Comparative study of acute and mid-term complications with leadless and transvenous cardiac pacemakers

Daniel J. Cantillon, MD, FHRS,* Srinivas R. Dukkipati, MD, FHRS,† John H. Ip, MD,‡ Derek V. Exner, MD, FHRS,§ Imran K. Niazi, MD,‖ Rajesh S. Banker, MD,¶ Mayer Rashtian, MD, FHRS,# Kenneth Plunkitt, MD, FHRS,** Gery F. Tomassoni, MD, FHRS,†† Yelena Nabutovsky, MS,‡‡ Kevin J. Davis, BS,‡‡ Vivek Y. Reddy, MD†

*From the *Cleveland Clinic, Cleveland, Ohio, †Icahn School of Medicine at Mount Sinai, New York, New York, ‡Sparrow Clinical Research Institute, Lansing, Michigan, §Libin Cardiovascular Institute of Alberta, Calgary, Alberta, Canada, ‖Aurora Medical Group, Milwaukee, Wisconsin, ¶Premier Cardiology, Newport Beach, California, #Huntington Memorial Hospital, Pasadena, California, **Naples Community Hospital, Naples, Florida, ††Central Baptist Hospital, Lexington, Kentucky, and ‡‡Abbott, Sylmar, California.*

BACKGROUND Leadless cardiac pacemakers (LCPs) aim to mitigate lead- and pocket-related complications seen with transvenous pacemakers (TVPs).

OBJECTIVE The purpose of this study was to compare complications between the LCP cohort from the LEADLESS Pacemaker IDE Study (Leadless II) trial and a propensity score–matched real-world TVP cohort.

METHODS The multicenter LEADLESS II trial evaluated the safety and efficacy of the Nanostim LCP (Abbott, Abbott Park, IL) using structured follow-up, with serious adverse device effects independently adjudicated. TVP data were obtained from Truven Health MarketScan claims databases for patients implanted with single-chamber TVPs between April 1, 2010 and March 31, 2014 and more than 1 year of preimplant enrollment data. Comorbidities and complications were identified via *International Classification of Diseases, Ninth Revision* and Current Procedural Terminology codes. Short-term ($\leq$1 months) and mid-term (>1–18 months) complications were compared between the LCP cohort and a propensity score–matched subset of the TVP cohort.

RESULTS Among 718 patients with LCPs (mean age 75.6 $\pm$ 11.9 years; 62% men) and 1436 patients with TVPs (mean age 76.1 $\pm$ 12.3 years; 63% men), patients with LCPs experienced fewer complications (hazard ratio 0.44; 95% confidence interval 0.32–0.60; $P < .001$), including short-term (5.8% vs 9.4%; $P = .01$) and mid-term (0.56% vs 4.9%; $P < .001$) events. In the short-term time frame, patients with LCPs had more pericardial effusions (1.53% vs 0.35%; $P = .005$); similar rates of vascular events (1.11% vs 0.42%; $P = .085$), dislodgments (0.97% vs 1.39%; $P = .54$), and generator complications (0.70% vs 0.28%; $P = .17$); and no thoracic trauma compared to patients with TVPs (rate of thoracic trauma 3.27%). In short- and mid-term time frames, TVP events absent from the LCP group included lead-related, pocket-related, and infectious complications.

CONCLUSION Patients with LCPs experienced fewer overall short- and mid-term complications, including infectious and lead- and pocket-related events, but more pericardial effusions, which were uncommon but serious.

KEYWORDS Complications; Leadless; Comparative Study; Pacemakers; Transvenous

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Introduction

Approximately 1 million transvenous pacemakers (TVP) are implanted annually worldwide.[1] Despite technological advances, the implantation technique involving a subcutaneous pulse generator and transvenous lead has remained unchanged and is the most common source of complications, occurring in up to 12% of device recipients.[2,3] Acute complications are related to implantation and include pneumothorax,

This study was funded by Abbott. **Address reprint requests and correspondence:** Dr Daniel J. Cantillon, Heart & Vascular Institute, Cleveland Clinic, 9500 Euclid Avenue J2-2, Cleveland, OH 44195. E-mail address: cantild@ccf.org.

