ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

Preoperative atrial fibrillation may not increase thromboembolic events in left ventricular assist device recipients on midterm follow-up

Yu Xia, MD, David Stern, MD, Patricia Friedmann, MS and Daniel Goldstein, MD

From the Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York.

KEYWORDS:
LVAD;
atrial fibrillation;
thromboembolic events;
patient survival;
INTERMACS

BACKGROUND: Atrial fibrillation (AF) is a well-established risk factor for thromboembolic (TE) complications. AF is frequently found in patients with advanced heart failure, including patients undergoing left ventricular assist device (LVAD) implantation. However, reports on whether preoperative AF increases the risk of TE events after LVAD implantation are scarce and limited to single-center or 2-center studies. We sought to evaluate the association of preoperative AF with TE events and patient survival using the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).

METHODS: A retrospective analysis of INTERMACS data of primary continuous-flow LVADs implanted between May 2012 and December 2013 was performed. Adult patients were dichotomized as having AF or no AF (NAF). TE events were defined as cerebrovascular accident, transient ischemic attack, hemolysis, arterial non–central nervous system embolism, or explant because of pump thrombosis. Kaplan-Meier analysis and multivariate Cox regression were performed for freedom from TE and patient survival.

RESULTS: Of 3,909 patients identified during the study period, 838 (21.4%) had preoperative AF. Patients with AF were older, were likely to be male, and had more comorbidities ($p < 0.01$). In the AF group, 236 TE events occurred in 175 (20.9%) patients. In the NAF group, 900 TE events occurred in 691 (22.5%) patients. The TE event rate was not significantly different between the 2 groups (0.36 events/patient-year in AF group vs 0.37 events/patient-year in NAF group, $p = 0.60$). On univariate analysis, AF was not significantly associated with freedom from TE but was associated with decreased patient survival (log-rank test $p = 0.03$). On multivariate analysis, AF was not significantly associated with either TE (adjusted hazard ratio 0.95; 95% confidence interval, 0.80–1.13) or patient survival (adjusted hazard ratio 1.09; 95% confidence interval, 0.91–1.31).

CONCLUSIONS: Analysis of INTERMACS suggests that preoperative AF may not increase the risk of postoperative TE complications or patient mortality on midterm follow-up. Longer follow-up to confirm these findings is warranted.

J Heart Lung Transplant ■■■■;■:■■■–■■■

Atrial fibrillation (AF) is the most common arrhythmia and is particularly common in patients with heart failure. The prevalence of AF increases with the severity of heart failure and coexists in up to 50% of patients with severe heart failure, increasing morbidity and mortality compared with either disorder alone.[1] Left ventricular assist device (LVAD) therapy is being increasingly used for treatment of end-stage heart failure, with >2,000 devices

Reprint requests: Daniel Goldstein, MD, 3400 Bainbridge Avenue, MAP 5, Bronx, NY 10467. Telephone: 718-920-2144. Fax: 718-231-7113.
E-mail address: dgoldste@montefiore.org

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2016.03.003

now being implanted annually in the United States.[2] With the increasing usage of LVADs, a significant number of patients with LVADs have preoperative AF. Preoperative AF is a risk factor for increased morbidity and mortality after valvular and coronary cardiac surgery.[3–7] To date, there are scant data published in the literature limited to single-center or two-center experiences regarding the impact of preoperative AF on outcomes after LVAD implantation. These reports present differing conclusions, with one group finding that AF may increase the risk of thromboembolic (TE) events, whereas other groups found no difference in TE events in patients with preoperative AF or patients who developed atrial arrhythmias post-operatively.[8–10] A preliminary review of data from our own center suggested a trend toward increased morbidity and mortality in LVAD recipients with preoperative AF.[11] To evaluate the association of preoperative AF with TE events and overall survival in a large cohort of LVAD recipients, we performed an analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).

