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Postoperative Atrial Fibrillation Is Associated with Increased Morbidity and Resource Utilization After Left Ventricular Assist Device Placement

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Abstract

Background—Postoperative atrial fibrillation (POAF) is a known risk factor for morbidity and mortality following cardiac surgery but has not been investigated in the left ventricular assist device (LVAD) population. We hypothesize that POAF will increase morbidity and resource utilization after LVAD placement.

Methods—Records were extracted for all patients in a regional database who underwent continuous flow LVAD placement (n=1064, 2009-2017). Patients without a history of atrial fibrillation (n=689) were stratified by POAF for univariate analysis. Multivariable regression models calculated the risk-adjusted association of arrhythmias on outcomes and resource utilization.

Results—The incidence of new onset POAF was 17.6% and patients who developed POAF were older and more likely to have moderate/severe mitral regurgitation, a history of stroke, and concomitant tricuspid surgery. After risk-adjustment, POAF was not associated with operative mortality or stroke, but was associated with major morbidity (OR 2.5 p=0.0004), prolonged ventilation (OR 2.7, p<0.0001), unplanned RVAD (OR 2.9, p=0.01), and a trend towards renal failure (OR 2.0, p=0.06). Additionally, POAF was associated with higher risk-adjusted resource

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Classifications: atrial fibrillation, ventricular assist device, resource utilization, cost

utilization including discharge to a facility (OR=2.2, p=0.007), an additional 4.9 postoperative days (p=0.02), and 88 hours in the ICU (p=0.01).

Conclusions—POAF was associated with increased major morbidity, possibly from worsening right heart failure leading to increased renal failure and unplanned RVAD placement. This led to POAF patients having longer ICU and hospital stays and more frequent discharges to a facility.

Graphical abstract

INTRODUCTION

Postoperative atrial fibrillation (POAF) after cardiac surgery is a common complication occurring after 10-40% of cardiac cases.[1–3] The causes of POAF are multifactorial and include preoperative structural changes and perioperative proarrhythmic adrenergic activation, inflammation and oxidative stress.[3] Development of POAF is associated with increased risk of morbidity, mortality, and resource utilization including length of stay, readmission and hospital cost.[4] However, the information regarding the impact of POAF after left ventricular assist device (LVAD) implantation is far less well understood. Ventricular arrhythmias garner far more concern than POAF, likely limiting investigation into the clinical and economic impacts of atrial arrhythmias.

While the complication rate after LVAD surgery is high, at a rate of approximately 30% POAF is one of the most common complications reported.[5–8] With the cost of LVAD implantation in the hundreds of thousands of dollars, this therapy warrants scrutiny to identify quality and cost improvement opportunities.[9–11] The Virginia Cardiac Services Quality Initiative (VCSQI) is a regional consortium of hospitals with the primary goal of

improving patient quality, outcomes and cost. The data available within this cohort represents an ideal opportunity to address quality and cost inefficiencies within a high-cost procedure.

The purpose of this analysis was to identify the potential associations of POAF with complications and resource utilization. We hypothesized that POAF is associated with risk-adjusted morbidity and mortality after LVAD implantation. Furthermore, we believe these differences will be evidenced by increased resource utilization including postoperative length of stay (LOS) as well as health care related cost.

PATIENTS AND METHODS

Patient Data

The VCSQI is a multi-state regional collaborative consisting of 19 hospitals and surgical practices. Eight of these hospitals perform LVAD surgeries. Member hospitals submit administrative, demographic and clinical data via the Society of Thoracic Surgeons (STS) standardized data entry forms to both VCSQI and the STS national adult cardiac surgery database. Early data versions collected mean pulmonary artery pressure which were converted to estimated pulmonary artery systolic pressure ((mean pulmonary artery pressure – 2)/0.61).