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hemothorax, cardiac perforation, pocket hematoma, and lead dislodgment.[4] Most long-term complications are associated with the pulse generator or lead and include pocket erosion, infection, lead fracture or insulation failure, tricuspid valve regurgitation, and venous thrombosis.[2,3,5–7]

Leadless cardiac pacemakers (LCPs) represent a new paradigm in cardiac pacing developed to mitigate complications by eliminating the need for a subcutaneous pocket and transvenous leads. These devices are small ($\sim$1 cm^3), entirely self-contained units that are delivered via a transfemoral venous catheter and affixed in the right ventricle using either an active (Nanostim, Abbott, Abbott Park, IL) or a passive (Micra, Medtronic, Minneapolis, MN) fixation mechanism.[8–13] The short-term safety and efficacy of these devices at 6 months have been established in nonrandomized comparisons to prespecified historical performance measures of TVPs.[8,9] Complications occurred in 4.0%–6.7% of patients, with cardiac perforation being the most common adverse event. While the quantity and type of complications were fewer and different from those reported with TVPs, comparison is limited by differences in patient comorbidities and study characteristics.

In this study, short-term and mid-term complications of the Nanostim LCP (Abbott, Abbott Park, IL) are compared with those of conventional single-chamber TVPs. The LCP safety data are obtained from the extended follow-up of the previously reported LEADLESS II IDE study.[8] Comparative safety data for TVPs are reported from a propensity score–matched cohort obtained from a large US real-world insurance claims database.

Methods

LCP study

The LEADLESS Pacemaker IDE Study (Leadless II) trial is a prospective, nonrandomized, multicenter clinical study conducted in the United States, Canada, and Australia. The trial design has been described in detail previously.[8] Patients with indications for permanent single-chamber ventricular pacing were implanted with a Nanostim LCP between February 1, 2014 and January 31, 2016. Full inclusion and exclusion criteria for the LEADLESS II trial are described in the Supplement. The LCP is a self-contained, active-fixation, rate-adaptive single-chamber pacemaker. The 42-mm-long, 5.99-mm-diameter device contains a helical screw-in fixation electrode at the distal end. A specially designed delivery catheter is used to percutaneously implant the LCP in the right ventricular apex or apical septum. Patients were evaluated before hospital discharge with device interrogation, chest radiography, and standard 12-lead electrocardiography. Subsequently, patients were followed at 2 weeks, 6 weeks, 3 months, 6 months, and every 6 months thereafter.

LCP safety data

All complications in the LEADLESS II trial were reported as part of the active clinical study follow-up and adhered to the International Standard Organization definition of a serious adverse device effect (SADE). A *SADE* is any untoward but not unanticipated medical occurrence that is related to the investigational device or procedure and that is classified as serious. A *"serious" event* is defined as any event that led to death or to a serious health deterioration that resulted in either a life-threatening illness or injury or a permanent impairment of a body structure or body function. It also includes events that led to an inpatient or prolonged hospitalization or medical or surgical intervention that was required to prevent the above-mentioned effects. All adverse events were adjudicated by an independent clinical events committee. SADEs were categorized into those related to cardiac perforation, vascular complications, device dislodgment, pacing threshold elevation, or other types of events. Complications were evaluated from implantation until 18 months or the time of withdrawal from the study, last available follow-up visit, or death.

TVP study

TVP data were extracted from the Truven Health MarketScan Research Databases, which contain more than 20 billion de-identified, person-specific health insurance claims from approximately 350 US private sector payers.[14] Data for this study were extracted from 2 MarketScan databases—the Commercial Claims and Encounters database and the Medicare Supplemental database—spanning the time period from April 1, 2010 to March 31, 2014. The Commercial Claims and Encounters database contains data from active employees, dependents, and early retirees covered by employer-sponsored health plans. The MarketScan database contains data from Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans.

The study population included patients 18 years and older implanted with single-chamber pacemakers from any device manufacturer. Patients with pacemaker were identified as those having the *International Classification of Diseases, Ninth Revision* procedure code 37.81 (initial insertion of a single-chamber device, not specified as rate responsive) or 37.82 (initial insertion of a single-chamber device, rate responsive) or the Current Procedural Terminology code 33207 (insertion or replacement of a permanent pacemaker and lower-chamber electrodes). Patients with any implantable cardiac rhythm management device-related codes at any time before pacemaker implantation (Supplemental Table S1) were excluded from the analysis to eliminate non–de novo implants.

To characterize baseline comorbidities in the study population with TVPs, relevant inpatient and outpatient diagnostic and procedure codes were identified over the entire available time period before implantation. To ensure completeness of baseline data, patients with less than 1 year of MarketScan enrollment data were excluded from the analysis. Codes that indicated a history of atrial fibrillation, hypertension, diabetes, coronary artery disease, vascular disease, or tricuspid valve disease were included in the baseline characterization (comorbidity codes are listed in Supplemental Table S2).

TVP safety data

Pacemaker-related complications were identified for the TVP cohort using inpatient and outpatient billing codes recorded