Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Anesthesiology. Author manuscript; available in PMC 2018 March 01.

Published in final edited form as:

Anesthesiology. 2017 March ; 126(3): 450–460. doi:10.1097/ALN.0000000000001488.

Complications, Risk Factors, and Staffing Patterns for Non-cardiac Surgery in Patients with Left Ventricular Assist Devices

Michael R. Mathis, MD[*] **[Lecturer]**, **Subramanian Sathishkumar, MBBS**[*] **[Assistant Professor]**, **Sachin Kheterpal, MD, MBA**[*] **[Associate Professor]**, **Matthew D. Caldwell, MD**[*] **[Assistant Professor]**, **Francis D. Pagani, MD, PhD**[†] **[Professor]**, **Elizabeth S. Jewell, MS**[*] **[Research Associate]**, and **Milo C. Engoren, MD**[*] **[Professor]**

[*]Department of Anesthesiology, University of Michigan Health System, University of Michigan, 1H247 UH, SPC 5048, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5048, Phone: 734-936-4280

[†]Department of Cardiac Surgery, University of Michigan Health System, University of Michigan, SPC 5852, Cardiovascular Center, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5852, Phone: 888-287-1082

Abstract

Background—Patients with left ventricular assist devices (LVADs) presenting for non-cardiac surgery (NCS) are increasingly commonplace; however, little is known about their outcomes. Accordingly, the authors sought to determine the frequency of complications, risk factors, and staffing patterns.

Methods—We performed a retrospective study at our academic tertiary care center, investigating all adult LVAD patients undergoing NCS from 2006 to 2015. We described perioperative profiles of NCS cases, including patient, LVAD, surgical case, and anesthetic characteristics, as well as staffing by cardiac/non-cardiac anesthesiologists. Through univariate and multivariable analyses, we studied acute kidney injury (AKI) as a primary outcome; secondary outcomes included elevated serum lactate dehydrogenase (LDH) suggestive of LVAD thrombosis, intraoperative bleeding complication, and intraoperative hypotension. We additionally studied major perioperative complications and mortality.

Results—Two hundred forty six patients underwent 702 procedures. Of 607 index cases, 110 (18%) experienced postoperative AKI, and 16 (2.6%) had elevated LDH. Of cases with complete blood pressure data, 176 (27%) experienced intraoperative hypotension. Bleeding complications occurred in 45 cases (6.4%). Thirteen (5.3%) patients died within 30 days of surgery. Independent risk factors associated with AKI included major surgical procedures (adjusted odds ratio [aOR] 4.4, 95% confidence interval [CI] 1.1–17.3, $p = 0.03$) and cases prompting invasive arterial line

Corresponding Author: Michael R. Mathis, MD, mathism@med.umich.edu, Department of Anesthesiology, University of Michigan, 1H247 UH, SPC 5048, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5048, Phone: 734-936-4280, Fax: 734-936-9091.

Summary Statement: We retrospectively studied 246 patients with left ventricular assist devices undergoing 702 non-cardiac surgical procedures over a ten year period. We describe trends in perioperative management, risk factors, and complications in this uniquely challenging population.

Conflict of Interest: No personal conflicts of interest among study authors. The University of Michigan performs contract research with St. Jude (Pleasanton, CA) and HeartWare (Framingham, MA).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

monitoring (aOR 3.6, 95% CI 1.3–10.3, $p = 0.02$) or preoperative fresh frozen plasma transfusion (aOR 1.7, 95% CI 1.1–2.8, $p = 0.02$).

Conclusions—Intraoperative hypotension and AKI were the most common complications in LVAD patients presenting for NCS; perioperative management remains a challenge.

Introduction

The left ventricular assist device (LVAD) was first successfully implemented in 1988. Over the ensuing three decades, numerous modifications and improvements have been made, allowing LVAD therapy to become increasingly commonplace.[1] More recent durable LVAD technologies have utilized smaller devices with continuous flow using either centrifugal or axial flow designs, leading to improved survival.[2] Used as either a bridge to heart transplant or as a "destination" therapy (i.e., permanent pump placement), patients with LVADs have made successful recoveries and are managed as outpatients. However, owing to illness and complications, related or unrelated to LVAD therapy, patients have inevitably presented for a wide array of non-cardiac surgeries.[3–14]

Within the patient population presenting for non-cardiac surgery (NCS), patients with LVADs present unique perioperative challenges to the anesthesiologist. Common anesthetic concerns include management of anticoagulation,[15,16] patient monitoring limitations inherent to minimally pulsatile blood flow,[10,17,18] modified surgical access to the operative site,[19–23] concern for intraoperative cardiovascular and cerebrovascular events,[24–26] management of intraoperative device malfunction,[6] and postoperative complications including bleeding[15,26–28] and infection.[29–34]

Currently, numerous studies have characterized the LVAD patient population presenting for NCS and have described management within the preoperative, intraoperative, and postoperative periods.[3–5,7–14,17,18,22,35–37] Profiles of this patient population have been described in terms of surgical procedure type, admission status, elective versus urgent/emergent status, as well as frequency of complications. Although complications have been described, studies have been limited in sample size, with the largest study to date comprising 271 adult cases,[13] and have been greatly underpowered when investigating adverse event frequency. Due to small study sizes, the range of surgical procedures described within the LVAD population has also been limited. Additionally, no study to date has currently addressed risk factors for perioperative complications within this patient population. Calls for such a study have been made, as identifying perioperative risk factors would provide a valuable evidence basis for clinical decision making in this uniquely high-risk population.[38]

To characterize the LVAD patient population presenting for NCS, we performed this retrospective observational study at our tertiary care facility. We hypothesized that patients with LVADs undergo a steadily increasing frequency of NCS procedures with anesthesia care increasingly from non-cardiac anesthesiologists, and that variations in perioperative management exist. Additionally, we hypothesized that specific perioperative characteristics exist that place this patient population at increased risk of complications.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Methods

The Institutional Review Board approved this retrospective study and waived informed consent (HUM00092710; Ann Arbor, Michigan, USA). The primary outcome, data collection process, and statistical analysis plan were prospectively established, presented at a departmental peer-review forum, and registered on August 27, 2014. The STROBE Statement checklist for reporting observational studies was followed. Data, including demographics, laboratory values, discharge diagnoses, anesthesia history and physical, and intraoperative record were extracted from our enterprise and departmental electronic health record systems (EPIC 9; EPIC Systems, Verona WI and Centricity© General Electric, Waukesha WI) Methods used for data validation, recording, storage, and extraction from a local, single-center database within the Multicenter Perioperative Outcomes Group (MPOG) enterprise have been described elsewhere and utilized in prior studies.[39–42]

Using the local Society for Thoracic Surgeons LVAD registry (which tracks all LVAD patients regardless of primary implantation hospital), we identified all adult (≥18 years) patients with durable LVADs of any type receiving care in our health system. We integrated this patient list with our local MPOG database to identify LVAD patients undergoing NCS procedures requiring an anesthesiologist between January 1, 2006 and August 13, 2015. NCS was determined on the basis of Anesthesiology Current Procedural Terminology (CPT) code; additionally, CPT code data were used to define NCS as minor (2011 American Society of Anesthesiologists (ASA) base unit values ≤5) or major (base unit values >5) procedures. All data were extracted from the electronic health record. Data quality assurance was maintained by a hand-review of all cases included in the study, including all perioperative complications, intraoperative vital signs, and preoperative patient anesthesia history and physical variables (Table 1; complete details provided in Supplemental Digital Content 1).