De-identified records for all continuous flow LVAD implantations from January 2009 through June of 2017 were extracted from the VCSQI data registry. Continuous flow LVADs included: HeartMate II and III (Thoratec Corp., Pleasanton, CA) and HVAD (HeartWare, Framingham, MA). Patients were excluded for missing baseline arrhythmia or POAF data. The primary outcomes of interest were short-term (in-hospital or 30-day) complications and resource utilization. Specifically, the risk adjusted associations between POAF and morbidity, mortality, length of stay and cost. Clinical variables utilized standard STS definitions.[12] Operative mortality is defined as either 30-day or in-hospital mortality. Major morbidity includes permanent stroke, prolonged ventilation, reoperation for any reason, renal failure and deep sternal wound infection.

The primary objective of VCSQI is quality improvement with implementation of solutions across the collaborative. Business associate agreements are in place between VCSQI, members and the database vendor (ARMUS Corporation, San Mateo, CA). This analysis represents a secondary analysis of the VCSQI data registry without Health Insurance Portability and Accountability Act patient identifiers and was exempted from IRB review at the University of Virginia (IRB #20321).

Cost Data

The VCSQI cost collection, pairing and estimation methodologies have been previously described.[13, 14] Briefly, STS clinical data is paired with patient-level hospital financial records using Uniform Billing-04 files, which include all final hospital charges. The matching success rate is 99%. The identified charges are sorted based on International Classification of Diseases, ninth revision, based revenue codes. Next, the charges are multiplied by a set of cost-to-charge ratios for each hospital that are publically available and

submitted to the Centers for Medicare and Medicaid Services. All costs are presented as 2016 dollars after adjusting for medical inflation using the market basket for the Centers for Medicare and Medicaid Services Inpatient Prospective Payment System.[15]

Statistical Analysis

Categorical variables are presented as counts (%) and continuous variables as median [25th, 75th percentile] due to skewedness except for cost data, which was also presented as mean ± standard deviation (SD). Cost data is presented as both median and mean to more fully understand cost outliers. Patients were stratified by POAF and preoperative atrial fibrillation and compared by univariate analysis. Categorical variables were analyzed by Chi-square test for and continuous variables by Mann-Whitney U test. For univariate analyses, no imputation for missing data was performed.

Multivariable regression modeling assessed the risk-adjusted associations between POAF and morbidity, mortality and resource utilization metrics. Predicted associations were adjusted for preoperative and operative risk factors, hospital volume and operative year with the complete list of covariates listed in Supplemental Table 1. All risk factors used in previous LVAD risk models were included, except for aspartate aminotransferase which is not captured in the data set and pulmonary artery pressures due to the high number missing (Supplemental Table 1).[16] For logistic regression models a stepwise selection methodology was utilized to limit the number of covariates to 1 per 10 events, while for linear regression models all potential covariates were included.

For univariate analyses missing data points were excluded from the corresponding analysis. For regression modeling data imputation was performed based on STS methodology utilized in the creation of the STS risk models.[17] For missing continuous variables the median cohort value and for categorical variables the lowest risk definition was applied. Some patients were missing multiple laboratory values, thus if patients were missing 4 or more values they were excluded from the regression models (n=203). All statistical analyses were carried out using SAS Version 9.4 (SAS Institutive, Cary, NC) with significance determined by a p-value less than 0.05.

RESULTS

Patient and Operative Characteristics

A total of 1,064 patients underwent implantation of a continuous flow LVAD, of whom 375 (35%) had a history of atrial fibrillation. Of the 689 patients without a history of atrial fibrillation, 568 (17.6%) developed POAF. The baseline descriptive statistics for patients without a history of atrial fibrillation are shown in Table 1 stratified by POAF. At baseline, patients who developed POAF were older with more frequent prior stroke. They had more frequent moderate/severe mitral regurgitation and higher pulmonary artery systolic pressures.

Patients who developed POAF had largely similar operative characteristics as demonstrated in Table 2 with neither cardiopulmonary bypass time nor application of a complete cross-clamp different by development of POAF. The rate of HeartWare HVAD implantation was

higher in the POAF cohort (27% vs 18%), with the converse true for HeartMate II (82% vs 72%, p=0.02). Patients who developed POAF also had a higher rate of concomitant tricuspid surgery.

