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Rate Control Versus Rhythm Control in Patients with Left Ventricular Assist Devices and Atrial Fibrillation

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Abstract

Background: Atrial fibrillation (AF) is a common comorbidity in patients with left ventricular assist devices (LVAD) with no defined guideline treatment strategy of rate versus rhythm control. The purpose of this study is to determine the effects of rate versus rhythm control for AF on the outcomes of patients with LVAD at our institution.

Methods: Consecutive patients who underwent LVAD implantation at St Vincent Hospital from January 1, 2015 to December 31, 2017 were retrospectively evaluated. Patients with AF were identified and divided into rate control or rhythm control groups. The primary outcome evaluated was a composite of death, heart failure admission, gastrointestinal bleed, ventricular tachycardia, cerebrovascular accident, hemolysis, and pump thrombosis. Secondary outcomes included the individual variables from the primary outcome.

Results: Out of 201 patients that underwent LVAD implantation, 81 had AF after implantation and were included with a median follow-up period of 384 days. The rate control group (n = 31; 38%) and the rhythm control group (n = 51; 62%) had no difference in composite outcomes (61% vs 59%, p = 0.83). When taken individually there was no difference in outcomes between the two groups. Thirteen patients underwent electrical cardioversion and successful conversion to normal sinus rhythm occurred in 71% of cases with a 60% recurrence rate.

Conclusions: There was no difference in primary outcome between rate and rhythm control groups. These data suggest that maintenance of sinus rhythm may not be necessary in all patients with LVAD.

Introduction

Atrial fibrillation (AF) is present in up to 50% of patients with congestive heart failure (CHF). [1,2,3] For patients with advanced CHF, left ventricular assist device (LVAD) has become a viable management strategy as a bridge to transplantation or destination therapy. The effect of AF on the outcomes of patients with LVADs is unknown.[1, 4,5,6,7] Specifically, current evidence remains equivocal on whether AF increases thromboembolic events, heart failure events or mortality in this population [8, 9, 10, 11] Furthermore, when AF is present in the LVAD patient, it is unclear whether rate or rhythm control is the most appropriate strategy. We retrospectively evaluated the effect of rate versus rhythm control for AF on the outcomes in our LVAD population.

Methods

Study Design and Participants

A retrospective single center review was performed of all 201 patients who underwent LVAD implantation at St Vincent Hospital in Indianapolis, IN from January 1, 2015, through December 31, 2017. Follow-up ended July 31, 2018. Patients were identified using the mechanical circulatory support database managed by our LVAD research team. Inclusion criteria consisted of any patient with AF post LVAD implantation irrespective of whether AF was present pre-operatively. Patients under the age of 18 were excluded. The primary outcome evaluated was a composite of death, CHF admission, gastrointestinal bleed (GIB), ventricular tachycardia (VT), cerebral vascular accident (CVA), hemolysis, and pump thrombosis. Secondary outcomes included the individual rates of death, CHF admission, GIB, VT, CVA, hemolysis and pump thrombosis. This study was approved by the local Institutional Review Board.

Study Arms and Clinical Data

Patients were separated into two groups based on AF management strategy: rate control vs. rhythm control. The definition of rate control included patients that did not receive therapy in attempts to restore normal sinus rhythm (NSR), while rhythm control included patients that received an antiarrhythmic drug (AAD) or electrical cardioversion in an attempt to restore and maintain NSR. Because many patients with LVAD are on AAD for ventricular tachycardia, only individuals treated with AAD with the intent to restore NSR were included in the rhythm control group; this intent was deduced by two independent

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chart reviewers and in the case of disagreement adjudicated by a third study member. AF was initially ascertained by chart review, but then confirmed by electrocardiogram, inpatient telemetry or data from cardiac implantable electronic device (CIED). CVA was defined as having a stroke, transient ischemic attack or intracranial hemorrhage diagnosed by the treating physician. Congestive heart failure admission was defined as patients requiring inotropes or readmission for IV diuretics. Time in therapeutic range (TTR) with warfarin was calculated for all patients using the Rosendaal method. [12]

Statistical Analysis

Continuous variables were compared using student T-test if normally distributed or Mann-Whitney test if non-normally distributed. Categorical variables were compared using Pearson Chi-square analysis or Fischer Exact Testing and expressed as percentages. Two tailed P values <0.05 were considered statistically significant.