Methods

Study population

INTERMACS data of all adult patients receiving continuous-flow LVADs between May 2012 and December 2013 as a first device were analyzed. Patients implanted with total artificial hearts and concomitant right ventricular assist devices were excluded. Patients were categorized as having a history of AF or no atrial fibrillation (NAF) based on a variable initiated at the relaunch of the INTERMACS registry in May 2012. Preoperative baseline characteristics were compared from the device data set along with variables in the follow-up data set.

Outcomes

The primary outcome was freedom from TE event defined as a composite of transient ischemic attack, cerebrovascular accident, hemolysis, arterial non–central nervous system thromboembolism, or explant secondary to pump thrombus. Patients were censored at the earliest occurrence of device explantation, transplantation, death, or last follow-up. The secondary outcome was patient mortality and overall incidence of adverse outcomes over the entire follow-up period for both the composite outcome and its parts. Incidence of bleeding events and subsequent TE events was compared between the NAF and AF groups.

Covariates

Covariates were selected based on perceived clinical relevance and included age $\geq$60 years, sex, body mass index $\geq$30, INTERMACS profile (1 or 2 vs $\geq$3), ischemic etiology, history of diabetes, liver dysfunction, pulmonary disease, major stroke, chronic renal disease, peripheral vascular disease, and any smoking. The appropriate functional form of model covariates was determined by exploratory data analysis and perceived impact on clinical relevance.

Statistical analysis

Categorical variables were expressed as proportions and compared by chi-square test. Continuous variables were expressed as mean $\pm$ SD and compared by *t*-test if normality criteria were met. Otherwise, they were expressed as median (interquartile range [IQR]) and compared with Wilcoxon rank sum test. Freedom from TE event and patient survival were analyzed with Kaplan-Meier curves. AF and NAF groups were compared using the log-rank test. The effects of AF and the other covariates on TE event and patient mortality were analyzed using Cox proportional hazards regression. No important departures from the proportional hazards assumption were observed. Ties in failure time were resolved using the Breslow method. Time to event was extracted from the INTERMACS events data set, with failure at time of TE or censoring at time of last contact, transplantation, or device explant. All *p*-values were 2-sided, and *p*-values < 0.05 were considered statistically significant. All data were analyzed using SAS software version 9.2 (SAS Institute Inc.).

Results

Patient characteristics

Our study population comprised 3,909 patients: 3,071 (78.6%) in the NAF group and 838 (21.4%) in the AF group. Baseline characteristics of AF and NAF patients are listed in Table 1. Patients with AF were older (age $\geq$60 years in 57.9% of AF patients vs 49.0% of NAF patients, $p < 0.01$), and there was a higher proportion of males among patients with AF (82.9% vs 77.8%, $p < 0.01$). New York Health Association functional class III or IV, INTERMACS profiles, and proportion of patients with ischemic cardiomyopathy were not significantly different. The AF group had a higher proportion of patients implanted for destination therapy (47.7% vs 43.1%, $p = 0.02$). Patients with AF also had more comorbidities, with a higher proportion of history of stroke, severe diabetes, chronic renal disease, peripheral vascular disease, pulmonary disease, pulmonary hypertension, liver dysfunction, chronic coagulopathy, gastrointestinal ulcers, smoking, and other comorbidities. In addition to LVAD implantation, patients with AF had a higher proportion of concomitant tricuspid valve repairs or replacement ($p < 0.01$) and other surgeries ($p < 0.01$). Concomitant surgeries among AF and NAF patients are depicted in Table 2.

Outcomes

Median follow-up time was 8.5 months (IQR 4.6–13.5 months) in the NAF group and 8.5 months (IQR 4.6–13.8 months) in the AF group ($p = 0.93$). Transplants occurred in 544 patients—425 (13.8%) in the NAF group and 119 (14.2%) in the AF group ($p = 0.79$). Median time to transplant was 6.2 months (IQR 3.8–9.8 months) and 6.2 months (IQR 4.1–10.4 months) in the NAF and AF groups, respectively ($p = 0.53$). Devices were explanted in 324 patients—78 (9.3%) in the AF group and 246 (8.0%) in the NAF group ($p = 0.23$). Median time to explant was 3.2 months (IQR 1.7–6.8 months) in the NAF