Postoperative Outcomes and Resource Utilization

By univariate analysis POAF was associated with higher rates of multiple morbidities as shown in Table 3. The rate of major morbidity was 16% higher in the POAF cohort (p=0.001) with many of the component complications similarly elevated. The rate of unplanned RVAD was more than double in the POAF group (4% vs 10%, p=0.02). In addition to complications, resource utilization was higher in patients who developed POAF. Postoperative atrial fibrillation was associated with a more than doubling of discharges to a facility (p<0.0001) although readmission rates were similar. Both intensive care unit (ICU) and postoperative LOS was longer in POAF patients (both p<0.001). The unadjusted median total hospital cost was significantly higher for patients who developed POAF ($300,281 [$247,120-360,327]) compared to those who did not ($272190 [$213,594-360,327]; p=0.003). Similarly, the unadjusted median ICU cost for POAF patients ($31,926 [$16,741-50,601]) was significantly higher than for patients without POAF ($36,506 [$21,745-64,634]; p=0.025). Examining average cost, POAF was associated with almost $30,000 higher mean hospital costs and over $4,000 higher mean ICU related costs.

Risk-Adjusted Outcomes and Resource Utilization

Postoperative atrial fibrillation continued to be associated with increased morbidity and resource utilization after risk-adjustment, as demonstrated in Table 4. This included higher risk of major morbidity (OR 2.46, p=0.0004) with a trend towards increased renal failure (OR 1.96, p=0.060). Postoperative atrial fibrillation was also independently associated with unplanned right ventricular assist device (RVAD) placement (OR 2.90, p=0.010). Resource utilization was higher with POAF including discharge to a facility (OR 2.23, p=0.007). Both postoperative and ICU LOS were higher with POAF (80 hours and 4.9 days, both p<0.05). Estimates for higher hospital ($19,183) and ICU ($5,488) costs associated with POAF did not reach statistical significance (both p>0.05). There was no association between POAF and operative mortality (OR 0.98, p=0.685) or stroke (1.19, p=0.667).

Additional risk factors included within each regression model are available in Supplemental Tables 2-12. The most widely associated variable was POAF, significant in 6 of 11 models. Also widely associated with outcomes were last hematocrit level (4 models) and last total albumin level (6 models). The least useful variables for risk prediction were preoperative inotropes (0 models), last platelet count (1 model), last international normalized ratio (1 model), HeartMate II device (1 model), LVAD volume by center (1 model), and year (1 model). The logistic regression model performance ranged from a c-statistic of 0.66 to 0.74. The linear regression model performance ranged from a r^2 of 0.09 to 0.18.

DISCUSSION

This study analyzes the impact of atrial fibrillation on risk adjusted morbidity, mortality, and resource utilization including hospital costs in a large regional cohort of continuous flow

LVAD patients. Of the 689 patients who underwent LVAD placement and did not have a history of atrial fibrillation, 121 (17.6%) developed POAF. The development of POAF was associated with a risk-adjusted increase in major morbidity (OR 2.5) but not mortality. There was a strong risk-adjusted association between POAF and unplanned RVAD (OR 2.9) as well as a trend towards renal failure (OR 2.0). In addition, POAF was broadly associated with increased resource utilization including discharges to a facility and length of stay. This includes a 5 day increase in postoperative length of stay, most of which was spent in the ICU (88 additional hours). While there are contemporary estimates of the impact of POAF in coronary and valve surgery, to our knowledge this represents the first estimates in the LVAD population.

