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Clinical Impact of Atrial Fibrillation in Patients With the HeartMate II Left Ventricular Assist Device

Alan D. Enriquez, MD,* Brandon Calenda, MD,† Parul U. Gandhi, MD,† Ajith P. Nair, MD,† Anelechi C. Anyanwu, MD,† Sean P. Pinney, MD†

ABSTRACT

BACKGROUND Atrial fibrillation (AF) is common in patients with the HeartMate II (HMII) left ventricular assist device (LVAD), but the impact of AF on clinical outcomes is uncertain.

OBJECTIVES This study sought to determine the effect of AF on outcomes in patients with the HMII LVAD.

METHODS Records of 106 patients who underwent HMII implantation at a single center were reviewed. The associations of paroxysmal atrial fibrillation (PAF) and persistent atrial fibrillation (PeAF) with survival, heart failure (HF) hospitalization, bleeding, and thromboembolism were examined using Kaplan-Meier survival analysis and Cox proportional hazards regression.

RESULTS Mean age was 56.6 ± 11.4 years, 87.7% of the implants were intended as a bridge to transplantation, and median length of support was 217 days (range: 1 to 952 days). AF was present in 55 patients (51.9%); 36 patients (34.0%) had PAF and 19 (17.9%) had PeAF. Twenty-one patients (19.8%) died, and 18 (17.0%) were hospitalized for HF. There were 0.75 major bleeding events and 0.28 thromboembolic events per patient year of follow-up. PAF was not associated with increased mortality, HF hospitalization, bleeding, or thromboembolism. PeAF, however, was an independent predictor of the composite endpoint of death or HF hospitalization (hazard ratio: 3.54; 95% confidence interval: 1.52 to 8.25; $p < 0.01$). Although there was no increase in bleeding or thromboembolism, patients with AF had thromboembolic events at higher international normalized ratios (INRs).

CONCLUSIONS Although PAF is not associated with worse outcomes in patients with the HMII LVAD, PeAF may be associated with increased mortality and HF hospitalization. Patients with AF also may have thromboembolic events at higher INR levels. (J Am Coll Cardiol 2014;64:1883–90) © 2014 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is common in patients with end-stage heart failure (HF) and is present in up to 50% of patients (1). AF prevalence in patients with continuous flow left ventricular assist devices (CF-LVADs) is similarly high (2). In conventional HF patients, AF has been associated with worse outcomes and increased mortality (1,3). In addition to an increased risk of thromboembolism, AF may lead to HF exacerbations because of a reduction in ventricular filling through the loss of atrial systole and rapid heart rates. However, the effect of AF on outcomes and mortality has not been well studied in LVAD patients.

AF may influence outcomes in patients with a CF-LVAD in several ways. Although LV filling is likely unaffected by AF due to support from the LVAD, right ventricular (RV) filling, and consequently cardiac output, may still be compromised by loss of atrial contraction, especially in patients with poor RV function and pulmonary hypertension. In addition, AF may confer an increased risk of thromboembolism in patients with a CF-LVAD (4), and some recommend

From the *Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts; and the †Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York. Dr. Pinney is on the advisory board of and has received consulting and speaker's fees from CareDX; is a paid consultant for Acorda Therapeutics; and has received clinical trial support and consulting and educational fees from Thoratec. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CF-LVAD = continuous flow left ventricular assist device

CPET = cardiopulmonary exercise test

CVA = cerebrovascular accident

HF = heart failure

HM II = HeartMate II

ICH = intracranial hemorrhage

PAF = paroxysmal atrial fibrillation

PeAF = persistent atrial fibrillation

RV = right ventricular/ventricle

TIA = transient ischemic attack

targeting an international normalized ratio (INR) of 1.5 to 2.0 for patients without AF and 2.0 to 2.5 for those with AF (5). Accordingly, AF may affect outcomes through an increased risk of bleeding due to the higher level of anticoagulation therapy. Therefore, we sought to determine the effect of AF on mortality, HF hospitalization, bleeding, and thromboembolism in patients with CF-LVADs.

