ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

Early elevations in pump power with the HeartMate II left ventricular assist device do not predict late adverse events

Christopher T. Salerno, MD,[a] Kartik S. Sundareswaran, PhD,[b] Thomas P. Schleeter, MD,[c] Sina L. Moanie, MD,[a] David J. Farrar, PhD,[b] and Mary Norine Walsh, MD[c]

From the [a]Department of Cardiothoracic Surgery, St. Vincent Heart Center of Indiana, Indianapolis, Indiana; [b]Research and Scientific Affairs, Thoratec Corporation, Pleasanton, California; and [c]Department of Cardiology, St. Vincent Heart Center of Indiana, Indianapolis, Indiana, USA.

KEYWORDS:
LVAD;
HeartMate II;
pump power;
thrombus;
HMII;
hemolysis

BACKGROUND: The aim of this study was to evaluate the prevalence of early pump power elevation events in patients with the HeartMate II (HMII) and its impact on subsequent development of stroke and pump thrombosis.

METHODS: We analyzed >45,000 measurements of pump power and pump speed measured during the initial hospitalization period and >12,000 follow-up measurements obtained from 138 consecutive patients implanted with a HMII between January 2009 and December 2012. An early power elevation (PEL) event was defined as power ≥10 W within the first 14 post-operative days. Patients were divided into two groups: those with an early PEL event and those without (NP).

RESULTS: Median follow-up duration was 316 (range 2 to 1,264) days. Twenty-seven (20%) patients had early PEL events that lasted for a total duration of 4 (range 1 to 77) hours per patient. Pump speed averaged 9,400 rpm in both groups. Although patients in the PEL group had higher median power (7.1 [6.0 to 9.9] W vs 6.7 [5.7 to 7.8] W, $p < 0.001$) in the immediate post-operative period, there was no difference between the two groups noted at first follow-up (6.6 [5.9 to 8.7] W vs 6.7 [5.5 to 7.7] W, $p = 0.940$). No differences in the prevalence of hemorrhagic stroke (4% vs 3%, $p = 0.56$), ischemic stroke (0% vs 4%, $p = 0.41$), hemolysis (7% vs 5%, $p = 0.32$), pump thrombosis (7% vs 4%, $p = 0.21$) or survival (76% at 1 year in both groups) were found between the two groups.

CONCLUSIONS: In this single-center experience, PEL events that occurred early all resolved by discharge. No relationship was found between early PEL events and subsequent development of pump thrombosis, hemorrhagic stroke or ischemic stroke.

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

The HeartMate II (HMII) is a left ventricular assist device (LVAD) approved by the U.S. Food and Drug Administration (FDA) for use as a bridge to transplant (BTT) and destination therapy (DT) in advanced heart failure patients who are refractory to medical therapy. Results of the pivotal clinical trial leading to FDA approval for both BTT and DT have been published[1,2] and suggested that the risk of bleeding was higher relative to the risk of thrombosis. In the recently published HMII BTT post-market study, the incidence of bleeding requiring blood transfusions was 1.44 events per patient-year (eppy), which was much higher compared with ischemic stroke (0.06 eppy), hemorrhagic stroke (0.01 eppy), hemolysis (0.04 eppy) and device replacement (0.01 eppy).[3] Similarly, in the DT experience,

Reprint requests: Christopher T. Salerno, MD, FACS, Department of Cardiothoracic Surgery, St. Vincent Heart Center of Indiana, 8433 Harcourt Road, Suite 100, Indianapolis, IN 46260. Telephone: 317-583-7602. Fax: 317-583-7644.

E-mail address: ctsalern@stvincent.org

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2014.02.024

the rate of bleeding requiring transfusions was higher (1.13 eppy) compared with ischemic stroke (0.05 eppy), hemorrhagic stroke (0.03 eppy), hemolysis (0.03 eppy) and device thrombosis (0.04 eppy).[4] With increasing clinical experience, there has been a general trend toward a lower incidence of bleeding and stroke, as reported in subsequent publications on BTT[5] and DT.[4] Some of these improvements in bleeding were realized through an altered anticoagulation protocol involving the use of heparin in the immediate post-operative period[6] and a revised international normalized ratio (INR) target of 1.5 to 2.5.[7] These findings were subsequently incorporated into the clinical management recommendations for LVADs.[8]

