Prognostic value of vasoactive-inotropic score following continuous flow left ventricular assist device implantation

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Abstract

BACKGROUND: The purpose of this study is to evaluate the utility of vasoactive-inotropic score (VIS) in predicting outcomes after left ventricular assist device (LVAD) implantation and explore possible mechanisms of post-operative hemodynamic instability.

METHODS: Retrospective review was performed in 418 consecutive patients with LVAD implantation. VIS was calculated as dopamine + dobutamine + 10 × milrinone + 100 × epinephrine + 100 × norepinephrine (all μg/kg/min) + 10000 × vasopressin (U/kg/min) after initial stabilization in the operating room and upon arrival at the intensive care unit. The primary outcome was in-hospital mortality. The secondary outcomes were a composite of in-hospital mortality, delayed right ventricular assist device (RVAD) implantation, and continuous renal replacement therapy. The pre-operative biomarkers of inflammation, oxidative stress, endotoxemia and gut-derived metabolite trimethylamine-N-oxide (TMAO) were measured in a subset of 61 patients.

RESULTS: Median VIS was 20.0 (interquartile range 13.3–27.9). VIS was an independent predictor of in-hospital mortality (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.03–1.09,

$p < 0.001$) and composite outcome (OR 1.03, 95% CI 1.01–1.06, $p = 0.008$). In-hospital mortality increased for each VIS quartile (0% vs 3.9% vs 7.6% vs 12.3%, $p = 0.002$). VIS was superior to other established LVAD risk models as a predictor of in-hospital mortality (area under the curve 0.73, 95% CI 0.64–0.82). The optimal cut-off point for VIS as a predictor of in-hospital mortality was 20. Pre-operative hemoglobin level was the only independent predictor of VIS   20 ($p = 0.003$). Patients with a high VIS were more likely to have elevated TMAO pre-operatively (53.6% vs 25.8%, $p = 0.03$).

CONCLUSIONS: A high post-operative VIS is associated with adverse in-hospital outcomes and is a better predictor of in-hospital mortality compared with existing LVAD risk models. Whether early hemodynamic stabilization using RVAD may benefit patients with a high VIS remains to be investigated.

Keywords

ventricular assist device; inotropes; vasopressors; in-hospital mortality; trimethylamine-N-oxide

The use of durable continuous flow left ventricular assist devices (LVADs) has been shown to improve the survival and quality of life in patients with advanced heart failure (HF).[1] However, in-hospital mortality at the time of LVAD implantation still remains as high as 6.0% in the modern era.[2] Post-operative complications such as the need for right ventricular assist device (RVAD) and continuous renal replacement therapy (RRT) are reported to be 6%–9%[3,4] and 14%,[5] respectively. The discriminatory ability of LVAD risk scores, such as HeartMate II Risk Score (HMRS) and Right Ventricular Failure Risk Score (RVFRS), for the prediction of post-operative outcomes has been limited.[6,7] In addition, the pathophysiological basis for early unfavorable outcomes following LVAD surgery is poorly understood. Inflammation, oxidative stress, endotoxemia and gut-derived metabolites, such as trimethylamine-N-oxide (TMAO), have been associated with HF progression and outcomes, and as such might predispose to untoward post-LVAD complications.[8–15] In addition, cardiac surgery provokes a vigorous inflammatory and oxidative response that together may culminate in severe peripheral vasodilatation and myocardial dysfunction.

Vasoactive-inotropic score (VIS) has been extensively studied in pediatric patients undergoing cardiopulmonary bypass (CPB) to measure illness severity and as a surrogate marker for hemodynamic cardiovascular derangement at the time of intensive care unit admission. The initial inotrope score was developed by Wernovsky et al[16] and then modified as VIS by Gaies et al[17] to include additional vasoactive medications used in modern clinical practice. Prior studies in infants and adults undergoing cardiac surgery showed that an elevated VIS was associated with in-hospital mortality and adverse events, including cardiac arrest, RRT, and neurological injury.[17–20] However, the utility of VIS in patients with LVAD implantation has never been studied.

Our main objectives were to (1) investigate whether VIS is an independent predictor of mortality, RVAD implantation, and RRT at index hospitalization among adult patients with HF undergoing LVAD implantation; (2) determine the optimal cut-off point of VIS as a predictor of outcomes; and (3) identify pre-operative and intraoperative predictors of a high VIS. In addition, as an exploratory aim, we investigated the association of pre-operative

inflammation, endotoxemia, oxidative stress, and TMAO with the development of post-operative hemodynamic instability in patients with advanced HF undergoing LVAD surgery.

Methods

Study population

This study was approved by the Columbia University Irving Medical Center Institutional Review Board with a waiver of consent. A total of 469 adult (age 18) patients received LVAD implantation from April 2004 to December 2015 at Columbia University Irving Medical Center. Of those, 418 (89.1%) patients were included in this study after excluding 19 (4.1%) patients who received concomitant RVAD at the time of initial LVAD implantation and 32 (6.8%) patients with limited chart availability.