METHODS

We reviewed the records of consecutive adult patients receiving the HeartMate II (HMII; Thoratec Corp., Pleasanton, California) LVAD at the Mount Sinai Medical Center in New York between June 2008 and April 2012. Patients were followed until 1 of the following endpoints was reached: death, transplantation, HMII explantation, end of follow-up period, or loss to follow-up. The Institutional Review Board of the Icahn School of Medicine at Mount Sinai approved this study.

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ATRIAL FIBRILLATION AND ANTICOAGULATION. Retrospective chart reviews of electrocardiograms, device interrogations, and progress notes were performed to evaluate for AF occurrence. AF was defined as the presence of preoperative AF or the development of AF post-LVAD past the perioperative period (>30 days). AF was further subdivided into paroxysmal atrial fibrillation (PAF) and persistent atrial fibrillation (PeAF), using standard definitions (1). Because outcomes may differ between these groups, patients were analyzed in 3 groups: 1) those who did not have AF; 2) those who had PAF; and 3) those who had PeAF. The management of AF post-LVAD was left to the discretion of the HF specialist. In terms of anticoagulation, all patients received aspirin, 81 mg daily, and warfarin. For patients without AF, the INR goal was 1.5 to 2.0. For all patients with AF, the INR goal was 2.0 to 2.5. If a patient had multiple bleeding events, the INR goal was decreased to 1.5 to 2.0 in patients with AF.

ATRIAL FIBRILLATION AND OUTCOMES. The focus of the study was the impact of PAF and PeAF on the following 3 outcomes: survival or HF hospitalization, thromboembolism, and bleeding. All deaths were confirmed through examination of the medical record, and the cause of death was noted. HF hospitalization was defined as hospitalization for signs of right HF (e.g., jugular venous distension, lower extremity edema) requiring escalation of diuretic therapy and/or initiation of inotrope therapy. Thromboembolism was defined as cerebrovascular accident (CVA), transient ischemic attack (TIA), arterial thromboembolism, or confirmed LVAD pump thrombosis. Major bleeding was defined using the Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) definition (6). However, intracranial hemorrhage (ICH) also was included in major bleeding. The INR at the time of each bleeding and thromboembolic event was recorded. For thromboembolic events, a 4-week mean INR prior to the event also was calculated.

ATRIAL FIBRILLATION AND FUNCTIONAL STATUS. Patients deemed suitable by the HF specialist underwent a cardiopulmonary exercise test (CPET) ≥3 months after LVAD implantation. The CPET was performed on a treadmill, using a modified Naughton protocol. Oxygen consumption (Vo_2) was continuously measured, and the test was symptom limited. Peak Vo_2 levels of patients without AF were compared with those of patients with PAF and PeAF.

STATISTICAL ANALYSIS. Categorical variables were evaluated using the chi-square or Fisher exact test. Continuous variables were analyzed with the *t*-test or Mann-Whitney *U* test. Normally distributed continuous variables were expressed as mean ± SD; nonnormal variables were expressed as medians with interquartile ranges (IQR). For survival analysis, Kaplan-Meier time-to-event curves stratified by AF status were generated for death or HF hospitalization, thromboembolism, and bleeding. Statistical significance between the curves was analyzed using the log-rank test. The effect of AF and other variables on each outcome was analyzed using Cox proportional hazards regression. Because of the relatively small number of events for each outcome, multivariable regression was performed only for the composite outcome. Variables with a p value of <0.10 in univariable analysis were included in the multivariable model. All p values were 2-tailed, and the level of significance for all p values was <0.05. No corrections were used for multiple comparisons. Confidence intervals (CIs) were computed at the 95% confidence level. All statistics were computed using Stata version 12.0 (StataCorp, College Station, Texas).

RESULTS

DEMOGRAPHICS. During the study period, 106 patients received the HMII device, and 9 patients also received a temporary RV assist device at the time of LVAD implantation. Only 1 patient underwent an (unsuccessful) Cryo-Maze (Medtronic, Minneapolis, Minnesota) procedure during LVAD implantation,