For descriptive purposes, variables studied included an array of surgical, anesthetic, and patient characteristics (Table 1). As has been investigated in previous similar studies, the involvement of a cardiac anesthesia provider, defined by faculty appointment and practice pattern within the cardiac anesthesia division of our department, was included as a study variable.[13,38] To account for evolving trends in LVAD management over the study period, the year of surgery, type of LVAD, and duration since LVAD placement were also included as study variables. Perioperative complications studied included those known to the ventricular assist device population (Table 2).[6,9–13]

Based upon previous studies assessing perioperative LVAD complications, expected complication frequencies, and clinical relevance, we chose acute kidney injury (AKI) as the primary outcome for this study. AKI was defined by established clinical practice guidelines as a postoperative increase in serum creatinine ≥1.5 times preoperative baseline within seven days as the primary outcome.[6,9–13,43] Secondary outcomes included elevated serum lactate dehydrogenase (LDH) concerning for possible LVAD-associated hemolysis (defined by current literature as a value greater than 600 IU/L, i.e. 2.5-times the upper limit of laboratory normal),[44–46] intraoperative bleeding complication (defined as an estimated blood loss >500 mL or blood product transfusion intraoperatively), and clinically significant intraoperative

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

hypotension. Given the seven-day postoperative measurement window defining AKI and elevated LDH, patients incurring multiple NCS procedures were restricted to one ("index") case evaluated per seven-day period to prevent duplication of a single outcome. To analyze clinically significant intraoperative hypotension as a secondary outcome, we selected mean arterial pressure (MAP) thresholds and durations established in current LVAD,[47,48] NCS,[49] and AKI[50] literature. For purposes of multivariable analyses, we planned *a priori* to select the MAP threshold and duration most associated with our primary outcome, AKI. This selected hypotension definition was studied as a covariate for primary and secondary outcomes, as well as an outcome itself.

Statistical Analysis

Basic descriptive statistics, including percentages, means, standard deviations (SDs), medians, and interquartile ranges (IQRs) were calculated for all factors listed in Table 1; complete details are available in Supplemental Digital Content 1. Factors were univariately compared using Fisher exact or Pearson chi-square tests for categorical variables and Student t-tests for continuous variables. To calculate adjusted odds ratios (aORs) via multivariable analysis, conditional binary logistic regressions were performed with patient as the strata and adjusting for factors with univariate p-values less than 0.20, followed by stepwise variable selection by Akaike information criterion (AIC). A 95% confidence interval (CI) excluding 1 or $p < 0.05$ was deemed statistically significant. Model discrimination was determined by Harrell's c-statistic. Internal model validation was evaluated using 1000 bootstrapped resamples. The resamples were chosen by patient with replacement. For each resample, a full model was fit, and then a reduced model was selected by stepwise variable selection by AIC. All analyses were done in R, version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Power analysis

An *a priori* power analysis was performed for the study to determine adequacy of sample size. Based upon an expected AKI incidence of 10%, a multivariable analysis including up to 10 variables would require approximately 100 primary outcomes to be observed, and thus 1,000 cases available for analysis.

Results

We identified 246 patients with LVADs presenting for 702 unique procedures. As stratified by Anesthesia CPT code, 270 (38%) were major surgical procedures and 432 (62%) were minor (complete details provided in Supplemental Digital Content 2). Upper or lower gastrointestinal endoscopies (n=263, 37%) and implantable cardioverter-defibrillator (ICD) procedures (n=248, 35%) were the most common procedures.

Case Characteristics – Preoperative

Most patients were males (n=197, 80%) and had continuous flow devices (n=227, 92%) including the Heartmate II™ (n=170, 69%) (St. Jude, Pleasanton, CA) and HVAD® (n=50, 20%) (HeartWare, Framingham, MA). Five hundred thirty nine of the NCS (77%) were performed on an inpatient basis; 47 were performed emergently (ASA "E" status). The

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

median duration from LVAD placement to NCS date was 370 days (IQR 87, 827) and preoperative mean arterial pressure (MAP) averaged 82 mmHg (± 12 mmHg SD) (Table 1).

Anesthetic Management

Given a transition to Heartmate II™ and HVAD® devices as routinely implanted LVADs after 2010 at our institution, we describe preoperative management before and after this transition ("early" and "late" study periods). Between the early and late study periods, cardiac anesthesiologist involvement decreased from 57% to 33% (p <0.001). The use of general anesthesia similarly decreased, from 31% to 23% (p = 0.03). Across study cases, 316 (45%) received preoperative hospital-administered anticoagulation of any type (unfractionated heparin (194), warfarin (154), enoxaparin (19), argatroban (14), clopidogrel (7), prasugrel (6), fondaparinux (1), eptifibatide (1), or bivalirudin (1)). Anticoagulation was rarely reversed preoperatively: fresh frozen plasma (FFP) was given in only 26 (3.7%) cases, vitamin K in 15 (2.1%) cases, platelets in 3 (0.4%) cases, and prothrombin complex concentrate in 2 (0.3%) cases. Cryoprecipitate, recombinant coagulation factor VIIa, and recombinant fibrinogen were not administered preoperatively for any case. Arterial line invasive blood pressure monitoring was used in 141 (20%) of cases. Arterial line monitoring was less commonly used for minor procedures (n=50, 12% of minor procedures, p <0.001) and cardiology procedures (n=39, 14% of cardiology procedures, p <0.001) compared to non-cardiology major procedures (n=55, 72% of non-cardiology major procedures, p <0.001). Arterial line monitoring was also more common for general anesthetics (n=114, 64%) compared to cases without general anesthesia (n=27, 5.1%, p <0.001). Between the early and late study periods, arterial line blood pressure monitoring decreased from an overall rate of 31% to 16% (p <0.001) (Table 3); among minor procedures, arterial line monitoring decreased from an overall rate of 30% to 7.6% (p <0.001) from early to late study periods.

Intraoperative Events

In more than half of NCS cases (n=386, 55%) there was a >20 minute intraoperative gap without recorded blood pressures. Furthermore, amongst the 141 cases with arterial line monitoring, 45 (32%) demonstrated a monitoring gap of >20 minutes, most commonly after anesthetic induction prior to placement of the arterial line. Amongst 561 cases without arterial line monitoring, 31 (5.5%) were devoid of any recorded intraoperative blood pressure (Table 4). In such cases, measures approximating vital organ perfusion were documented, including patient responsiveness (e.g. "patient following commands", "patient alert", etc.) in 11 cases and serial documentation of stable LVAD parameters (i.e. flow, power, pulsatility index) in 29 cases. In one remaining case, documentation describing attempts at blood pressure monitoring were made; in all cases lacking blood pressure recording, anesthesiologists subsequently documented a postoperative anesthesia evaluation including an assessment of mental function prior to recovery unit discharge.

Use of vasoactive medications beyond phenylephrine was rare: only four cases received epinephrine >10 mcg and 15 cases received vasopressin >1 unit. In three cases, amiodarone 150mg was administered: one administration occurred in the setting of ventricular tachycardia, another in the setting of supraventricular tachycardia, and a third

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

prophylactically. Malignant dysrhythmias were rare: ventricular tachycardia occurred in seven cases; ventricular fibrillation and asystole once each. All were successfully managed pharmacologically or with electrical defibrillation; chest compressions were used in one patient.

Outcomes

Among primary and secondary outcomes studied, AKI and intraoperative hypotension regularly occurred; elevated LDH and bleeding complications were less common (Tables 1, 2; Supplemental Digital Content 1). Among the 607 index cases, 110 (18%) developed AKI. Patients who developed AKI were more likely to have preoperative organ dysfunction, comorbidities, and lower blood pressures (Table 1). After adjusting for other factors, three processes of care demonstrated statistically significant independent associations with AKI: major procedures (adjusted odds ratio [aOR] 4.4, 95% confidence interval [CI] 1.1–17.3, $p = 0.03$), invasive arterial blood pressure monitoring (aOR 3.6, 95% CI 1.3–10.3, $p = 0.02$), and FFP transfusion preoperatively (aOR 1.7, 95% CI 1.1–2.8, $p = 0.02$) (Figure 1). The model had fair predictive discrimination (Harrell's c = 0.645). Of the 1000 bootstrapped models, 875 of the full and reduced models converged. All of the variables in the reduced model remained in greater than 45% of the bootstrapped reduced models, with major procedures remaining in 66%, invasive arterial blood pressure monitoring remaining in 70%, and FFP transfusion preoperatively remaining in 59% of the models. All of the confidence intervals for the original model estimates overlapped with the 95% percentile bootstrapped confidence intervals.

