non-bleeders (Tukey-adjusted $p < 0.001$). Furthermore, post LVAD implantation, sCD40L levels remained 100% higher (i.e., twice as much) in future bleeders on the first day ($p = 0.002$) and 175% higher on post-op day 3 ($p = 0.010$) (Figure 4B). No significant differences were observed in sCD40L levels in the outcomes of stroke, pump thrombosis, drive-line infection, or mortality.

Discussion

In this study, we performed an extensive characterization of thromboinflammatory responses to LVAD support to date, in order to identify early clinically-relevant signatures to predict long-term adverse events such as bleeding and thrombosis. Immediately following LVAD implantation, platelet count declined and was accompanied by a subsequent increase in MPV, presumably reflecting the release of young platelets from sites of production such as the bone marrow and lung (Lefrancais et al., 2017). We and others have recently published that persistent thrombocytopenia after TAVR predicts mortality, and several studies have suggested an association between the severity of thrombocytopenia and long-term mortality

after surgical interventions (Lefrancais et al., 2017, Overgaard et al., 2008). The reason for this remains elusive. In this study, MPV was also significantly higher in patients who developed GI bleeding. The increase in MPV suggests that a reactive thrombocytosis occurs, and is possible that it is this response, rather than the decline in platelet count, that accounts for associated long-term adverse outcomes.

To analyze platelet activity in LVAD recipients, we selected the Multiplate aggregometry method, as this assay has been demonstrated to predict both clinical bleeding and thrombosis after percutaneous coronary intervention (Raphael et al., 2016). Following implantation, we found that aggregate platelet dysfunction developed, with more persistent changes observed in ADP and ristocetin-induced aggregation pathways. However, collagen-induced platelet aggregation was significantly different among patients who subsequently bled and those that did not, even during the early post-implantation period when no patients were exposed to anticoagulants that act on the ADP-platelet receptor. Future GI bleeding was also strongly associated with particular responses in the ristocetin-induced pathway, which requires von Willebrand Factor (vWF). While activity through the ristocetin pathway was decreased in future bleeders relative to non-bleeders during the first week on LVAD support, the activity profile changed by follow-up. This is particularly interesting as it is known that patients on LVAD support develop an acquired vWF syndrome (Meyer et al., 2010). Perhaps although measured vWF does in fact decrease, patients most at risk of developing bleeding eventually foster an innate protective response. In general, there was a trend towards higher platelet function at follow-up. The presence of heparin at early time points may have particularly impaired vWR-dependent platelet function. Whether there is a biologic significance to the differences in ristocetin-platelet function is not clear at this point. Further evaluation of platelet activity during the follow-up period is underway.

Conclusions

Profiling patient risks is before and immediately following LVAD implantation is a particularly opportune time because they are hospitalized and early identification of patients at risk could improve clinical management, allow for tailored anticoagulation and appointments, and even improve patient education. Our findings suggest that LVAD implantation elicits a thromboinflammatory state that may contribute to post-procedural thrombocytopenia. Importantly, our results add to the growing body of literature that suggests the thromboinflammatory changes that occur early after implantation may predict long-term outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Significance

Left ventricular assist devices provide support for patients with end-stage heart failure. Over the last decade, platelets have been shown to play vital roles that extend well beyond hemostasis. In this work, the authors demonstrate that analyzing platelet parameters following LVAD implantation may be able to stratify risk for longer term adverse events. The findings suggest that LVAD implantation elicits a thromboinflammatory state that may contribute to post-procedural thrombocytopenia. The findings suggest that early trends in routine bloodwork and platelet function may serve as novel signatures of patients at risk to later develop adverse events.

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Figure 1. Acute post-surgical platelet count and MPV predict 12-month bleeding events.

No significant differences were observed in platelet count over the first week following VAD implants between the HeartMate II (white boxes) and HeartWare devices (gray boxes) (A). Patients who developed GI bleeding within one-years following VAD implant had significantly slower platelet count recovery within the first week compared to non-bleeders (B). No significant differences were observed in mean platelet volumes (MPV) over the first week following VAD implants (C). There was a significant difference over the first week in MPV between one-year Non-bleeders and bleeders (D). Boxes represent the 25%–75% IQR with the horizontal line within the box as the median. Whiskers represent the extent of the data range. Significant differences at specific time points are indicated by * where $p < 0.05$.

Figure 2. MPV is associated with one-year mortality.

No significant difference over the first 168 hours after pump implant was observed between survivors and non-survivors in platelet count (A). A significant difference over the first 168 hours was seen in MPV between survivors and non-survivors. Boxes represent the 25%–75% IQR with the horizontal line within the box as the median. Whiskers represent the extent of the data range. Significant differences at specific time points are indicated by * where $p < 0.05$.

Figure 3. Follow-up ristocetin-induced platelet activity predict one-year bleeding events.

No significant difference over the time course after pump implant was observed between one-year bleeder (gray bars) and non-bleeders (white bars) in TRAP-induced (A) or ADP-induced (B), or collagen-induced (C) platelet aggregation. Ristocetin-induced aggregation had significant a difference at follow-up between bleeders and non-bleeders. Significant differences at specific time points are indicated by * where $p < 0.05$.