Calculation of VIS and hemodynamic data

VIS was calculated using the following formula[14,15]: dopamine + dobutamine + milrinone ($\times$ 10) + epinephrine ($\times$ 100) + norepinephrine ($\times$ 100) (all μg/kg/min) + vasopressin ($\times$ 10000) (U/kg/min). VIS and hemodynamic data (Fick cardiac index, systemic vascular resistance [SVR], mean arterial pressure [MAP], central venous pressure [CVP], and mean pulmonary artery pressure [PAP]) were acquired after initial stabilization in the operating room and upon arrival to the intensive care unit.

Data collection

Patient data were obtained from electronic medical records by coauthors (JH and AP). Pre-operative laboratory values and hemodynamics were collected within 24–48 hours prior to LVAD implantation. Pre-operative inotrope support was defined as the use of milrinone, dobutamine, and dopamine immediately prior to LVAD implantation. Pre-operative vasopressor support was defined as the use of norepinephrine, epinephrine, and vasopressin. The primary outcome was all-cause in-hospital mortality. The secondary outcome was a composite of in-hospital mortality, delayed RVAD implantation, or a need for RRT during index hospitalization. The existing risk models for patients with LVAD implantation, such as HMRS and RVFRS, were calculated to assess their relationship with in-hospital mortality as well as with VIS.

Measurements of plasma and serum biomarkers

As an exploratory analysis, in a cohort of 61 patients who underwent LVAD implantation from February 2016 to December 2017, we prospectively obtained measures of biomarkers of inflammation, oxidative stress, endotoxemia, and TMAO at a single time point pre-operatively (median 3, interquartile range [IQR] 1–8; days before surgery). The biomarkers of endotoxemia (lipopolysaccharide [LPS] and soluble CD14 [sCD14]), inflammation (C-reactive protein [CRP], interleukin-6 [IL-6], tumor necrosis factor-α [TNF-α], endothelin-1 [ET-1], and adiponectin), and oxidative stress (isoprostane) were measured in plasma or serum. Serum CRP was measured using a high sensitivity (0.3 mg/liter) particle enhanced turbidimetric assay on the automated analyzer, Integra 400 plus (Roche Diagnostics, Indianapolis, IN). Serum IL-6, TNF-α, sCD14, and ET-1 were assessed using a high-sensitivity enzyme-linked immunoassay (ELISA) kit (RD Systems, Minneapolis, MN).

Serum adiponectin was measured using a Millipore Radioimmunoassay (RIA) kit (cat no. HADP-61HK, Billerica, MA). Plasma LPS was measured using a Limulus Amebocyte Lysate Chromogenic Endotoxin Quantitation Kit (Pierce Thermo Scientific, Rockford, IL). Plasma isoprostane (8, 12-iso-iPF2a-VI) was measured in butylated hydroxytoluene-treated human plasma samples using liquid chromatography-tandem mass spectrometry (LC-MS)/ tandem mass spectrometry (MS) on Acquity UPLC-Xevo TQS (Waters. Milford, MA). TMAO was measured in human plasma samples using ultraperformance LC-MS after protein precipitation using deuterated (D9)-TMAO as the internal standard. LC-MS analysis was performed on a platform comprising Eksigent UPLC 100 integrated to an API 4,000 mass spectrometer, which was controlled by Analyst 1.6 (AB Sciex, Foster City, CA).

Statistical analysis

Stata 14 software (Stata Corp, College Station, TX) was used in statistical analyses. Statistical significance was determined based on a pre-determined two-sided a of 0.05. Logistic regression models were derived for a range of VIS cut-off points and Youden's index was used to identify the optimal cut-off point of VIS for in-hospital mortality. The entire cohort was dichotomized into high vs low VIS groups based on the optimal cut-off point. The categorical variables are summarized with frequencies and percentages and were compared across VIS groups using chi-squared or Fisher's exact tests as appropriate. The continuous variables are summarized as mean ± standard deviation (among all patients) or mean ± standard error (among VIS groups) for normally distributed data and as median (IQR) for non-normally distributed data. The differences in continuous variables between VIS groups were compared with either two-sample t-tests or Mann-Whitney-Wilcoxon tests, as appropriate. A series of univariate logistic models from pre-and intraoperative characteristics listed in Table 1 were used to determine whether VIS was an independent predictor of in-hospital mortality as the primary outcome and composite in-hospital mortality, delayed RVAD implantation, and RRT as secondary outcomes. The pre-operative variables at threshold of $p < 0.1$ and potential confounders including age, body mass index, and gender were then entered into a multivariate model. The final model was selected using Mallow's C_P as a criterion. To identify pre-and intraoperative predictors of high VIS, a series of univariate logistic models regressed high VIS on pre-and intraoperative predictors of high VIS. The variables at a threshold of $p < 0.1$ and clinically relevant variables were then entered into a multivariate model. The final model was selected using Mallow's C_P as a criterion. In a subset of patients with biomarker values, the biomarkers were dichotomized using a median split and were compared across high and low VIS groups using chi-squared tests. For TMAO, we further utilized a linear regression model to additionally assess the relationship between log TMAO values and continuous VIS.