Elevated LDH occurred in 16 of 607 index cases (2.6%) and bleeding complications in 45 of 702 cases (6.4%). Intraoperative hypotension defined by a MAP <70 mmHg for >20 minutes demonstrated the strongest univariate association with AKI ($p = 0.02$); using this definition, clinically significant intraoperative hypotension occurred in 176 of 664 cases (27%). While there were several risk factors associated with elevated LDH, bleeding complication, or intraoperative hypotension (including surgery characteristics, emergency cases, longer cases, cases with general anesthesia, and cases with preoperative elevated LDH [Supplemental Digital Content 1]) multivariable analyses failed to demonstrate any significant independent associations. Among cases with preoperative and postoperative LDH values available, absolute and relative changes in LDH levels were varied (-12 IU/L median, −49 to 20 IU/L IQR; −9% median, −26 to 15% IQR, for absolute and relative changes respectively). Furthermore, thirteen of sixteen cases with postoperative elevated LDH had LDH elevated (>600 IU/L) preoperatively. A post-hoc sensitivity analysis defining elevated LDH as >480 IU/L demonstrated similar results through univariate and multivariate analyses (available as Supplemental Digital Content 3).

We compared cases for which the majority of care was performed by a cardiac versus a non-cardiac anesthesiologist (described in Supplemental Digital Content 4). Through univariate analyses performed, cardiac anesthesiologists were associated with a population of patients more likely to have HeartMate II™ devices, more frequently undergoing cardiology procedures, and less frequently having had a recent surgery within 30 days. Cardiac anesthesiologists were more frequently associated with elevated troponin levels but less

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

frequently associated with bleeding complications. Of note, cardiology procedures were primarily managed by cardiac anesthesiologists (n = 212, 75% of cardiology procedures (284), $p < 0.001$), whereas gastroenterology procedures were overwhelmingly managed by non-cardiac anesthesiologists (n = 255, 97% of gastroenterology procedures (263), $p < 0.001$); among gastroenterology procedures, seven patients received intraoperative PRBC transfusions. Among major surgeries, unadjusted 30-day mortality rates were 7.1% among non-cardiac anesthesiologists versus 2.2% among cardiac anesthesiologists; however, this did not meet statistical significance ($p = 0.07$). For all study outcomes including AKI, elevated LDH, bleeding complication, intraoperative hypotension, and mortality, no independent associations between cardiac anesthesiologist versus non-cardiac anesthesiologist were demonstrated via multivariable analysis.

Intraoperative bleeding complications occurred in 45 cases (6.4%). Among these cases, 30 (4.2%) required packed red blood cell (PRBC) transfusion, 21 (3.0%) FFP transfusion, 14 (2.0%) platelet transfusion, 2 (0.3%) desmopressin administration, and 1 (0.1%) recombinant coagulation factor VIIa administration. In no cases were cryoprecipitate, prothrombin complex concentrate, or recombinant fibrinogen administered. Fifteen cases were minor NCS, seven of which were gastrointestinal endoscopies for bleeding. The 30 major NCS cases with bleeding complications were most commonly general surgical procedures (n=8), neurosurgical procedures (n=8), and vascular procedures (n=4). In the postoperative period, blood product administration occurred in 92 cases; 56 were gastrointestinal endoscopies. Among 29 major NCS receiving postoperative transfusions, general surgical (n=11) and cardiology (n=7) procedures were the most common.

We also found several other less frequent adverse events (Table 2). LVAD thrombosis, defined by administration of hemolytics and/or requiring LVAD exchange prior to hospital discharge, was observed in four cases (0.6%). All patients received tissue plasminogen activator and none required LVAD exchange. LVAD device malfunction occurred in one case, in which an LVAD device controller engineering defect required controller replacement. One patient also required device exchange for major driveline infection not resolved with medical therapy. While there were no intraoperative deaths, 13 patients (5.3%) died within 30 days postoperatively. Among these patients, most (n = 10) had been operated on as emergency salvage procedures.

Discussion

Enabled by improvements in device technology and LVAD-specific care infrastructure, the LVAD patient presenting for NCS is increasingly common. Descriptive analyses of LVAD patients safely managed for NCS are well-documented. Our study builds upon prior literature by providing greater perioperative detail and performing risk factor analyses for which prior studies have been underpowered. We report 246 LVAD patients presenting for 702 NCS procedures, with complications including perioperative mortality (5.3%), AKI (18%), elevated LDH (2.6%), intraoperative bleeding (6.4%), and hypotension (MAP <70 mmHg >20 minutes, 27%).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

We found that perioperative characteristics independently associated with AKI included major procedures, invasive arterial blood pressure monitoring, and preoperative FFP transfusion; no clinically significant independent associations with secondary outcomes were identified. The independent association between arterial line monitoring and AKI underscores arterial line use as a marker of case complexity not measured by other covariates, and reinforces the importance of anesthesiologist vigilance for hemodynamic instability during cases in which arterial line monitoring is deemed necessary. FFP transfusion, also independently associated with AKI, may serve as a similar marker, reflecting cases requiring rapid anticoagulation reversal or patients with on-going hemorrhage and decreased renal perfusion. The acuity of such cases may explain increased AKI risk; however, it is also possible that a causal relationship between FFP transfusion and AKI may exist. This association has been demonstrated in patients undergoing cardiothoracic surgery.[51,52]

Among hypotension measures studied, a MAP <70 mmHg >20 minutes demonstrated the strongest univariate association with AKI ($p < 0.001$). This finding is in contrast to prior studies of the general surgical population involving primarily non-LVAD patients, in which MAP values <55–60 mmHg have been established as thresholds for postoperative complications.[49,50,53] Given altered hemodynamics imparted by an LVAD as evidenced by changes in organ perfusion after implantation,[54,55] it is reasonable that intraoperative hemodynamic goals, including target MAP range, may differ from the general surgical population as well. Furthermore, the etiology of hypotension in LVAD patients commonly differs from the general surgical population (e.g. thrombus, suction events, right ventricular failure, and limited compensatory response to vasodilation) and thus treatment may differ as well. Our study represents an initial step towards defining the impact of intraoperative hypotension on outcomes in these patients; further studies are needed to investigate hypotension treatment in the LVAD population. Our study results support the current recommended minimum MAP target of 70 mmHg; current recommended maximum MAP values range from 80 to 90 mmHg.[47,48]

In agreement with Stone et al., we found that non-cardiac anesthesiologists provided an increased proportion of care over time.[13] This can be attributed to a developing familiarity with LVADs, as well as an increasing LVAD patient caseload, with a shift towards minor procedures, requiring a wider range of anesthesiology staff resources. Although limited by provider-specific case clustering, our study offers evidence justifying this trend, demonstrating no independent association with perioperative complications among non-cardiac anesthesiologists when adjusted by the perioperative characteristics in Supplemental Digital Content 4. Among major surgeries, it is possible that our study failed to demonstrate a univariate association between cardiac anesthesiologists and decreased perioperative mortality ($p = 0.07$) due to limited sample size. After adjustment for case complexity via multivariable analysis, however, we continued to find no independent association. Our provider-specific findings should be interpreted with caution, as the extent of cardiac anesthesiologist involvement continues to vary widely among institutions, due to a lack of consensus on LVAD patient management as well as intra- and inter-institutional variation in anesthesia provider skills and experience.[13,14,37]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

As similar to previous literature, we found a decrease in invasive arterial blood pressure monitoring over the study period.[13] Much of this has been attributed to the increase in minor NCS procedures, most notably those in the endoscopy suite.[37,38,56] However, our study offers caution in this regard. As we observed intraoperative blood pressure monitoring gaps >20 minutes in a majority of cases despite anesthesiologist attempts to obtain blood pressure measurements or document vital organ perfusion, opportunities for unrecognized hypotension were common. Our study suggests a need for improved blood pressure monitoring for detection and treatment of hypotension in LVAD patients, and sheds light on prior conflicting literature either supporting [9,37] or refuting [14,56] this concept.