Results

Baseline Characteristics

From January 1, 2015, through December 31, 2017, 201 patients underwent LVAD implantation. Of these patients, 82 (41%) had AF after device implantation. Among these, 31 (38%) underwent rate control and 51 (62%) underwent rhythm control treatment approaches. The baseline demographics are summarized in [Table 1]. In the rate control group, the median (interquartile range) age was 62 (57, 66) years and only 9.7% of the patients were female, while in the rhythm control group, the median (interquartile range) age was 60 (53, 67) years and 17.6% of the patients were female, with no difference in age or sex between the two groups. The two groups had similar CHA_2DS_2VASc scores (CHF, hypertension, age ≥ 75 years, diabetes, stroke/TIA/thromboembolism, vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) and duration of follow up. Other basic demographic characteristics were also similar between the two groups including TTR.

Antiarrhythmic Therapy and Electrical Cardioversion

Eight patients (26%) in the rate control group were taking amiodarone for VT suppression with no intention of restoring sinus rhythm (chart review agreement 100%). In the rhythm control group, 98% (n = 49) of patients received therapy with an antiarrhythmic drug (amiodarone in all but one patient who was given dofetilide) and 59% of patients had antiarrhythmic therapy long-term. Electrical cardioversion (CV) was performed in 28% of patients in the rhythm control group and immediately restored NSR in 71% (10 of 14 patients). There was a recurrence rate of 60% (n = 6) in long term follow up despite successful cardioversion.

Outcomes According to Treatment Arm

Overall, there was no difference in the combined endpoint of death, CVA, GIB, CHF admission, VT, hemolysis and pump thrombosis (p = 0.83). There was also no difference in secondary outcomes between the two groups. Ventricular tachycardia was the secondary outcome that occurred most frequently in the rate control and rhythm control group (29% and 43% respectively, p = 0.3). In the rate control group, there was a 26% mortality rate during follow-up while it was 18% in the rhythm control group (p = 0.38) The primary and secondary outcomes are summarized in [Table 2]. Additionally, a comparison of all rate control patients not taking amiodarone were compared to those in the rhythm control group. Fourteen (58%) patients in the rate control arm that were not taking amiodarone met the primary endpoint compared to the 30 (59%) patients in the rhythm control group (p = 0.95). Furthermore, we compared all patients who were taking amiodarone compared to those not taking amiodarone. Fifteen (63%) of the patients that were not taking amiodarone met the primary endpoint compared to the 33 (58%) patients taking amiodarone (p = 0.7).

Discussion

The current study adds to the limited body of literature evaluating the impact of AF management in patients with LVADs. We found that AF occurred in 41% of patients after implantation of LVAD, which was lower than previous reports.[10,11,12] There was no difference in composite outcome of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis between rate and rhythm control strategies (61% vs 59%, p = 0.83). To our knowledge, this is the first study to determine the acute success rate of cardioversions in AF patients with LVADs, with

Table 1: **Baseline Characteristics. Values are median (interquartile range) or n (%). Abbreviation are IMACS – International registry for mechanically assisted circulatory support; LVAD – Left Ventricular assist Device; CHADsVASc – CHF, hypertension, age >= 75 years, diabetes, stroke/TIA/thromboembolism, vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]; INR – International normalized ratio.**

	Rate Control 31 (38%)	Rhythm Control 51 (62%)	p-value
Median Age, years	62 (57, 66)	60 (53, 67)	0.49
Female Sex	3 (9.7%)	9 (17.6%)	0.32
BMI	29 (25, 33)	29 (26, 33)	0.73
Medical History			
Atrial fibrillation	23 (74.2%)	33 (64.7%)	0.37
Coronary Artery Disease	12 (38.7%)	26 (51%)	0.28
Ventricular Tachycardia	15 (48.4%)	20 (39.2%)	0.42
Hypertension	16 (51.6%)	35 (68.6%)	0.12
Diabetes	14 (45.2%)	28 (54.9%)	0.39
Hyperlipidemia	20 (64.5%)	36 (70.6%)	0.57
Stroke	4 (12.9%)	5 (9.8%)	0.66
ICD	25 (80.6%)	36 (70.6%)	0.31
Destination Therapy	15 (48.4%)	25 (49%)	0.96
IMACS profile			0.57
1	6	7	
2	1	7	
3	17	26	
4	5	9	
7	0	1	
LVAD Type			0.4
Heart Ware	16	18	
Heart Mate 2	6	18	
Heart Mate 3	8	13	
CHADsVASc Score	3 (2, 4)	3 (3, 4)	0.4
Follow-up (median LVAD days)	409 (275, 743)	343 (231, 693)	0.37
Time in Therapeutic Range, INR	67 (56, 75%)	67 (55, 75%)	0.93