Results

VIS as a predictor of clinical outcomes

Pre- and intraoperative characteristics of all patients are outlined in Table 1. In the entire cohort, the mean age was 57.8 1 13.1 years, 82.1% were male, 36.6% were undergoing destination therapy, and 40.4% had ischemic etiology. A total of 83.7% of patients were on inotrope support and 8.4% patients were on vasopressors pre-operatively. The median VIS

was 20.0 (IQR 13.3–27.9). The maximum VIS score was 85.0, and the overall distribution is shown in the boxplot and histogram in Figure 1. VIS was a significant predictor for in-hospital mortality with an OR of 1.06 per each unit increase in VIS (95% CI 1.03–1.09, $p < 0.001$) after adjusting for destination therapy, pre-operative vasopressor use, and pre-operative hemoglobin and creatinine levels (Table 2). Receiver operating curve (ROC) analyses (Figure 2) showed that VIS as a predictor of in-hospital mortality had an area under the curve (AUC) of 0.73 (95% CI 0.64–0.82) compared with other risk models for LVAD, such as HMRS (AUC 0.68, 95% CI 0.58–0.78) and RVFRS (AUC 0.53, 95% CI 0.35–0.70). VIS was also a significant predictor for the composite outcome of in-hospital mortality, delayed RVAD implantation, and the need for RRT therapy during index hospitalization with an OR of 1.03 for each unit increase in VIS (95% CI 1.01 –1.06, $p = 0.008$) after adjusting for pre-operative hemoglobin, albumin, and creatinine levels (Table 2).

Optimal VIS cut-off point for prediction of clinical outcomes

An initial ROC analysis found VIS   20 as the optimal threshold for creating a dichotomous VIS variable. Based on Youden's index, VIS   20 as a predictor of in-hospital mortality yielded a sensitivity of 0.84 and a specificity of 0.53. The results were nearly identical for the composite outcome with a cut-off point of 19.7 with a sensitivity of 0.72 and a specificity of 0.52.

Clinical characteristics based on a cut-off point of VIS   20

There were 210 (51.5%) patients with a high VIS (20) and 208 (48.5%) with a low VIS (<20). The patients with a high VIS had a lower body mass index and were more likely to have prior sternotomy, be on mechanical circulatory support, be on amiodarone, and have an INTERMACS 1 profile than patients with a low VIS (Table 1). In addition, the patients with a high VIS had lower hemoglobin and albumin and higher aspartate aminotransferase levels than those with a low VIS. The majority of patients ($n = 329$, 78.7%) received HeartMate II (Abbott Laboratories, Chicago, IL). A total of 44 (10.5%) patients received HeartWare (Medtronic, Minneapolis, MN) and 45 (10.8%) had other continuous flow devices. There was no association between device selection and VIS levels ($p = 0.24$). The patients with a high VIS were more likely to have required longer CPB time (97 minutes [IQR 67–130] vs 79 minutes [IQR 59–104], $p < 0.001$), concomitant valve procedures (48.1% vs 33.7%, $p = 0.003$), as well as a greater use of packed red blood cells (55.6% vs 35.1%, $p < 0.001$) and fresh frozen plasma (75.9% vs 66.3%, $p = 0.033$) intraoperatively.

Pre-and intraoperative predictors of VIS   20 after LVAD implantation

The multivariate logistic regression models showed that pre-operative hemoglobin level (OR 0.82, 95% CI 0.72–0.93, $p = 0.003$) was associated with increased post-operative VIS   20 (Table 3). Pre-operative thyroid function test, use of angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, or amiodarone were not predictors of VIS   20. There was no correlation between existing pre-operative LVAD risk models, such as HMRS ($R^2 < 0.001$, $p = 0.62$) and RVFRS (Kruskal–Wallis $p = 0.58$), with post-operative VIS   20. However, a high-risk pre-operative INTERMACS profile   2 was associated with a high VIS (Mann-U-Whitney $p < 0.001$) (Figure 3).

Early post-operative clinical outcomes according to VIS 20 cut-off point

Table 4 shows early post-operative outcomes during index hospitalization. Twenty-five (6.0%) patients died. The most common causes of death were multi-organ failure ($n = 10$, 40.0%) followed by stroke ($n = 5$, 20.0%), bleeding (n = 2, 8.0%), and right HF ($n = 2$, 8.0%). A high VIS was associated with increased in-hospital mortality (10.0% vs 1.9%, $p < 0.001$). In-hospital mortality increased for each VIS quartile (0% [VIS 2.5–13.0] vs 3.9% [VIS 13.2–19.7] vs 7.6% [VIS 19.8–27.9] vs 12.3% [VIS 27.9–85.0], $p = 0.002$). A total of 37 (8.9%) patients needed post-operative RRT, and 12.9% of patients with a high VIS required RRT compared with 4.8% of patients with a low VIS ($p = 0.004$). There were 19 (4.5%) patients requiring delayed RVAD implantation without any significant difference among the VIS groups ($p = 0.44$). The patients with a high VIS spent longer periods of time in intensive care units than those with a low VIS (8 days [IQR 6–14] vs 7 days [IQR 5–11], $p = 0.013$) and a higher incidence of ventricular arrhythmias (31.8% vs 22.6%, $p = 0.04$).