Our results differ from studies noting no difficulty with non-invasive blood pressure monitoring.[14,56] This may relate to differences in monitor type, patient and surgical characteristics, and anesthetic management. In particular, the use of a Doppler probe with a manual sphygomomanometer, as well as a slow-deflation cuff (e.g. Elemano, Terumo Medical Corp, Somerset, NJ), have been shown to increase success rates.[57–59] Within the continuous-flow LVAD population, non-invasive monitoring success rates improved from 50–63% for automated measurements to 91–100% when utilizing such methods.[57–59] Although shortcomings have been described, including limitations in accuracy[57] as well as lack of widespread availability, these alternative non-invasive monitoring devices allow for a blood pressure to be measured in patients for which automated non-invasive monitoring would otherwise be unsuccessful. Of note, our institution in 2012 implemented elective use of a Doppler probe with sphygmomanometer among patients with continuous-flow LVADs; however documentation of this method was frequently not present. In our study, cases lacking a recorded blood pressure documented other measures approximating organ perfusion, including patient responsiveness and LVAD flow parameters. In light of these findings, our study illustrates how the LVAD patient can create difficulties in observing ASA basic monitoring standards, including systemic blood pressure monitoring every five minutes, and suggests a need for more widespread use of alternative blood pressure monitoring techniques in order to meet these standards.[60]

Anticoagulation management during the perioperative period remains controversial for LVAD patients. Although manufacturer guidelines and institutional standards exist for target INR levels postoperatively, no clear guidelines exist for the preoperative and intraoperative periods. Postoperatively, Heartmate II™ manufacturer guidelines recommend an INR range of 2.0 to 3.0.[61] Among studies investigating patients transitioned to vitamin K antagonists postoperatively, goal INR values vary from 1.5 to 3.5.[62] Whereas previously a lower INR range (1.5–2.5) was recommended in LVAD patients,[63] recent reports of hemolysis and thrombotic complications[64] have prompted some centers to adopt higher ranges (2.0–3.0).[44,62,65] In the preoperative context among patients in our study, we observed a mean INR of 1.7. In some cases, INR values were below target ranges and unaccompanied by hospital-administered perioperative bridging anticoagulation within 24 hours of surgery. These findings shed light on the need for consensus guidelines for preoperative anticoagulation management in the LVAD population.[66,67] Of additional consideration is the emerging role of point-of-care viscoelastic coagulation testing. Although studies within the LVAD population are limited, such testing has shown associations with thromboembolic complications after NCS in the non-LVAD population.[68] In the absence of prospective

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

studies, anticoagulation management for LVAD patients remains challenging for the perioperative clinician; current management most likely should be determined on a case-by-case basis.

Management of LVAD-induced hemolysis also remains challenging for the perioperative clinician; we found postoperative LDH levels >600 IU/L in 2.6% of cases. Prior studies have cited LDH thresholds ranging from 250–1000 IU/L to define LVAD-associated hemolysis, among other accompanying markers, including elevated plasma free hemoglobin and bilirubin, decreased haptoglobin, anemia, hemoglobinuria, and altered pump parameters.[65,69,70] We chose an LDH >600 IU/L based upon recent literature and expert guidelines.[44,46] In addition to increased risk of device thrombosis, elevated LDH is also a marker of increased cell-free heme, which has been causally implicated in AKI.[71,72] While we found a univariate association among elevated LDH and AKI, this did not persist after multivariable adjustment. Although in only four instances did patients receive postoperative thrombolytics, our study is limited by the short-term follow-up. Some patients with suspected thrombosis may not have been treated due to increased risk of hemorrhage.

Our study has several limitations. As characteristic to retrospective reviews, no specific interventions were mandated, although standard clinical practices were employed. Additionally, data were limited to that which was recorded for clinical care purposes. Our study was performed at a single tertiary care center, and thus variation related to our practice patterns and patient population may limit generalizability. In our characterization of cases performed primarily by non-cardiac anesthesiologists, it is possible that a cardiac anesthesiologist participated in patient care, either for a minority of the case duration, or through informal case discussion. As the 702 cases studied were comprised of 246 patients, patients undergoing multiple procedures may have skewed our results, although our AKI and elevated LDH outcomes were restricted to index cases to minimize this impact. Finally, as most complications were rare, it is possible multivariable analyses were underpowered to detect risk factors with small effect size.

Despite limitations, our review of LVAD patients presenting for NCS represents the largest, most in-depth study to date. The increased prevalence of such patients demands a knowledgebase and familiarity with LVADs among cardiac and non-cardiac anesthesiologists alike. Through reporting trends in clinical decision-making, complications, and risk factors, our study offers unparalleled insight into perioperative management of LVAD patients. In conclusion, we report AKI, hypotension, elevated LDH, and bleeding to comprise the leading major complications within our LVAD patient population, and a 30-day postoperative mortality rate of 5.3%.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Acknowledgments

The authors would like to acknowledge Anik Sinha, M.S. (Department of Anesthesiology, University of Michigan Health System, Ann Arbor, MI, USA) for his contributions in data acquisition and electronic search query programming for this project.

Sources of Financial Support:

All work and partial funding attributed to the Department of Anesthesiology, University of Michigan Medical School (Ann Arbor, Michigan, USA). The project described was supported in part by the National Center for Research Resources, Grant UL1RR024986, which is now at the National Center for Advancing Translational Sciences, Grant 2UL1TR000433 (Bethesda, Maryland, USA). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, Miller MA, Baldwin JT, Young JB. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transplant. 2015; 34:1495–1504. [PubMed: 26520247]
2. Dell'aquila AM, Schneider SR, Stypmann J, Ellger B, Redwan B, Schlarb D, Martens S, Sindermann JR. Survival Results After Implantation of Intrapericardial Third-Generation Centrifugal Assist Device: An INTERMACS-Matched Comparison Analysis. Artif Organs. 2014; 38:383–390. [PubMed: 24117675]
3. Votapka TV, Pennington DG, McBride LR, Kaminski DL, Andrus CH, Swartz MT. Noncardiac operations in patients supported with mechanical circulatory support devices. J Am Coll Surg. 1994; 179:318–320. [PubMed: 8069428]
4. Khoo KA. Ventricular assist devices and anesthetic implications for noncardiac procedures. AANA J. 2010; 78:483–488. [PubMed: 21309296]
5. Ficke DJ, Lee J, Chaney MA, Bas H, Vidal-Melo MF, Stone ME. Case 6-2010: Noncardiac surgery in patients with a left ventricular assist device. J Cardiothorac Vasc Anesth. 2010; 24:1002–1009. [PubMed: 21109156]
6. Morgan JA, Paone G, Nemeh HW, Henry SE, Gerlach B, Williams CT, Lanfear DE, Tita C, Brewer RJ. Non-cardiac surgery in patients on long-term left ventricular assist device support. J Heart Lung Transplant. 2012; 31:757–763. [PubMed: 22425233]
7. Bhat G, Kumar S, Aggarwal A, Pauwaa S, Rossell G, Kurien S, Kumar A, Pappas PS, Tatooles A. Experience with noncardiac surgery in destination therapy left ventricular assist devices patients. ASAIO J. 2012; 58:396–401. [PubMed: 22713727]
8. Ahmed M, Le H, Aranda JM Jr, Klodell CT. Elective noncardiac surgery in patients with left ventricular assist devices. J Card Surg. 2012; 27:639–642. [PubMed: 22978844]
9. Slininger KA, Haddadin AS, Mangi AA. Perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. J Cardiothorac Vasc Anesth. 2013; 27:752–759. [PubMed: 23332965]
10. Barbara DW, Wetzel DR, Pulido JN, Pershing BS, Park SJ, Stulak JM, Zietlow SP, Morris DS, Boilson BA, Mauermann WJ. The perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. Mayo Clin Proc. 2013; 88:674–682. [PubMed: 23809318]
11. Hessel EA 2nd. Management of patients with implanted ventricular assist devices for noncardiac surgery: a clinical review. Semin Cardiothorac Vasc Anesth. 2014; 18:57–70. [PubMed: 24132353]
12. Evans AS, Stone ME. A patient safety model for patients with ventricular assist devices undergoing noncardiac procedures. Am J Med Qual. 2014; 29:173–174. [PubMed: 24589753]
13. Stone M, Hinchey J, Sattler C, Evans A. Trends in the Management of Patients With Left Ventricular Assist Devices Presenting for Noncardiac Surgery: A 10-Year Institutional Experience. Semin Cardiothorac Vasc Anesth.
14. Nelson EW, Heinke T, Finley A, Guldan GJ, Gaddy P, Matthew Toole J, Mims R, Abernathy JH 3rd. Management of LVAD Patients for Noncardiac Surgery: A Single-Institution Study. J Cardiothorac Vasc Anesth. 2015; 29:898–900. [PubMed: 25990267]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