Table 2: Outcomes. Values are n (%). CHF – congestive heart failure

	Rate Control	Rhythm Control	
	Events	Events	p-value
Composite Outcome	19 (61%)	30 (59%)	0.83
Ventricular Tachycardia	9 (29%)	22 (43%)	0.3
Cerebrovascular Accident	2 (6%)	9 (18%)	0.15
Gastrointestinal Bleed	6 (19%)	16 (31%)	0.23
CHF admission	5 (16%)	14 (27%)	0.24
Hemolysis	1 (3%)	2 (4%)	0.86
Thrombosis	1 (3%)	2 (4%)	0.87
Death	8 (26%)	9 (18%)	0.38

14 patients undergoing cardioversion and an acute success rate of 71%.

Primary and Secondary Endpoints

The primary outcome including a composite of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis revealed no statistical difference between rate versus rhythm control groups (61% vs 59%, p = 0.83). Conclusions from previously published studies evaluating whether or not AF contributes to morbidity and mortality in this unique population were equivocal. [1,4,5,6,7] As a result, clinicians caring for this group of patients have few data to identify what risk AF may pose and the best therapeutic approach. Recently, Noll et al attempted to bridge this void of literature by retrospectively evaluating what effects rhythm control may have over rate control. They concluded that a rhythm control strategy for atrial arrhythmias in patients with LVAD does not decrease the risk of mortality, thromboembolism or bleeding. [13] Our data also support that a rhythm control strategy to maintain sinus rhythm may not improve outcomes in patients with LVAD.

The secondary outcomes included the rate of death, CHF admission, GIB, VT, CVA, hemolysis and pump thrombosis and revealed no statistical difference. These secondary outcomes were selected given the putative risks of AF in this select population include blood stasis secondary to decreased atrial contractility resulting in clot formation, CVA, pump thrombosis and hemolysis; rapid and irregular ventricular contractions precipitating CHF exacerbations and ventricular arrhythmias; and treatment with additional medications, such as amiodarone, that may result in labile INRs. Amiodarone was almost exclusively used in the rhythm control group and did not result in a significant difference in TTR despite drug-drug interactions. There was no difference in rate of GIB or CVA between the two groups. However, there was a trend towards higher rate of CVA (18% vs 6%) and GIB (31% vs 19%) in the rhythm control group that did not meet statistical significance. Larger scale trials are needed to ensure this difference doesn't expand with larger numbers. This also demonstrates the importance of appropriate international normalized ratio (INR) monitoring if additional medications are prescribed with significant warfarin interactions. There was also no difference in CHF admissions between the two groups suggesting rate control for AF should suffice for heart failure mitigation.

Electrical Cardioversion for AF

To our knowledge, this is the first study to determine the success rate of cardioversions in AF patients with LVADs, with 14 patients undergoing cardioversion. The success rate of 71%, is similar to previous reports in patients without LVAD ranging from 68-90%. [14, 15] It is important to note that 71% (n = 10 of 14) of these patients were taking amiodarone at the time of electrical cardioversion. After successful cardioversion, 60% had eventual AF recurrence despite continued antiarrhythmic medication. Of the 14 patients who underwent cardioversion, 1 had a CVA within 1 month after the CV. The patient had a therapeutic INR at time of CV, and had no left atrial appendage thrombus identified on a transesophageal echocardiogram immediately prior to CV. Nine days after the CV, the patient presented with a small right middle cerebral artery infarct and a subtherapeutic INR.

Limitations

This study has the limitation of being a retrospective, nonrandomized, single-center study with a limited number of patients. As a result, we are unable to account for confounding factors that may play a significant role in the results. These confounding factors include, but are not limited to selection bias toward early cardioversion or AADs for patients perceived to have benefit from an early rhythm control strategy (e.g. patients with severe heart failure and uncontrolled ventricular rates), ventricular arrhythmias requiring anti-arrhythmic therapies that may also aid in AF rhythm control and those requiring prolonged inotropic therapy making rate control medications difficult to use.

Conclusions

In patients with AF in the setting of LVAD, there was no difference in composite or individual outcomes of death, CVA, CHF admission, GIB, VT, hemolysis and pump thrombosis between rate and rhythm control groups. Electrical CV can be accomplished with reasonable safety and efficacy in patients with LVAD.

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