Post-operative hemodynamic parameters based on VIS 20 cut-off point

Patients with a high VIS had lower SVR (median 1,380 dynes sec cm^{-5}, [IQR: 1,034–1,831] vs 1,562 [IQR: 1,199–1,963] dynes sec cm^{-5}, $p = 0.03$), lower MAP (median 77 mmHg [IQR: 71–84] vs 81 [IQR: 75–87] mmHg, $p < 0.001$) and lower mean PAP (median 22 mmHg [IQR: 18–26] vs 25 [IQR: 20–29] mmHg, $p = 0.03$) compared to those with a low VIS. There was no difference in VIS and Fick cardiac index (median 3.75 liter/min/m^2 [IQR 3.03–5.02] vs 3.51 liter/min/ m^2 [IQR 2.87–4.51], $p = 0.17$) and CVP (median 9.5 mm Hg [IQR 7–13] vs 10 mm Hg [IQR 8–13], $p = 0.58$).

Biomarkers and VIS

Overall, the baseline characteristics and the distribution of VIS between patients with biomarkers measured (2016–2017) and those in whom biomarkers were not measured (2004–2015) were similar (refer to Supplementary Material 1 available online at www.jhltonline.org and Figure S1). The patients with high post-operative VIS 20 were more likely to have elevated TMAO pre-operatively (53.6% vs 25.8%, $p = 0.03$). The relationship between VIS and log transformation of TMAO is shown in Figure 4 ($R^2 = 0.09$). There was no significant association between VIS and pre-operative biomarkers of inflammation (IL-6, TNF-α, CRP, adiponectin, and ET-1), oxidative stress (isoprostane), and endotoxemia (sCD14 and LPS).

Discussion

The purpose of this study was to evaluate the utility of post-operative VIS (a combined marker of inotrope and vasopressor requirement) to predict adverse outcomes when calculated after initial stabilization in the OR and upon arrival at the intensive care unit and to explore possible mechanisms for post-operative hemodynamic instability.

The findings show that VIS is an independent predictor and composite outcome of in-hospital mortality, delayed RVAD implantation and RRT, and the optimal cut-off point of VIS as a predictor of outcome is 20. Additionally, VIS is a better discriminator of in-hospital mortality compared with established LVAD risk models. Furthermore, pre-operative

hemoglobin level is an independent predictor of elevated VIS and higher pre-operative plasma levels of TMAO are associated with a high VIS, while other biomarkers of inflammation, oxidative stress, and endotoxemia are not.

Prior studies in patients with LVAD implantation focused on identifying pre-operative predictors of short-term adverse events to allow better patient selection.[21–26] However, few studies have tried to risk stratify patients immediately after LVAD surgery. Tecson et al[27] recently reported that post-operative vasoplegia (defined as the "occurrence of normal cardiac index but with the need for intravenous vasopressors within 48 hours following surgery for >24 hours to maintain a MAP > 70 mm Hg") was associated with poor post-operative outcomes, including mortality. Our study expands on this initial observation, by providing a reliable prediction tool that (1) integrates information on both vasopressor and inotrope requirement into one score that summarizes the severity of cardiovascular derangement, and (2) is calculated after initial stabilization in the OR and upon arrival at the intensive care unit. For this purpose and for the first time in the adult LVAD population, we are adopting VIS—a surrogate marker of overall cardiovascular derangement that has been associated with poor post-operative outcomes in pediatric and adult patients undergoing cardiac surgery.

Initial studies of VIS in pediatric patients used 24- or 48-hour maximum doses of drugs to calculate VIS.[17–20] The results from our cohort show that VIS at a single time point still remains a significant predictor of in-hospital mortality and composite outcome of in-hospital mortality, delayed RVAD implantation, and RRT. The optimal cut-off point of VIS as a predictor of poor outcome in our cohort was 20. In a recent article by Yamazaki et al[20] that utilized VIS as a predictor of morbidity and mortality in patients who underwent adult cardiac surgery, the optimal cut-off point was 5.5. This discrepancy in cut-off values is likely due to the differences in baseline characteristics and surgical procedures between studies, because the majority of the patients in their cohort had elective valve surgery, few had a left ventricular ejection fraction < 30%, and none underwent LVAD surgery for the treatment of endstage HF.[21] Thus, VIS appears to maintain a prognostic role throughout a wide range of surgical procedures, although cut-off points may vary depending on patients' characteristics and the type of intervention.

A high VIS captures the complex interplay between right ventricular dysfunction and vasoplegia, which one may define as "vasoplegia with relative RVF" that frequently follows LVAD implantation. Our results indicate that patients with a VIS ≥ 20 have a lower SVR [median 1,380 dynes sec cm^{-5} (IQR 1,034–1,831) vs 1,562 dynes sec cm^{-5} (IQR 1,199–1,963), $p = 0.03$], a lower MAP [median 77 mm Hg (IQR 71–84) vs 81 mm Hg (IQR 75–87), $p < 0.001$], and increased RRT requirement (12.9% vs 4.8%, $p = 0.004$) than those with a VIS < 20. Importantly, these data suggest that exposure to high, "toxic" doses of vasopressors to maintain MAP in a setting of marginal cardiac output may further limit perfusion of critical end-organs, particularly the kidneys, eventually causing acute kidney injury and ultimately patients' demise.[28] In addition, a greater incidence of ventricular arrhythmias in high VIS population (31.8% vs 22.6%, $p = 0.04$) may be driven by arrhythmogenic properties of inotropes and vasopressors. LVAD recipients with a high VIS deserve closer attention. In our opinion, these patients may benefit from early consideration

of RVAD therapy, either surgical or percutaneous, to maintain a higher cardiac output and minimize vasopressor requirement before the kidneys and other organs sustain meaningful and eventually irreversible damage. Late interventions are often futile as demonstrated in our prior published experience.[29] Our results indicate that VIS is a better predictor of in-hospital mortality than existing pre-operative risk models, such as HMRS or RVFRS, in patients with LVAD implantation.[22–25] Notably, a high-risk INTERMACS profile (2) was a predictor of VIS 20, while the above LVAD risk models were not.

