Long-term outcomes in leadless Micra transcatheter pacemakers with elevated thresholds at implantation: Results from the Micra Transcatheter Pacing System Global Clinical Trial

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BACKGROUND Device repositioning during Micra leadless pacemaker implantation may be required to achieve optimal pacing thresholds.

OBJECTIVE The purpose of this study was to describe the natural history of acute elevated Micra vs traditional transvenous lead thresholds.

METHODS Micra study VVI patients with threshold data (at 0.24 ms) at implant (n = 711) were compared with Capture study patients with de novo transvenous leads at 0.4 ms (n = 538). In both cohorts, high thresholds were defined as >1.0 V and very high as >1.5 V. Change in pacing threshold (0–6 months) with high (1.0 to ≤1.5 V) or very high (>1.5 V) thresholds were compared using the Wilcoxon signed-rank test.

RESULTS Of the 711 Micra patients, 83 (11.7%) had an implant threshold of >1.0 V at 0.24 ms. Of the 538 Capture patients, 50 (9.3%) had an implant threshold of >1.0 V at 0.40 ms. There were no significant differences in patient characteristics between those with and without an implant threshold of >1.0 V, with the exception of left ventricular ejection fraction in the Capture cohort (high vs low thresholds, 53% vs 58%; $P = .011$). Patients with an implant threshold of >1.0 V decreased significantly ($P < .001$) in both cohorts. Micra patients with high and very high thresholds decreased significantly ($P < .01$) by 1 month, with 87% and 85% having 6-month thresholds lower than the implant value. However, when the capture threshold at implant was >2 V, only 18.2% had a threshold of ≤1 V at 6 months and 45.5% had a capture threshold of >2 V.

CONCLUSIONS Pacing thresholds in most Micra patients with elevated thresholds decrease after implant. Micra device repositioning may not be necessary if the pacing threshold is ≤2 V.

KEYWORDS Bradycardia; VVI; Pacemaker; Leadless pacemaker; Capture threshold; Clinical trial; Outcomes

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Introduction

Permanent pacing has been a long-standing effective therapy for symptomatic bradycardia, with >350,000 procedures performed each year in the United States alone.[1] However, pacemaker implantation is associated with several risks including an 11% lead complication rate and a pocket complication rate of nearly 7% at 5 years.[2] Furthermore, lead failures are associated with significant morbidity and a 16% risk of subsequent major complications.[3] In contrast to traditional transvenous pacemakers, the leadless transcatheter Micra pacemaker is a miniaturized (0.8 mL) single-chamber ventricular pacemaker that is implanted directly in the right ventricle. The Micra leadless pacemaker is associated with a 51% lower risk of complications in the first 6 months after implant compared with transvenous pacemakers, including a lower risk of infection.[4] The Micra leadless pacemaker has been shown to be effective with low and stable pacing thresholds. The device's nitinol tines, which are separate from the electrode, are used to anchor the device and stimulate less fibrosis, allowing for lower pacing thresholds. Implant of the Micra leadless pacing system is safe and efficient; however, device capture, repositioning, and redeployment may be required to obtain an optimal pacing threshold. Multiple repositioning is associated with a small but increased risk of adverse events, including pericardial bleeding. While thresholds may be elevated after initial deployment, the natural history of capture thresholds in Micra leadless devices are not well defined. More specifically, it is not known what percentage of patients with an elevated (>1 V) threshold at implant will have a lower threshold at follow-up. Finally, the differences between threshold progression in leadless devices relative to traditional transvenous devices have not been well described. The objective of this analysis was to test the hypothesis that acute elevated Micra pacing thresholds would improve after implant in a manner comparable to transvenous leads.

Methods

Micra study cohort

`The rationale and design of the Micra pivotal investigational device exemption (IDE) study has been described previously.[5] Pertinent national regulatory authorities and ethics committees at each participating site approved the protocol. In brief, patients with a class I or II guideline indication for de novo ventricular pacing were eligible for enrollment. There was no prespecified exclusion based on patient comorbidity (eg, chronic obstructive pulmonary disease). The study enrolled 745 patients, of whom 726 (97.4%) underwent implant attempts at 56 centers in 19 countries between December 2013 and May 2015. All Micra patients with a successful implant and pacing threshold data measured at a pulse duration of 0.24 ms at implant (711 of the 720 successfully implanted patients) were included in this analysis.

Comparator cohort

In order to compare the Micra pacing thresholds with transvenous thresholds, we analyzed transvenous pacing thresholds from the Capture study.[6] The Capture study was a contemporary study designed to assess pacing thresholds in EnPulse dual-chamber devices. Right ventricular leads in Capture patients included multiple lead models and both active and passive fixation models (Medtronic: 4074, 4076, 4092, 5054, 5076, 5092; St. Jude Medical: 1388TC, 1470T, 1688TC; others). The devices in Capture were programmed to DDD or DDD(R) since both atrial and ventricular pacing capture thresholds were being analyzed. The Capture cohort also served as a good comparator study because the EnPulse pacing thresholds could be measured by the device in 1/8 V increments (the same as Micra). Capture study patients who had their right ventricular lead implanted on the same day as their pulse generator and had a ventricular pacing threshold measured at 0.40 ms at implant were included as the comparator group (n = 538). Follow-up capture thresholds in the Capture cohort were taken from capture management testing performed during clinic visits.

Statistical analysis

For the purposes of this analysis, in both studies, high pacing thresholds were defined as >1.0 V and very high thresholds as >1.5 V. Patient demographic characteristics, comorbidities, and pacing electrode location were compared within pacing systems for patients with high and low thresholds using the *t* test or Fisher exact test. We analyzed changes in pacing threshold among those patients with a high (1.0 to ≤1.5 V) or very high (>1.5 V) threshold with paired implant and 6-month pacing threshold measurements within pacing systems using the Wilcoxon signed-rank test and between pacing systems using the Wilcoxon rank-sum test. In addition, the Wilcoxon signed-rank test was used to compare implant and postimplant pacing threshold measurements within pacing systems among patients with a pacing threshold of >1.0 V. Mean Micra pacing thresholds and percentage of patients with a pacing threshold of >1 V by number of device deployments were analyzed using linear and logistic regression, respectively. Multivariable logistic regression was used to identify factors associated with an implant threshold of >1 V at 0.24 ms. Candidate variables included the following baseline variables: pacing indication associated with permanent or persistent atrial fibrillation, hypertension, congestive heart failure, coronary artery disease, prior myocardial infarction, diabetes, renal dysfunction, age >75 years, female sex, body mass index <25 kg/m^2, and history of pulmonary disorder (including chronic obstructive pulmonary disease). Candidate variables also included the following procedural variables: use of heparin bolus during implant, number of Micra deployments, and apical location. Finally, correlations between the change in pacing threshold and impedance and sensing amplitude were assessed using the Pearson correlation coefficient. Significance was determined with a 2-tailed α value of <.05 for all analyses.

Results

Baseline characteristics

The baseline characteristics, comorbidities, and electrode location of the Micra (n = 711) and Capture (n = 538) study