15. Kurien S, Hughes KA. Anticoagulation and bleeding in patients with ventricular assist devices: walking the tightrope. AACN Adv Crit Care. 2012; 23:91–98. [PubMed: 22290095]
16. Whitson BA, Eckman P, Kamdar F, Lacey A, Shumway SJ, Liao KK, John R. Hemolysis, pump thrombus, and neurologic events in continuous-flow left ventricular assist device recipients. Ann Thorac Surg. 2014; 97:2097–2103. [PubMed: 24775803]
17. Riha H, Netuka I, Kotulak T, Maly J, Pindak M, Sedlacek J, Lomova J. Anesthesia management of a patient with a ventricular assist device for noncardiac surgery. Semin Cardiothorac Vasc Anesth. 2010; 14:29–31. [PubMed: 20472619]
18. Oleyar M, Stone M, Neustein SM. Perioperative management of a patient with a nonpulsatile left ventricular-assist device presenting for noncardiac surgery. J Cardiothorac Vasc Anesth. 2010; 24:820–823. [PubMed: 19695906]
19. Livi U, Guzzi G, Tursi V, Martinez B, Albanese MC, Corno C, Badano LP. Laparoscopic approach for urgent abdominal surgery in patients with left ventricular assist devices. J Cardiovasc Med (Hagerstown). 2009; 10:741–744. [PubMed: 19525857]
20. Samoukovic G, Vassiliou M, Giannetti N, Al-Sabah S, Lash V, Cecere R. Laparoscopic splenectomy in a patient with a Heartmate((R)) II left ventricular assist device. J Laparoendosc Adv Surg Tech A. 2011; 21:535–538. [PubMed: 21767119]
21. Khemees TA, Shabsigh A. Feasibility of robotic-assisted laparoscopic nephroureterectomy in left ventricular assist device patient. Case Rep Urol. 2012; 2012:282680. [PubMed: 23094186]
22. Sathishkumar S, Kodavatiganti R, Plummer S, High K. Perioperative management of a patient with an axial-flow rotary ventricular assist device for laparoscopic ileo-colectomy. J Anaesthesiol Clin Pharmacol. 2012; 28:101–105. [PubMed: 22345955]
23. Connors CW, Poltak JM, Christie AA. Noncardiac surgery in the prone position in patients with ventricular assist devices. J Cardiothorac Vasc Anesth. 2012; 26:e6–e7.
24. Backes D, van den Bergh WM, van Duijn AL, Lahpor JR, van Dijk D, Slooter AJ. Cerebrovascular complications of left ventricular assist devices. Eur J Cardiothorac Surg. 2012; 42:612–620. [PubMed: 22659892]
25. Morgan JA, Brewer RJ, Nemeh HW, Gerlach B, Lanfear DE, Williams CT, Paone G. Stroke while on Long-Term Left Ventricular Assist Device Support: Incidence, Outcome, and Predictors. ASAIO J. 2014; 60:284–289. [PubMed: 24625532]
26. Boyle AJ, Jorde UP, Sun B, Park SJ, Milano CA, Frazier OH, Sundareswaran KS, Farrar DJ, Russell SD. Pre-operative risk factors of bleeding and stroke during left ventricular assist device support: an analysis of more than 900 HeartMate II outpatients. J Am Coll Cardiol. 2014; 63:880–888. [PubMed: 24316083]
27. Islam S, Cevik C, Madonna R, Frandah W, Islam E, Nugent K. Left ventricular assist devices and gastrointestinal bleeding: a narrative review of case reports and case series. Clin Cardiol. 2013; 36:190–200. [PubMed: 23378047]
28. Shrode CW, Draper KV, Huang RJ, Kennedy JL, Godsey AC, Morrison CC, Shami VM, Wang AY, Kern JA, Bergin JD, Ailawadi G, Banerjee D, Gerson LB, Sauer BG. Significantly higher rates of gastrointestinal bleeding and thromboembolic events with left ventricular assist devices. Clin Gastroenterol Hepatol. 2014; 12:1461–1467. [PubMed: 24480675]
29. Schmid C, Hammel D, Deng MC, Weyand M, Baba H, Tjan TD, Drees G, Roeder N, Schmidt C, Scheld HH. Ambulatory care of patients with left ventricular assist devices. Circulation. 1999; 100:II224–II228. [PubMed: 10567308]
30. Simon D, Fischer S, Grossman A, Downer C, Hota B, Heroux A, Trenholme G. Left ventricular assist device-related infection: treatment and outcome. Clin Infect Dis. 2005; 40:1108–1115. [PubMed: 15791509]
31. Topkara VK, Kondareddy S, Malik F, Wang IW, Mann DL, Ewald GA, Moazami N. Infectious complications in patients with left ventricular assist device: etiology and outcomes in the continuous-flow era. Ann Thorac Surg. 2010; 90:1270–1277. [PubMed: 20868826]
32. Schaffer JM, Allen JG, Weiss ES, Arnaoutakis GJ, Patel ND, Russell SD, Shah AS, Conte JV. Infectious complications after pulsatile-flow and continuous-flow left ventricular assist device implantation. J Heart Lung Transplant. 2011; 30:164–174. [PubMed: 20888258]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

33. Goldstein DJ, Naftel D, Holman W, Bellumkonda L, Pamboukian SV, Pagani FD, Kirklin J. Continuous-flow devices and percutaneous site infections: clinical outcomes. J Heart Lung Transplant. 2012; 31:1151–1157. [PubMed: 22766022]
34. Jennings DL, Chopra A, Chambers R, Morgan JA. Clinical outcomes associated with chronic antimicrobial suppression therapy in patients with continuous-flow left ventricular assist devices. Artif Organs. 2014; 38:875–879. [PubMed: 24571683]
35. Stehlik J, Nelson DM, Kfoury AG, Reid BB, Clayson SE, Nelson KE, Christensen BJ, Renlund DG, Movsesian MA, Cowley CG, Smith HK, Rasmusson BY, Long JW. Outcome of noncardiac surgery in patients with ventricular assist devices. Am J Cardiol. 2009; 103:709–712. [PubMed: 19231338]
36. Garatti A, Bruschi G, Colombo T, Russo C, Milazzo F, Catena E, Lanfranconi M, Vitali E. Noncardiac surgical procedures in patient supported with long-term implantable left ventricular assist device. Am J Surg. 2009; 197:710–714. [PubMed: 18926514]
37. Barbara DW, Olsen DA, Pulido JN, Boilson BA, Bruining DH, Stulak JM, Mauermann WJ. Periprocedural Management of 172 Gastrointestinal Endoscopies in Patients with Left Ventricular Assist Devices. Asaio j. 2015; 61:670–675. [PubMed: 26181710]
38. Sheu R, Joshi B, High K, Thinh Pham D, Ferreira R, Cobey F. Perioperative management of patients with left ventricular assist devices undergoing noncardiac procedures: a survey of current practices. J Cardiothorac Vasc Anesth. 2015; 29:17–26. [PubMed: 25440639]
39. Freundlich RE, Kheterpal S. Perioperative effectiveness research using large databases. Best Pract Res Clin Anaesthesiol. 2011; 25:489–498. [PubMed: 22099915]
40. Kheterpal S. Clinical research using an information system: the multicenter perioperative outcomes group. Anesthesiol Clin. 2011; 29:377–388. [PubMed: 21871400]
41. Bateman BT, Mhyre JM, Ehrenfeld J, Kheterpal S, Abbey KR, Argalious M, Berman MF, Jacques PS, Levy W, Loeb RG, Paganelli W, Smith KW, Wethington KL, Wax D, Pace NL, Tremper K, Sandberg WS. The risk and outcomes of epidural hematomas after perioperative and obstetric epidural catheterization: a report from the Multicenter Perioperative Outcomes Group Research Consortium. Anesth Analg. 2013; 116:1380–1385. [PubMed: 22504213]
42. Kheterpal S, Healy D, Aziz MF, Shanks AM, Freundlich RE, Linton F, Martin LD, Linton J, Epps JL, Fernandez-Bustamante A, Jameson LC, Tremper T, Tremper KK. Incidence, Predictors, and Outcome of Difficult Mask Ventilation Combined with Difficult LaryngoscopyA Report from the Multicenter Perioperative Outcomes Group. Anesthesiology. 2013; 119:1360–1369. [PubMed: 24071617]
43. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012; 120:c179–c184. [PubMed: 22890468]
44. Cowger JA, Romano MA, Shah P, Shah N, Mehta V, Haft JW, Aaronson KD, Pagani FD. Hemolysis: a harbinger of adverse outcome after left ventricular assist device implant. J Heart Lung Transplant. 2014; 33:35–43. [PubMed: 24418732]
45. Shah P, Mehta VM, Cowger JA, Aaronson KD, Pagani FD. Diagnosis of hemolysis and device thrombosis with lactate dehydrogenase during left ventricular assist device support. J Heart Lung Transplant. 2014; 33:102–104. [PubMed: 23968811]
46. INTERMACS Adverse Event Definitions: Adult and Pediatric patients, Hemolysis. Birmingham, AL: 2016.
47. Slaughter MS, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD, Starling RC, Chen L, Boyle AJ, Chillcott S, Adamson RM, Blood MS, Camacho MT, Idrissi KA, Petty M, Sobieski M, Wright S, Myers TJ, Farrar DJ. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. J Heart Lung Transplant. 2010; 29:S1–S39. [PubMed: 20181499]
48. Wilson SR, Givertz MM, Stewart GC, Mudge GH Jr. Ventricular assist devices the challenges of outpatient management. J Am Coll Cardiol. 2009; 54:1647–1659. [PubMed: 19850205]
49. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L, Sessler DI. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology. 2013; 119:507–515. [PubMed: 23835589]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

50. Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology. 2015; 123:515–523. [PubMed: 26181335]
51. Cappabianca G, Mariscalco G, Biancari F, Maselli D, Papesso F, Cottini M, Crosta S, Banescu S, Ahmed AB, Beghi C. Safety and efficacy of prothrombin complex concentrate as first-line treatment in bleeding after cardiac surgery. Crit Care. 2016; 20:5. [PubMed: 26738468]
52. Kim WH, Park MH, Kim HJ, Lim HY, Shim HS, Sohn JT, Kim CS, Lee SM. Potentially modifiable risk factors for acute kidney injury after surgery on the thoracic aorta: a propensity score matched case-control study. Medicine (Baltimore). 2015; 94:e273. [PubMed: 25590836]
53. Bijker JB, van Klei WA, Vergouwe Y, Eleveld DJ, van Wolfswinkel L, Moons KG, Kalkman CJ. Intraoperative hypotension and 1-year mortality after noncardiac surgery. Anesthesiology. 2009; 111:1217–1226. [PubMed: 19934864]
54. Slaughter MS. Long-term continuous flow left ventricular assist device support and end-organ function: prospects for destination therapy. J Card Surg. 2010; 25:490–494. [PubMed: 20642766]
55. Hasin T, Topilsky Y, Schirger JA, Li Z, Zhao Y, Boilson BA, Clavell AL, Rodeheffer RJ, Frantz RP, Edwards BS, Pereira NL, Joyce L, Daly R, Park SJ, Kushwaha SS. Changes in renal function after implantation of continuous-flow left ventricular assist devices. J Am Coll Cardiol. 2012; 59:26–36. [PubMed: 22192665]
56. Goudra BG, Singh PM. Anesthesia for gastrointestinal endoscopy in patients with left ventricular assist devices: initial experience with 68 procedures. Ann Card Anaesth. 2013; 16:250–256. [PubMed: 24107691]
57. Lanier GM, Orlanes K, Hayashi Y, Murphy J, Flannery M, Te-Frey R, Uriel N, Yuzefpolskaya M, Mancini DM, Naka Y, Takayama H, Jorde UP, Demmer RT, Colombo PC. Validity and reliability of a novel slow cuff-deflation system for noninvasive blood pressure monitoring in patients with continuous-flow left ventricular assist device. Circ Heart Fail. 2013; 6:1005–1012. [PubMed: 23811966]
58. Woldendorp K, Gupta S, Lai J, Dhital K, Hayward CS. A novel method of blood pressure measurement in patients with continuous-flow left ventricular assist devices. J Heart Lung Transplant. 2014; 33:1183–1186. [PubMed: 25438163]
59. Bennett MK, Roberts CA, Dordunoo D, Shah A, Russell SD. Ideal methodology to assess systemic blood pressure in patients with continuous-flow left ventricular assist devices. J Heart Lung Transplant. 2010; 29:593–594. [PubMed: 20060321]
60. American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring.
61. Russell, SSM., Pagani, F., Moore, S., Idrissi, K., Klodell, C. HeartMate II LVAS: Patient Management Guidelines. Administration USFaD. , editor. 2006. p. 35
62. Baumann Kreuziger LM, Kim B, Wieselthaler GM. Antithrombotic therapy for left ventricular assist devices in adults: a systematic review. J Thromb Haemost. 2015; 13:946–955. [PubMed: 25845489]
63. Suarez J, Patel CB, Felker GM, Becker R, Hernandez AF, Rogers JG. Mechanisms of bleeding and approach to patients with axial-flow left ventricular assist devices. Circ Heart Fail. 2011; 4:779–784. [PubMed: 22086831]
64. Starling RC, Moazami N, Silvestry SC, Ewald G, Rogers JG, Milano CA, Rame JE, Acker MA, Blackstone EH, Ehrlinger J, Thuita L, Mountis MM, Soltesz EG, Lytle BW, Smedira NG. Unexpected abrupt increase in left ventricular assist device thrombosis. N Engl J Med. 2014; 370:33–40. [PubMed: 24283197]
65. Ravichandran AK, Parker J, Novak E, Joseph SM, Schilling JD, Ewald GA, Silvestry S. Hemolysis in left ventricular assist device: a retrospective analysis of outcomes. J Heart Lung Transplant. 2014; 33:44–50. [PubMed: 24418733]
66. Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, Garcia DA, Jacobson A, Jaffer AK, Kong DF, Schulman S, Turpie AG, Hasselblad V, Ortel TL. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. N Engl J Med. 2015; 373:823–833. [PubMed: 26095867]
67. Rechenmacher SJ, Fang JC. Bridging Anticoagulation: Primum Non Nocere. J Am Coll Cardiol. 2015; 66:1392–1403. [PubMed: 26383727]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

68. Hincker A, Feit J, Sladen RN, Wagener G. Rotational thromboelastometry predicts thromboembolic complications after major non-cardiac surgery. Crit Care. 2014; 18:549. [PubMed: 25292221]

69. Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD, Conte JV, Naka Y, Mancini D, Delgado RM, MacGillivray TE, Farrar DJ, Frazier OH. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med. 2007; 357:885–896. [PubMed: 17761592]

70. Tchantchaleishvili V, Sagebin F, Ross RE, Hallinan W, Schwarz KQ, Massey HT. Evaluation and treatment of pump thrombosis and hemolysis. Ann Cardiothorac Surg. 2014; 3:490–495. [PubMed: 25452909]

71. Jarmi T, Agarwal A. Heme oxygenase and renal disease. Curr Hypertens Rep. 2009; 11:56–62. [PubMed: 19146802]

72. Tracz MJ, Alam J, Nath KA. Physiology and pathophysiology of heme: implications for kidney disease. J Am Soc Nephrol. 2007; 18:414–420. [PubMed: 17229906]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