The incidence of POAF after cardiac surgery has been reported to range from 10-40%.[4] However, there are far fewer estimates for rates of atrial fibrillation after LVAD surgery. In this analysis the overall rate of POAF was 17.6%. This rate is both consistent with the coronary and valve surgery rates, as well as previously reported rates after LVAD implantation of 13-32%.[5, 7,8, 18] These numbers are somewhat surprising given that LVAD implantation decreases left atrial pressure and size and has been shown to reduce atrial arrhythmias in the long-term, where over 40% of patients with prior atrial fibrillation will never have a recurrence in long-term follow-up.[18] While POAF is thought to be brought on by unique perioperative stressors, insight can be gained by noting paroxysmal and permanent atrial fibrillation have drastically different trajectories after LVAD placement, with the former improving and the latter causing increased risk of long-term mortality.[18, 19] Right heart failure is the likely culprit as permanent atrial fibrillation will continue to compromise right ventricular filling.[20, 21] This is supported by the fact that these patients have higher rates of hospitalization for heart failure and right heart failure as a cause of death.[19, 22]

While POAF increases the risk of mortality after coronary and valve surgery, this was neither demonstrated in this study nor was POAF found to increase the risk of short or long-term mortality after LVAD placement in other studies.[1, 4, 5, 7] Despite a lack of impact on operative mortality, POAF was highly associated with STS defined major morbidities. This correlates with the coronary and valve literature, but has not been shown previously in the LVAD population.[4, 23] This association appears to be driven by right heart dysfunction and results in a significantly higher risk for unplanned RVAD and a trend of increased renal failure. While the risk factors for heart failure and atrial fibrillation are similar and the causality cannot be determined from this study, evidence would suggest that POAF is both a cause and symptom of right heart failure. Similar arguments for why permanent atrial fibrillation disrupt right ventricular function apply to POAF. Additionally, many patients after LVAD placement have high right sided pressures increasing the risk of both heart failure and atrial fibrillation, which is born out by the higher median pulmonary artery pressures in the POAF cohort.[21] Finally, it is also been shown that treatment of atrial fibrillation with ablation improves right heart symptoms.[24]

Importantly, the component complication of permanent stroke was not associated with development of POAF.[5] This is contrary to other cardiac surgery populations where POAF increases the risk of stroke, although these patients are not routinely anticoagulated.[4]

Additionally, the current literature is mixed with regards to atrial fibrillation and risk of thromboembolic events, with controversy ignited when preoperative atrial fibrillation was found to increase the risk of late events.[25] Recent literature is more consistent with our findings that neither preoperative or postoperative atrial fibrillation are associated with increased rate of stroke.[5, 19, 26, 27]

Resource utilization was found to be increased in LVAD patients who develop POAF, both in the unadjusted and risk-adjusted analyses. In other cardiac surgery procedures POAF is associated with increases of 48 hours in the ICU and 3 additional postoperative days.[4, 23] These represent approximately 100% and 50% increases based on respective median LOS for patients without POAF. Similarly, in this study POAF was associated with a risk-adjusted increase in ICU LOS of 88 hours, a 52% increase over the median ICU LOS of 168 hours for non-POAF patients. The increase of 5 days postoperatively in the POAF group represents a 26% increase over the median of 19 days in the non-POAF cohort. These results and a lack of association with mortality indicate that POAF has similar effects in LVAD and other cardiac procedures, although the relative effect size is smaller in this population. However, due to the high complication rates and resource utilization the impact is still decidedly notable and clinically relevant with larger absolute increases in LOS. This is the first time POAF has been identified as predictive of increase length of stay after LVAD implantation as other analyses have not included this as a risk factor in their models.[28]

This study has limitations, many of which are inherent to any retrospective analysis of a multi-institutional database such as a risk of selection bias. This design prevents causal determination and in particular the timing and relationship of atrial fibrillation to other complications cannot determined. Furthermore, we are constrained by the dataset available that includes unique information such as cost, but also lacks detailed information present in other databases or common in atrial fibrillation specific trials as well as INTERMACS. Some patients were missing multiple laboratory values preventing the entire cohort from being included in the risk-adjustment analysis. The risk-adjustment performed requires regression models be built for each outcome of interest, increasing the risk of a type I error, the false positive rate. However, compared to other options this has the advantage of not requiring matching on a postoperative event and utilizing risk models that have been previously validated in large cohorts. Finally, findings were limited by the short-term nature of all STS related databases.