In our study, a lower hemoglobin level is associated with increased VIS. Our result is consistent with a prior study that showed anemia is associated with post-operative vasoplegia in patients with LVAD implantation.[30] Pre-operative anemia is likely multifactorial. Determinants may include an underlying inflammatory state (anemia of chronic disease), poor nutrition and recurrent phlebotomies causing iron deficiency anemia, as well as hemolysis in patients on pre-operative mechanical circulatory support. While prior reports have identified the use of ACE inhibitors or beta-blockers as risk factors for post-bypass vasodilatory state and adverse events,[31–33] our model does not show any association in the present cohort. Byrne et al [34] similarly reported that ACE inhibitors were not predictors of post-heart transplant vasoplegia. The long-term compensatory activation of the renin-angiotensin system in patients with HF (i.e., ACE escape) may explain this lack of association between ACE inhibitors and vasoplegia in this patient population.[35]

Our understanding of the pathophysiology that contributes to post-operative vasoplegia is incomplete. Cardiopulmonary bypass causes inflammation and smooth muscle relaxation via the release of nitric oxide.[36] The pro-inflammatory milieu of advanced HF may also contribute to this hemodynamic response during Cardiopulmonary bypass. We investigated the association between VIS and biomarkers of inflammation, oxidative stress, and endotoxemia as well as the gut-derived metabolite TMAO in a subset of our study cohort. We report that a pre-operative value of TMAO is associated with a high VIS. Prior studies have shown that high TMAO levels are predictors of increased mortality in patients with chronic and acute HF,[9–11] supporting the so-called gut-inflammatory hypothesis for the progression of this disease.[12–14] One could speculate that TMAO may promote post-operative vasodilation through activation of nuclear factor-kB in endothelial cells and smooth muscle cells,[15] although TMAO is a relatively novel biomarker and its precise role in the pathophysiology of vasoplegia is yet to be determined.

This investigation has limitations. First, this is a single-center retrospective study that lacks an external validation cohort. Future prospective multi-institutional studies are necessary to fully evaluate the utility of VIS in patients with LVAD implantation. Second, VIS is measured at a single time point rather than the precise definition of maximum doses within the first 24 hours. However, we believe that a single value offers a simple and rapid calculation of VIS, which helps to identify high-risk patients with LVAD implantation immediately after the surgery.

In conclusion, a high VIS after initial stabilization in the operating room and upon arrival at the intensive care unit is associated with adverse clinical outcomes and is a better predictor of in-hospital mortality compared with existing LVAD risk models. A lower hemoglobin