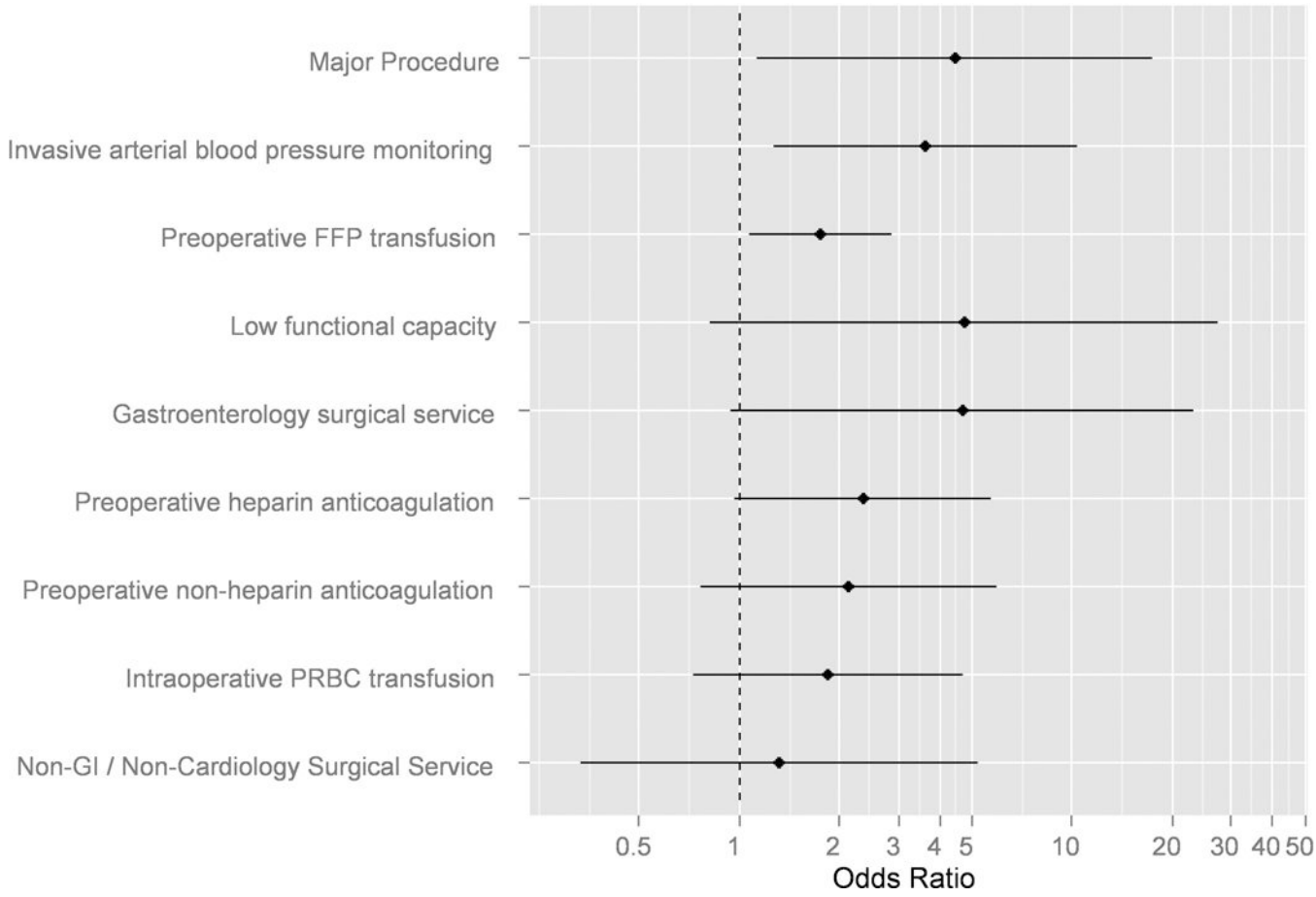

Figure 1.

Multivariable Analysis – Independent Associations with Postoperative Acute Kidney Injury

FFP = fresh frozen plasma; PRBC = packed red blood cells; GI = gastroenterology

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Anesthesiology. Author manuscript; available in PMC 2018 March 01.

Table 1

Study Variables & Univariate Analyses – Primary Outcome

Descriptor			**Acute kidney injury Index Cases**				
	All cases (n= 702)		**Yes (n=110, 18%)**		**No (n=497, 82%)**		
Patient History Data	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p-value**
Age	58	12	56	13	59	12	0.05
Weight (kg)	92	23	93	25	92	23	0.53
Height (cm)	175	9	175	10	175	9	0.64
Body Mass Index (BMI)	29.7	6.0	30.3	6.4	29.7	6.0	0.34
	Median	IQR	Median	IQR	Median	IQR	p-value
LVAD Duration since Placement (days)	370	(87, 827)	84	(25, 513)	390	(128, 825)	<0.001
	N	%	N	%	N	%	p-value
Gender							0.42
Male	585	83.3	87	79.1	412	82.9	
Female	117	16.7	23	20.9	85	17.1	
Race / Ethnicity							0.29
Caucasian	527	75.1	82	74.5	378	76.1	
African American	164	23.4	24	21.8	112	22.5	
Other	11	1.6	4	3.6	7	1.4	
LVAD Type							0.87
HeartMate II™	504	71.8	78	70.9	353	71	
HVAD®	144	20.5	25	22.7	106	21.3	
Other*	54	7.7	7	6.4	38	7.6	
Cardiomyopathy							0.77
Ichemic	395	56.3	60	54.5	279	56.1	
Non-ischemic	307	43.7	50	45.5	218	43.9	
Recent Surgical Procedure <30 days	186	26.5	27	24.5	64	12.9	0.003
Preoperative Laboratory Values within 30 Days	Mean	SD	Mean	SD	Mean	SD	p-value
INR	1.7	0.7	1.5	0.6	1.8	0.7	<0.001

Descriptor	All cases (n= 702)		Acute kidney injury Index Cases				
			Yes (n=110, 18%)		No (n=497, 82%)		
Patient History Data	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p-value**
PTT (sec)	36.7	13.5	37.8	14.1	36.2	13.3	0.28
Hematocrit (%)	29.5	6.8	28.2	5.5	30.6	7.2	<0.001
Creatinine Level (mg/dL)	1.3	0.6	1.4	0.8	1.2	0.5	0.03
Lactate Dehydrogenase (IU/L)	336	186	395	260	324	170	0.008
Platelet Count (K/μL)	222	95	245	107	221	92	0.03
Preoperative Vital Signs	Mean	SD	Mean	SD	Mean	SD	p-value
SBP (mmHg)	100	16	96	17	101	15	0.002
MAP (mmHg)	82	12	79	13	83	12	0.005
HR (beats/min)	80	13	83	14	79	13	0.01
Surgical/Anesthetic Characteristics	Median	IQR	Median	IQR	Median	IQR	p-value
Surgical Duration (minutes)	65	(34, 108)	82	(47, 138)	61	(33, 100)	<0.001
Anesthetic Duration (minutes)	117	(75, 182)	155	(96, 225)	112	(75, 174)	<0.001
	N	%	N	%	N	%	p-value
ASA Status							0.21
3	92	13.1	14	12.7	73	14.7	
4	602	85.8	93	84.5	420	84.5	
5	8	1.1	3	2.7	4	0.8	
Emergent Status	47	6.7	14	12.7	25	5	0.006
Surgical Service							0.06
Gastroenterology	261	37.2	33	30	179	36	
Cardiology	284	40.5	44	40	219	44.1	
All Others	157	22.4	33	30	99	19.9	
Inpatient Admission Status	539	76.8	102	92.7	343	69	<0.001
Major Procedure	270	38.5	63	57.3	171	34.4	<0.001
General Anesthesia Used	177	25.2	43	39.1	105	21.1	<0.001
Cardiac Anesthesiologist Primary Provider	278	39.6	58	52.7	193	38.8	0.01
Preoperative Management	N	%	N	%	N	%	p-value

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Descriptor	All cases (n= 702)		Acute kidney injury Index Cases				
			Yes (n=110, 18%)		No (n=497, 82%)		
Patient History Data	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p-value**
Arterial Line Used	141	20.1	41	37.3	81	16.3	<0.001
Central Venous Line Used	32	4.6	14	12.7	10	2	<0.001
Pulmonary Arterial Catheter Used	11	1.6	8	7.3	1	0.2	<0.001
Preoperative Heparin Anticoagulation**	194	27.6	45	40.9	120	24.1	<0.001
Preoperative Non-heparin Anticoagulation**	174	24.8	33	30	114	22.9	0.15
Preoperative PRBC Transfusion***	83	11.8	11	10	55	11.1	0.88
Preoperative FFP Transfusion***	26	3.7	7	6.4	16	3.2	0.2
Preoperative Platelet Transfusion***	3	0.4	1	0.9	2	0.4	0.45
Intraoperative Occurrences	N	%	N	%	N	%	p-value
Blood Pressure Monitoring Gap >20 minutes	386	55.0	66	60	271	54.5	0.35
Intraoperative Hypotension	176	26.5	44	41.9	108	23	<0.001
Intraoperative Estimated Blood Loss > 500 mL	10	1.4	5	4.5	4	0.8	0.01
Intraoperative PRBC Transfusion	30	4.3	10	9.1	13	2.6	0.003
Intraoperative FFP Transfusion	21	3.0	8	7.3	11	2.2	0.01
Intraoperative Platelet Transfusion	14	2.0	5	4.5	6	1.2	0.05

ASA = American Society of Anesthesiologists; FFP = fresh frozen plasma; HR = heart rate; INR = international normalized ratio; IQR = interquartile range; LDH = lactate dehydrogenase; LVAD = left ventricular assist device; MAP = mean arterial pressure; NCS = non-cardiac surgery; PRBC = packed red blood cells; PTT = partial thromboplastin time; SBP = systolic blood pressure; SD = standard deviation

Acute kidney outcome included 607 index cases; additional cases within 7 day postoperative measurement window were excluded.