CONCLUSION

Postoperative atrial fibrillation is an underappreciated complication after LVAD implantation. The development of POAF was associated with a risk-adjusted increase in not only major morbidity, but also resource utilization. This is likely driven by right ventricular failure both causing and worsened by the atrial fibrillation. This correlated with increased renal failure and unplanned RVAD placement. The result is both ICU and postoperative length of stays significantly increase with POAF. Contrary to some findings and the coronary/valve literature, postoperative atrial fibrillation was not associated with either mortality or permanent stroke. The significant implications of POAF in the setting of a high resource utilization surgery make it a prime target for quality improvement measures.

Lessons learned in prophylaxis and treatment with other cardiac surgeries may translate to the LVAD population. Further study is warranted to help limit the burden identified by this analysis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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ABBREVIATIONS

ECMO	extracorporeal membrane oxygenation
ICU	intensive care unit
LOS	length of stay
LVAD	left ventricular assist device
NYHA	New York Heart Association
POAF	postoperative atrial fibrillation
PRBC	packed red blood cells
RVAD	right ventricular assist device
STS	Society of Thoracic Surgeons
VCSQI	Virginia Cardiac Services Quality Initiative

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CENTRAL PICTURE

Legend: HeartMate II Left Ventricular Assist Device (Images provided by St. Jude Medical, Inc.) (88/90)

CENTRAL MESSAGE

POAF was associated with increased major morbidity, likely due to worsening right heart failure. This led to POAF patients having longer ICU and hospital stays, and more discharged to facilities. (196/200)

PERSPECTIVE STATEMENT

This study clarifies that some known associations of POAF apply to the LVAD population including increased morbidity and resource utilization. The likely detrimental impact on right heart function should spur further investigation to prevent complications. The impact of these complications represent a great opportunity to translate quality improvement initiatives into the LVAD population. (392/405)

Table 1

Baseline characteristics by POAF status

	No POAF (n = 568)	POAF (n = 121)	p value
Age	54 [42-61]	58 [52-64]	<0.0001
Body mass index	28 [24-33]	29 [25-35]	0.349
Female	159 (28.0%)	30 (24.8%)	0.474
Ventricular arrhythmia	146 (25.7%)	33 (27.3%)	0.721
Hypertension	367 (64.7%)	79 (65.3%)	0.906
Diabetes	235 (41.5%)	60 (49.6%)	0.101
Dialysis dependent renal failure	13 (2.3%)	2 (1.7%)	0.662
Prior stroke	46 (8.3%)	17 (14.2%)	0.047
Chronic lung disease (moderate/severe)	88 (15.7%)	21 (17.7%)	0.596
Prior myocardial infarction	194 (34.3%)	50 (41.3%)	0.142
NYHA Class IV	492 (86.9%)	108 (90.0%)	0.320
Ejection fraction (%)	15 [10-20]	15 [10-20]	0.271
Pulmonary artery systolic pressure (mmHg)	47.5 [36-60]	55 [41-62]	0.015
Aortic regurgitation (moderate/severe)	19 (4.9%)	4 (4.8%)	0.984
Mitral regurgitation (moderate/severe)	243 (49.5%)	62 (61.4%)	0.029
Tricuspid regurgitation (moderate/severe)	166 (35.5%)	46 (45.5%)	0.058
Preoperative albumin (g/dL)	3.6 [3.2-4.0]	3.5 [3.1-3.9]	0.066
Preoperative bilirubin (mg/dL)	0.8 [0.5-1.4]	0.9 [0.6-1.4]	0.259
Preoperative hematocrit (%)	35 [31-39]	35 [30-39]	0.986
Prior cardiac surgery	153 (26.9%)	23 (19.0%)	0.069
Urgent or Emergent status	447 (78.7%)	95 (78.5%)	0.964
Preoperative inotropes	423 (74.5%)	92 (76.0%)	0.720
Preoperative intraaortic balloon pump	89 (15.7%)	21 (17.4%)	0.651
Preoperative ECMO	17 (4.5%)	4 (4.1%)	0.862

NYHA = New York Heart Association; POAF = postoperative atrial fibrillation; ECMO = extracorporeal membrane oxygenation