level is an independent predictor of post-operative cardiovascular derangement. Based on an exploratory analysis, elevated preoperative TMAO levels are also associated with a high VIS. Whether early correction of hemodynamic compromise through mechanical right ventricular support therapy may prevent continued end-organ damage and improve clinical outcomes remains to be established.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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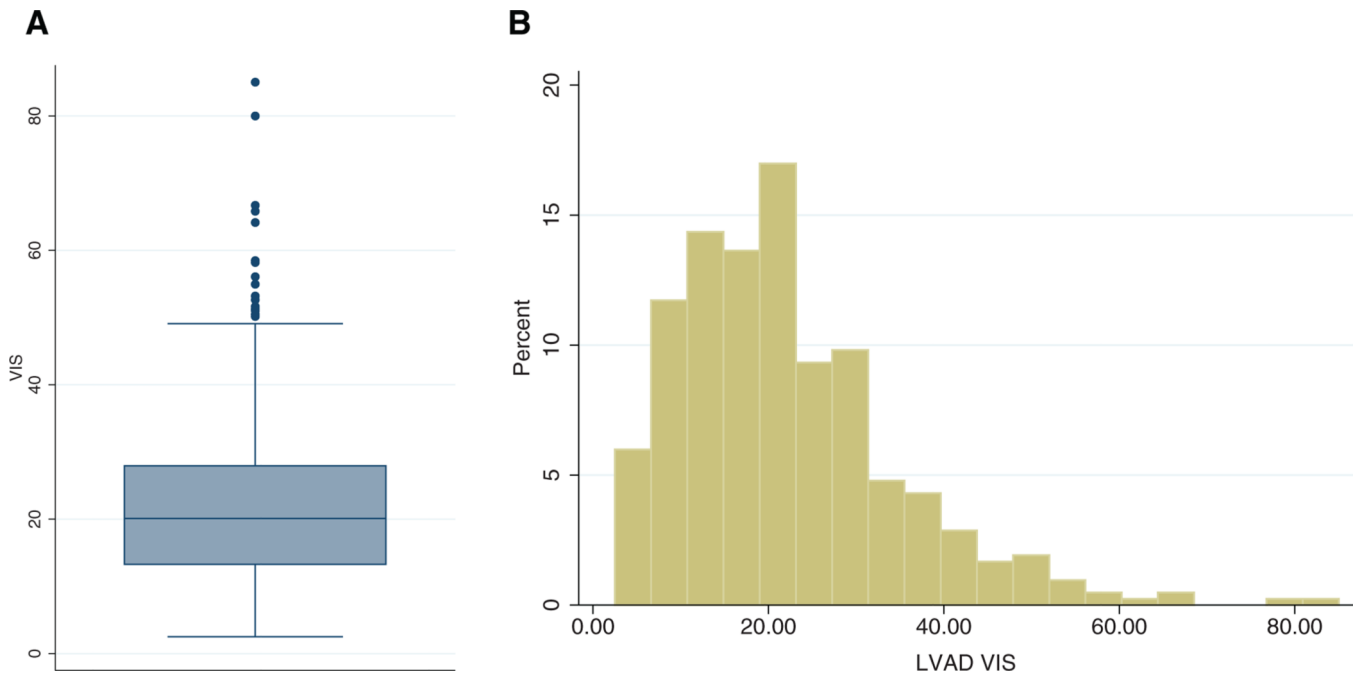
Figure 1.
Distribution of vasoactive-inotropic score (VIS). (A) Boxplot of VIS. (B) Histogram of VIS.
LVAD, left ventricular assist device.
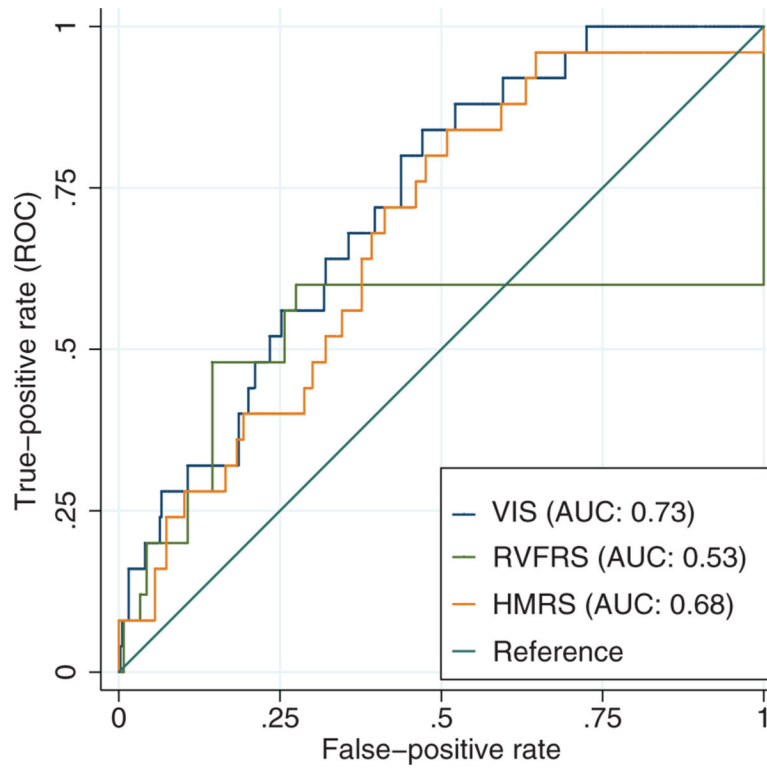
Figure 2.
Receiver operating curve (ROC) for comparison of vasoactive-inotropic score (VIS) and left ventricular assist device (LVAD) risk models (HeartMate II Risk Score [HMRS] and Right Ventricular Failure Risk Score [RVFRS]) in the prediction of in-hospital mortality. AUC, area under the curve.

Figure 3.
Vasoactive-inotropic score (VIS) values across INTERMACS profiles. LVAD, left ventricular assist device.