Although the incidence of thromboembolic events is low, as shown in both single- and multi-center studies,[2–7,9–11] recent reports have suggested that thrombosis may be a growing, vexing problem.[12–18] A recent publication on management of pump thrombosis shows it is a complex multi-factorial event that presents with a variety of signs or symptoms including: power elevations; isolated increases in serum lactate dehydrogenase (LDH); clinically significant hemolysis; failure to adequately unload the left ventricle; and heart failure.[19] Factors potentially contributing to pump thrombosis may be pump-related (e.g., bearing heat, blood–contact surface interactions, shear-induced platelet activation, regions of flow stasis), patient-related (e.g., atrial fibrillation, atrial/ventricular thrombus, infection, sepsis, hypercoagulable state) or management-related (e.g., sub-therapeutic anticoagulation, absence of anti-platelet therapy, inflow cannula malposition at implant, infection management).[19]

One of the signs that may occur with an intra-pump thrombus is elevation in pump power. In the early post-operative period, episodes of early power elevations are common, due to the wide variation in patient-specific conditions immediately after implantation. However, these early power elevations may not necessarily be an indication of pump thrombus in the absence of other clinical symptoms. Also, it is not known whether these early pump power elevations are risk factors for later adverse events, especially thromboembolic events. Hence, the objectives of this study were to: (a) characterize early power elevations observed in the immediate post-operative period; and (b) determine whether this phenomenon was relatable to future pump-related complications, such as development of hemorrhagic stroke, ischemic stroke, hemolysis, pump thrombosis and overall survival.

Methods

This study is a retrospective review of pump data manually collected over a period of 4 years from the HMII system monitor. One hundred forty-two consecutive patients received the HMII LVAD at a single institution from January 2009 to December 2012. One hundred thirty-eight of the 142 patients had pump data recorded at regular intervals post-implantation, and were the subjects of this investigation. Over 45,000 measurements of pump power, pump speed, pulsatility index (PI) and flow were made during initial hospitalization in these patients. These data were recorded from the system monitor by nurses approximately every hour when the patient was in the intensive care unit (ICU), with the frequency gradually decreasing as the patient became nearer to discharge.

In addition, INR, partial thromboplastin time (PTT), platelet count (PLT) and mean arterial pressure (MAP), evaluated using the Doppler technique, were also recorded for each patient. One hundred five of the 138 patients also had measurements of pump parameters after initial hospital discharge ($>12{,}000$ follow-up measurements). Patients who did not have follow-up power measurements were missing the data for a variety of reasons, but the main reason for missing data was that the patient reached an outcome (death or transplantation) before follow-up pump data were recorded. Nineteen of the 33 patients with missing follow-up power data had an outcome within the first 90 days, 16 of whom died with 3 being transplanted. For the remaining 14 patients, follow-up power was unavailable in the database, for unknown reasons. Early power and outcomes data were available for all 138 patients.

Patient outcomes analyzed included death while on device support, heart transplantation and recovery. In addition, hemorrhagic stroke, ischemic stroke, hemolysis and pump thrombosis were also obtained. Definitions utilized for evaluating the adverse events were as follows:

Stroke: Neurologic deficit lasting ≥ 24 hours.

Hemorrhagic stroke: If there is computed tomographic (CT) evidence of hemorrhage.

Ischemic stroke: If there is CT evidence of ischemic infarction.

Hemolysis: Clinical evidence of hemolysis as evidenced by elevated LDH, plasma hemoglobin (PHGB) and/or hemoglobinuria.

Pump thrombosis: Any suspected thrombus within the device as evidenced by impaired pump performance (e.g., lack of left ventricular unloading) requiring surgical intervention, urgent transplantation, pump exchange or death.

Data analysis

Measurements of pump power were plotted as a function of time for all 138 patients. Along with measurements of pump power, pulsatility index, pump flow, MAP, INR and PTT were also plotted to assess any observable correlations for any of these parameters with pump power. Any recorded power measurement ≥ 10 W was considered to be a power elevation event. Patients were divided into two groups based on whether an early power elevation event was experienced or not:

Normal power (NP) group: Maximum power measured <10 W in the first 14 days post-implantation.

Power elevation (PEL) group: At least one measurement of power ≥ 10 W in the first 14 days post-implantation.

Example power graphs of a patient with normal pump power and a patient with early power elevation events are shown in Figure 1.

Survival and adverse events were compared across both groups of patients. The analysis was performed on data as of March 11, 2013. Data are presented as mean $\pm$ standard deviation (SD) or median (5th to 95th percentile) for continuous variables and as percentage of patients for categorical variables. Adverse events are presented both as percentage of patients and as number of events per patient-year. Continuous variables were compared using the *t*-test (when the parameters were normally distributed) or the