Table 2

Operative characteristics by POAF status

Operative Characteristics	No POAF (n=586)	POAF (n=121)	p value
VAD exchange	44 (7.8%)	4 (3.3%)	0.084
LVAD Device			0.023
HeartMate II	463 (81.5%)	87 (71.9%)	
HeartMate III	2 (0.4%)	2 (1.7%)	
HeartWare HVAD	103 (18.1%)	32 (26.5%)	
Tricuspid valve operation	49 (8.7%)	19 (15.7%)	0.019
Cross clamp utilized	108 (19.6%)	30 (24.8%)	0.200
Cardiopulmonary bypass time (min)	99 [73-131]	103 [77-146]	0.076

LVAD = left ventricular assist device; POAF = postoperative atrial fibrillation

Table 3

Unadjusted outcomes by POAF status

Characteristics	No POAF (n=568)	POAF (n=121)	p value
STS operative mortality	78 (13.7%)	15 (12.4%)	0.696
STS Major morbidity	325 (57.2%)	88 (73.3%)	0.001
Permanent stroke	24 (4.2%)	5 (4.2%)	0.977
Cardiac arrest	12 (2.1%)	7 (5.8%)	0.024
Pneumonia	42 (7.4%)	15 (12.5%)	0.065
Prolonged ventilation	300 (52.8%)	87 (72.5%)	<0.0001
Unplanned RVAD	25 (4.4%)	12 (9.9%)	0.015
Renal failure	54 (9.5%)	18 (15.0%)	0.074
Renal failure requiring dialysis	39 (6.9%)	13 (10.8%)	0.135
Deep sternal wound infection	1 (0.2%)	0 (0%)	0.646
Transfusion, any	390 (68.9%)	90 (74.4%)	0.233
Transfusion, PRBC	377 (66.7%)	87 (71.9%)	0.270
Reoperation for bleeding	82 (14.4%)	25 (20.8%)	0.079
Reoperation for any reason	111 (19.5%)	34 (28.3%)	0.032
Discharge to facility	63 (12.5%)	29 (26.9%)	0.0002
Readmission	73 (14.7%)	18 (17.1%)	0.534
Total cost	$305,832 ± 160,276	$334,512 ± 143,733	0.003
ICU cost	$41,984 ± 42,186	$476,043 ± 34,279	0.025
Postoperative LOS (days)	19 [14-28]	24 [17-36]	<0.0001
ICU LOS (hours)	168 [116-293]	249 [161-447]	<0.0001

ICU = intensive care unit; LOS = length of stay; POAF = postoperative atrial fibrillation; PRBC = packed red blood cells; STS = Society of Thoracic Surgeons

Table 4

Risk-adjusted association between POAF and short-term outcomes

	Odds Ratio	95% CI	p-value	C-statistic
Operative mortality	0.98	(0.51-1.87)	0.944	0.685
Major morbidity[†]	2.46	(1.49-4.06)	0.0004	0.667
Permanent stroke	1.19	(0.42-3.40)	0.747	0.714
Unplanned RVAD	2.90	(1.30-6.49)	0.010	0.720
Renal failure	1.96	(0.97-3.97)	0.060	0.740
Cardiac Arrest	3.42	(1.21-9.71)	0.021	0.713
Prolonged ventilation	2.68	(1.64-4.37)	<0.0001	0.662
Reoperation	1.87	(1.10-3.18)	0.020	0.659
Discharge to facility	2.23	(1.25-4.01)	0.007	0.733
	Estimate	95% CI	p-value	R^2
Intensive Care Unit LOS (hrs)	87.7	(22.5-153.0)	0.009	0.124
Postoperative LOS (days)	4.9	(0.7-9.2)	0.022	0.091
Intensive care unit cost	$5,488	(-2539-13,515)	0.180	0.184
Total hospital cost	$19,183	(−16,918-55,283)	0.297	0.099

LOS= length of stay; POAF = postoperative atrial fibrillation; RVAD = right ventricular assist device