Figure 4.
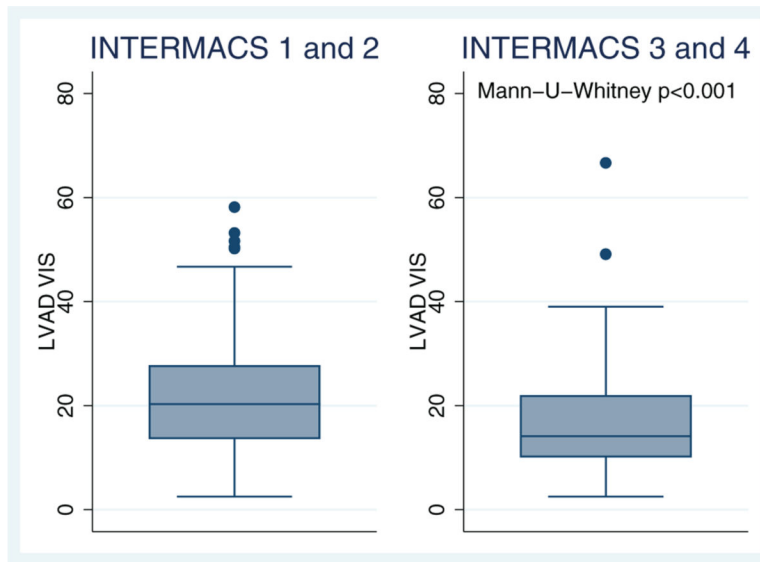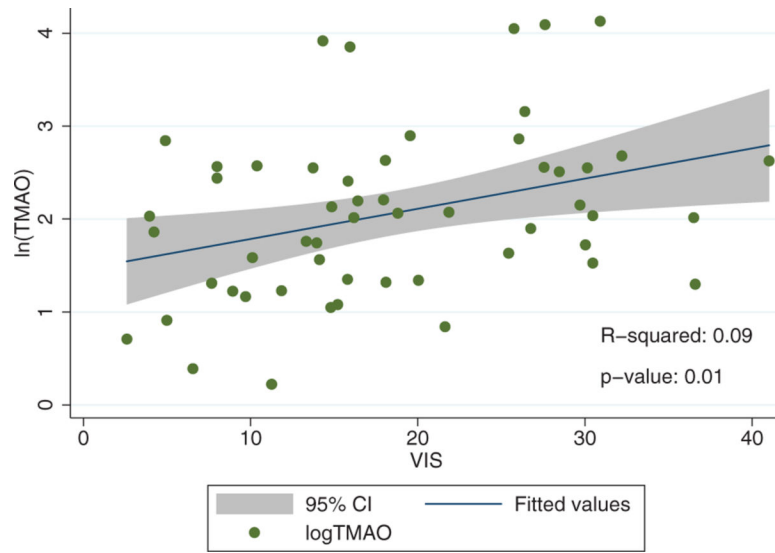Scatter plot of Log transformation of trimethyl-amine-N-oxide (TMAO) versus vasoactive-inotropic score (VIS). CI, confidence interval

Table 1

Pre-Operative and Intraoperative Baseline Characteristics

	All patients(n = 418)	VIS ≥ 20(n = 210)	VIS < 20(n = 208)	p-value
Demographic data				
Age (years)	57.8 ± 13.1	59.0 ± 0.88	56.6 ± 0.93	0.06
BMI (kg/m²)	26.3 ± 5.4	25.4 ± 0.35	27.2 ± 0.39	<0.001
Male, n (%)	343 (82.1)	172 (81.9)	171 (82.2)	0.94
Ischemic etiology, n (%)	169 (40.4)	86 (41.0)	83 (39.9)	0.06
LVAD indication				0.86
BTT, n (%)	265 (63.4)	134 (63.8)	131 (63.0)	
DT, n (%)	153 (36.6)	76 (36.2)	77 (37.0)	
Prior sternotomy (%)	132 (32.0)	79 (37.8)	53 (26.0)	0.010
Pre-operative inotrope support	350 (83.7)	172 (81.9)	178 (85.6)	0.31
Pre-operative vasopressor, n (%)	34 (8.4)	18 (8.8)	16 (7.9)	0.73
Pre-operative ventilator, n (%)	17 (4.2)	12 (5.9)	5 (2.5)	0.08
Pre-operative IABP, n (%)	119 (28.5)	69 (33.0)	50 (24.0)	0.042
Pre-operative mechanical				
Circulatory support, n (%)	41 (9.8)	29 (13.8)	12 (5.8)	0.006
ECMO	7 (1.7)	5 (2.4)	2 (1.0)	0.25
Impella	6 (1.4)	5 (2.4)	1 (0.5)	0.10
CentriMag VAD	32 (7.7)	23 (11.0)	9 (4.3)	0.011
INTERMACS profile				0.004
1	32 (7.7)	22 (10.5)	10 (4.8)	
2	129 (30.9)	62 (29.5)	67 (32.2)	
3	58 (13.9)	27 (8.1)	41 (19.7)	
4	10 (2.4)	4 (1.9)	6 (2.9)	
Hemodynamic data				
CVP (mm Hg)	10.8 ± 5.3	10.7 ± 0.4	11.0 ± 0.4	0.58
Mean PAP (mm Hg)	35.0 ± 9.8	34.3 ± 0.7	35.7 ± 0.7	0.17
PCWP (mm Hg)	23.7 ± 7.9	24.0 ± 0.6	23.4 ± 0.6	0.52
CO (liter/min)	3.48 ± 1.11	3.48 ± 0.1	3.46 ± 0.1	0.11