Figure 4. sCD40L strongly predicted one-year bleeding outcomes.

No significant difference over time was observed in sCD40L levels between the HeartMate II (white bars) and HeartWare devices (gray bars) (A). A strong significance was observed in the levels of sCD40L over time between bleeders within in first year incidence (gray bars) and those that did not (white bars) (B, $p < 0.001$). Means with standard deviations are reported. Significant differences at specific time points are indicated by * where $p < 0.05$.

Study Flow Chart

Table 1.
Baseline demographics and clinical characteristics of study participants:

The majority of cohort participants were male, Caucasian, had New York Heart Association CHF class IV before LVAD implantation, and received a HeartMate II device. Mean (SD) age of participants at time of implant are presented. Comparison between device groups revealed no significant differences other than the goal of VAD therapy. P-values for qualitative variables were calculated using Fisher's Exact test. P-values for quantitative variables were calculated with a two-sample t-test. MI = myocardial infarction, CHF = congestive heart failure.

	Cohort	HeartMate II	HeartWare	p value
Demographics				
Men	52 (85%)	40 (87%)	12 (80%)	0.676
Women	9 (15%)	6 (13%)	3 (20%)	0.676
Age	55.7 (10.1)	56.8 (9.5)	52.2 (11.3)	0.169
Caucasian	52 (85%)	39 (85%)	13 (87%)	1.000
African-American	9 (15%)	7 (15%)	2 (13%)	1.000
Medical History				
Hypertension	46 (75%)	35 (76%)	11 (73%)	1.000
Hyperlipidemia	34 (56%)	24 (52%)	10 (67%)	0.382
Diabetes	31 (51%)	24 (52%)	7 (47%)	0.772
Prior MI	24 (39%)	20 (43%)	4 (27%)	0.363
CHF class III	9 (15%)	8 (17%)	1 (7%)	0.430
CHF class IV	52 (85%)	38 (83%)	14 (93%)	0.430
Ischemic etiology	32 (52%)	24 (52%)	8 (53%)	1.000
Destination therapy	47 (77%)	45 (98%)	2 (13%)	<0.001
Bridge therapy	14 (23%)	1 (2%)	13 (87%)	<0.001

Table 2.
Adverse clinical events within one-year following LVAD implantation:

Presented are the number of cohort participants who experienced at least one adverse event within one year after having VAD implant.

	Cohort (n = 61)	HeartMate II	HeartWare	p value
Gastrointestinal (GI) bleeding	13 (21%)	11 (24%)	2 (13%)	0.489
Multiple GI bleeding episodes 2	9 (15%)	8 (17%)	1 (7%)	0.430
Stroke (all types)	13 (21%)	9 (20%)	4 (27%)	0.718
Hemorrhagic Stroke	6 (10%)	5 (11%)	1 (7%)	1.000
Pump thrombosis	8 (13%)	7 (15%)	1 (7%)	0.666
Drive-line infection (DLI)	18 (30%)	11 (24%)	7 (47%)	0.112
All-cause mortality	12 (20%)	10 (22%)	2 (13%)	0.712
Stroke and GI bleeding	4 (7%)	3 (7%)	1 (7%)	1.000
Stroke + pump thrombosis	4 (7%)	4 (9%)	0 (0%)	0.564
Bleeding + pump thrombosis	2 (3%)	2 (4%)	0 (0%)	1.000
No adverse clinical events	26 (43%)	21 (46%)	3 (20%)	0.127

Table 3:

Platelet Count and Mean Platelet Volume response following LVAD implantation

	Baseline	Post-Op	POD1	POD2	POD3	POD4	POD5	POD6	POD7
Platelet Count	200 (150–247)	139 (101–187) *	122 (102–144) *	109 (88–144) *	108 (94–140) *	124 (104–168) *	135 (111–179) *	171 (117214) *	221 (149–256)
MPV (fl)	10.6 (9.9–11.0)	10.5 (9.9–10.8)	10.8 (10.0–11.2)	10.9 (10.2–11.6) *	10.8 (10.3–11.4) *	10.6 (10.1–11.3) *	10.6 (10.1–11.4) *	10.6 (9.9–11.2)	10.5 (9.8–11.2)

Median values and ranges presented.

*

=p< 0.05 from baseline.

POD= Post-op day from LVAD implantation.

Table 4.

Platelet activity decreases transiently following LVAD implantation

	Baseline	Post-Op	POD1	POD3	POD6	Follow-up (30–160 days)
TRAP	764 (421)	573 (386) *	566 (327) *	471 (310) *	553 (453) *	847 (347)
ADP	533 (263)	335 (243) *	366 (226) *	326 (212) *	474 (344)	659 (341) *
Collagen	309 (200)	262 (230)	336 (223)	273 (177)	231 (179)	275 (176)
Ristocetin	602 (495)	214 (202) *	319 (285) *	416 (341) *	402 (245)	625 (368)

Mean values and standard errors presented.

*
=p< 0.05 from baseline.

POD= Post-op day from LVAD implantation.