Intraoperative hypotension defined as a mean arterial pressure <70 mmHg for a cumulative duration >20 minutes intraoperatively (664 cases with complete data).

Cases with complete laboratory value data varied by laboratory value: INR (n=592); PTT (n= 542); hematocrit (n=586); creatinine (n=585); lactate dehydrogenase (n=555); platelet count (n=585).

Preoperative variables in table refer to NCS cases studied (i.e. not prior to LVAD surgery).

* Including Heartmate® XVE (St. Jude, Pleasanton, CA) (28), DuraHeart® (Terumo, Tokyo, Japan) (12), Novacor® (WorldHeart, Salt Lake City, UT) (6), IVAD® (St. Jude, Pleasanton, CA) (4), and Heartmate III™ (St. Jude, Pleasanton, CA) (4).

** Heparin anticoagulation defined as bolus/infusion administered preoperatively on day of surgery or one calendar day prior, non-heparin anticoagulation defined as hospital-administered administered preoperatively on day of surgery or within three prior calendar days.

*** Within one calendar day of surgery.

Anesthesiology. Author manuscript; available in PMC 2018 March 01.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2

Perioperative Complications Studied

Complication	Frequency (%)
Intraoperative Clinically Significant Hypotension	176 (27%) †
Intraoperative Bleeding Complication	45 (6.4%)
Intraoperative Malignant Dysrhythmia	9 (1.3%)
Acute Kidney Injury	110 (18%) *
Postoperative Mortality **	13 (5.3%) ***
Elevated LDH	18 (3.0%) *
Elevated troponin >0.10 ng/mL **	17 (2.4%)
Stroke ****	5 (0.7%)
Device Thrombosis treated with Thrombolytics	4 (0.6%)
Pulmonary Embolism / Deep Venous Thrombosis *****	3 (0.4%)
Seizure ******	2 (0.3%)
Device Failure ******	1 (0.1%)
Driveline Infection Requiring Device Replacement ******	1 (0.1%)

† Hypotension measured among cases with complete data (664 cases)

* Acute kidney injury and elevated LDH measured among index cases only (607 index cases)

** Within 30 days postoperatively; confirmed via hand review

*** Postoperative mortality on a per-patient basis (246 patients)

**** Defined by discharge diagnosis or positive head computed tomography / magnetic resonance imaging within 30 days postoperatively; confirmed via hand review

***** Defined by ICD-9 discharge diagnoses and/or positive ventilation/perfusion scan or pulmonary embolism computed tomography scan within 30 days postoperatively; confirmed via hand review

****** Defined by ICD-9 discharge diagnoses; confirmed via hand review

LDH = lactate dehydrogenase

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3

Case Management Characteristics

		2004-2010 (n = 185)		2011-2015 (n = 517)		*p*-value	Total	
		N	%	N	%		N	%
Anesthesia Providers	Cardiac Anesthesiologist Present for Entire Case	76	41	123	24	<0.001	199	28
	Cardiac Anesthesiologist Primary Provider	106	57	172	33	<0.001	278	40
	Cardiac Anesthesiologist Present for Start of Case	108	58	168	33	<0.001	276	39
	Non-cardiac Anesthesiologist Primary Provider	79	43	345	67	<0.001	424	60
Anesthetic Technique	General	58	31	119	23	0.03	177	25
	Neuraxial	0	0	0	0	---	0	0
	MAC	127	69	398	77	0.03	525	75
	Supplemented by Regional Block	5	2.7	1	0.2	0.006	6	0.9
Case Type	Major (ASA base units >5)	109	59	161	31	<0.001	270	38
	Minor (ASA base units ≤5)	76	41	356	69	<0.001	432	62
Anticoagulation	Heparin Infusion within 1 Day Preoperative	64	35	130	25	0.02	194	28
	Hospital Administered Warfarin Anticoagulation with 3 Days Preoperative	37	20	117	23	0.52	154	22
	Hospital Administered Other Anticoagulation * within 3 Days Preoperative	7	3.8	38	7.4	0.13	45	6.4
Transfusion / Anticoagulation Reversal	Fresh Frozen Plasma	3	1.6	23	4.4	0.13	26	3.7
	Packed Red Blood Cells	10	5.4	73	14	0.003	83	12

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

		2004-2010 (n = 185)		2011-2015 (n = 517)		*p*-value	Total	
		N	%	N	%		N	%
Within 1 Day Preoperative	Platelets	2	1.1	1	0.2	0.35	3	0.4
	Cryoprecipitate	0	0	0	0	---	0	0
	Vitamin K	2	1.1	13	2.5	0.38	15	2.1
	Desmopressin	0	0	0	0	---	0	0
	Prothrombin Complex Concentrate	0	0	2	0.4	*0.99*	2	0.3
	Recombinant Coagulation Factor VIIa	0	0	0	0	---	0	0
	Recombinant Fibrinogen	0	0	0	0	---	0	0
Monitors	Arterial Line	58	31	83	16	<0.001	141	20
	Central Line **	10	5.4	22	4.3	0.66	32	4.6
	PA Catheter	3	1.6	8	1.5	0.99	11	1.6
	TEE	2	1.1	8	1.5	0.92	10	1.4

* Including enoxaparin, argatroban, clopidogrel, prasugrel, bivalirudin, eptifibatide, and fondaparinux

** Excluding peripherally inserted central catheter lines

ASA = American Society of Anesthesiologists, MAC = monitored anesthesia care; PA = pulmonary artery, TEE = transesophageal echocardiography

Anesthesiology. Author manuscript; available in PMC 2018 March 01.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4

Intraoperative Characteristics

	Median	Interquartile Range
Surgical Duration (min)	65	34 – 108
Anesthesia Duration (min)	117	75 – 182
	N	%
Blood Pressure Monitoring Gaps		
Blood Pressure Monitoring Gap > 20 Minutes	386	55
Blood Pressure Monitoring <20% of Intraoperative Minutes	335	48
Blood Pressure Monitoring <10% of Intraoperative Minutes	115	16
Hypotension		
MAP <70 mmHg for >20 min *	176	27
MAP <60 mmHg for >20 min	43	6.5
MAP <50 mmHg for >20 min	10	1.5
MAP <70 mmHg for >10 min	285	43
MAP <60 mmHg for >10 min	81	12
MAP <50 mmHg for >10 min	17	2.6
Intraoperative Bleeding/Transfusion/Anticoagulation Reversal		
EBL >500cc	10	1.4
Fresh Frozen Plasma transfusion	21	3.0
Packed Red Blood Cell transfusion	30	4.3
Platelet transfusion	14	2.0
Cryoprecipitate transfusion	0	0
Desmopressin	2	0.3
Malignant Dysrhythmia		
Asystole	1	0.1
Ventricular Tachycardia	7	1.0
Ventricular Fibrillation	1	0.1
Torsades de Pointes	0	0
Hemodynamic Medications Given		
Epinephrine >10 mcg	4	0.6
Vasopressin > 1 unit	15	2.1
Amiodarone ≥ 150 mg	3	0.4
Adenosine ≥ 6mg	0	0

* MAP <70 mmHg for >20 min used as hypotension measure for univariate/multivariable analyses. Hypotension measures out of 664 cases with sufficient blood pressure monitoring data.

EBL = estimated blood loss; MAP = mean arterial pressure; min= minutes