	All patients(*n* = 418)	VIS ≥ 20(*n* = 210)	VIS < 20(*n* = 208)	*p*-value
PVR (Wood units)	4.02 ± 2.64	3.98 ± 0.2	4.05 ± 0.2	0.81
Laboratory values				
Hemoglobin (g/dl)	11.4 ± 2.1	10.9 ± 0.1	11.9 ± 0.1	<0.001
Creatinine (mg/dl)	1.4 (1.1–1.7)	1.4 (1.1–1.7)	1.4 (1.1–1.7)	0.58
Albumin (g/dl)	3.7 (3.2–4.0)	3.6 (3.1–3.9)	3.7 (3.4–4.1)	0.007
AST (IU/liter)	24 (18–34)	25 (19–40)	22 (18–31)	0.032
Total bilirubin (mg/dl)	1.0 (0.7–1.7)	1.1 (0.7–1.9)	1.0 (0.7–1.5)	0.11
Medications				
ACE inhibitor use, *n* (%)	116 (31.0)	51 (27.4)	65 (34.6)	0.14
Beta blocker use, *n* (%)	285 (75.8)	139 (74.7)	146 (76.8)	0.63
Amiodarone use, *n* (%)	190 (50.8)	111 (59.7)	79 (42.0)	0.001
Intraoperative characteristics				
CPB time (min)	87 (63–119)	97 (67–130)	79 (59–104)	<0.001
Intraoperative blood products				
PRBC use, *n* (%)	187 (45.4)	115 (55.6)	72 (35.1)	<0.001
FFP use, *n* (%)	293 (71.1)	157 (75.9)	136 (66.3)	0.033
Platelets use, *n* (%)	335 (81.3)	173 (83.6)	162 (79.0)	0.236
Concomitant valve procedures	171 (40.9)	101 (48.1)	70 (33.7)	0.003
Tricuspid valve	75 (17.9)	49 (23.3)	26 (12.5)	0.004
Mitral valve	77 (18.4)	48 (22.9)	29 (13.9)	0.019
Aortic valve	60 (14.3)	25 (11.9)	35 (16.8)	0.15

ACE, angiotensin-converting enzyme; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; BTT, bridge-to-transplantation; CO, cardiac output; CPB, cardiopulmonary bypass; CVP, central venous pressure; DT, destination therapy; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PRBC, packed red blood cells; PVR, peripheral vascular resistance; VAD, ventricular assist device; VIS, vasoactive-inotropic score.

Table 2

Final Model for All Outcomes

Final model for in-hospital mortality (Mallow's C$_P$ 4.629)

Variable	OR	95% CI	*p-value*
Destination therapy	4.52	1.79–12.53	0.002
Pre-operative vasopressor use	3.37	0.91–11.07	0.053
Pre-operative hemoglobin	0.72	0.55–0.92	0.013
Pre-operative creatinine	1.81	1.10–3.21	0.026
Vasoactive-inotropic score	1.06	1.03–1.09	<0.001

Final model for composite outcome (Mallow's C$_P$ 4.937)

Variable	OR	95% CI	*p-value*
Pre-operative hemoglobin	0.81	0.66–0.97	0.030
Pre-operative albumin	0.42	0.21–0.83	0.014
Pre-operative creatinine	2.27	1.45–3.71	0.001
Vasoactive-inotropic score	1.03	1.01–1.06	0.008

CI, confidence interval; OR, odds ratio.

Table 3

Predictors of Vasoactive-Inotropic Score (VIS) 20

Predictors	OR	SE	(95% CI)	*p*-value
Age	1.017	0.010	(0.997–1.038)	0.089
BMI	0.958	0.022	(0.916–1.002)	0.063
Pre-operative hemoglobin	0.817	0.055	(0.716–0.934)	0.003
Pre-operative SBP	1.002	0.010	(0.983–1.022)	0.820
Pre-operative albumin	0.853	0.231	(0.502–1.450)	0.557
Pre-operative MCS	1.816	0.955	(0.648–5.089)	0.257
Re-sternotomy	1.252	0.355	(0.718–2.182)	0.429
Number of valve procedures	1.356	0.245	(0.952–1.930)	0.092
Amiodarone use	1.548	0.380	(0.957–2.505)	0.075
ACE inhibitor use	0.715	0.161	(0.460–1.111)	0.135
Beta blocker use	0.891	0.215	(0.556–1.429)	0.633

ACE, angiotensin-converting enzyme; BMI, body mass index; CI confidence interval; MCS, mechanical circulatory support; OR, odds ratio; SBP, systolic blood pressure; SE, standard error.

Table 4

Post-Operative Morbidity and Mortality during Index Hospitalization for Left Ventricular Assist Device (LVAD) Implantation

	All patients(N = 418)	VIS ≥ 20(n = 210)	VIS < 20(n = 208)	p-value
In-hospital mortality, n (%)	25 (6.0)	21 (10.0)	4 (1.9)	<0.001
Composite outcome [a], n (%)	54 (12.9)	37 (17.6)	17 (8.2)	0.004
Renal failure requiring RRT	37 (8.9)	27 (12.9)	10 (4.8)	0.004
Delayed RVAD implantation, n (%)	19 (4.6)	12 (5.8)	7 (3.3)	0.44
ICU stay (days)	7 (5–12)	8 (6–14)	7 (5–11)	0.013
Post-operative complications, n (%)				
Take back for bleeding	72 (18.3)	43 (22.1)	29 (14.7)	0.06
VF/VT	107 (27.2)	62 (31.8)	45 (22.6)	0.04
Atrial fibrillation	120 (28.7)	55 (26.2)	65 (31.3)	0.43
Sepsis	33 (8.5)	20 (10.5)	13 (6.6)	0.45
Cerebral vascular accident [b]	26 (6.3)	14 (6.7)	12 (5.8)	0.70

ICU, intensive care unit; RRT, renal replacement therapy; RVAD, right ventricular assist device; VF, ventricular fibrillation; VIS, vasoactive-inotropic score; VT, ventricular tachycardia.

[a] In-hospital mortality, delayed RVAD implantation, or a need for RRT during index hospitalization

[b] Cerebral vascular accident was defined as new acute neurological deficit lasting >24 hours associated with acute infarction or hemorrhage on imaging