Midterm Safety and Performance of a Leadless Cardiac Pacemaker

3-Year Follow-up to the LEADLESS Trial (Nanostim Safety and Performance Trial for a Leadless Cardiac Pacemaker System)

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Leadless cardiac pacemakers (LCPs) have been introduced to decrease lead- and pocket-related complications. Initial studies have shown short-term complication rates of 4% to 6.7% and adequate electric performance in up to 12 months of follow-up.[1–3] However, to fully appreciate the clinical impact and the robustness of this novel technology, additional follow-up is required to determine the long-term safety and performance. In this study, we report the longest clinical follow-up to date: the 3-year results of the LEADLESS trial (Nanostim Safety and Performance Trial for a Leadless Cardiac Pacemaker System).[4]

Patients implanted with an LCP (Nanostim, St. Jude Medical/Abbott) were retrospectively assessed to evaluate the safety and performance of this device with a minimum of 3 years of follow-up. No patients were lost to follow-up. Medical records were analyzed from June 2014 until May 2016 and evaluated for (1) serious adverse device effects (SADEs) and (2) electric performance of the LCP. The primary outcome was freedom from SADEs (Kaplan-Meier estimate) at 40 months of follow-up. Categorical variables are presented as frequencies and continuous variables as means (±SD). Permission of the local institutional review boards was obtained for this retrospective analysis, and all participants gave written informed consent.

Thirty-three patients (age 77±8 years, 67% male) were enrolled and were followed for a median duration of 38 months (range, 21–41 months). Two patients were not implanted with an LCP: 1 patient did not receive an LCP because of a complicated and aborted implant procedure, and the other patient was converted to an implantable cardioverter defibrillator.[3,4] At 3-year follow-up, 23 of the 31 (74%) patients were alive. None of the deaths were attributed to the LCP.

We found freedom from SADEs in 89.9% (95% confidence interval, 79.5%–100%) of patients at 40 months of follow-up (Figure, A). In total, 3 of 33 patients experienced device-related complications, of whom 2 patients had procedure-related SADEs (freedom from procedure-related SADEs is 93.9% [95% confidence interval, 86.1%–100%]).[4] One patient had a perforation during the implant procedure leading to cardiac tamponade, was operated on successfully, but died of a cerebral ischemic infarct 5 days postimplant. The second patient had an inadvertent placement of the LCP in the left ventricle through a persistent foramen ovale, requiring acute device retrieval and subsequent implant of a second LCP in the right ventricle. The third device-related complication occurred after 37 months of follow-up. This patient experienced device malfunction presenting as an abrupt loss of communication and pacing attributable to battery malfunction. The LCP was retrieved successfully and replaced with a new LCP. Later, a battery advisory was issued by the manufacturer addressing this battery issue. No occurrences of late LCP dislodgements, device infection, or pacemaker syndrome were reported.

The electric performance of the LCP was adequate up to 36 months of follow-up (Figure, B). Pacing thresholds were at baseline, prehospital discharge, 3, 12,

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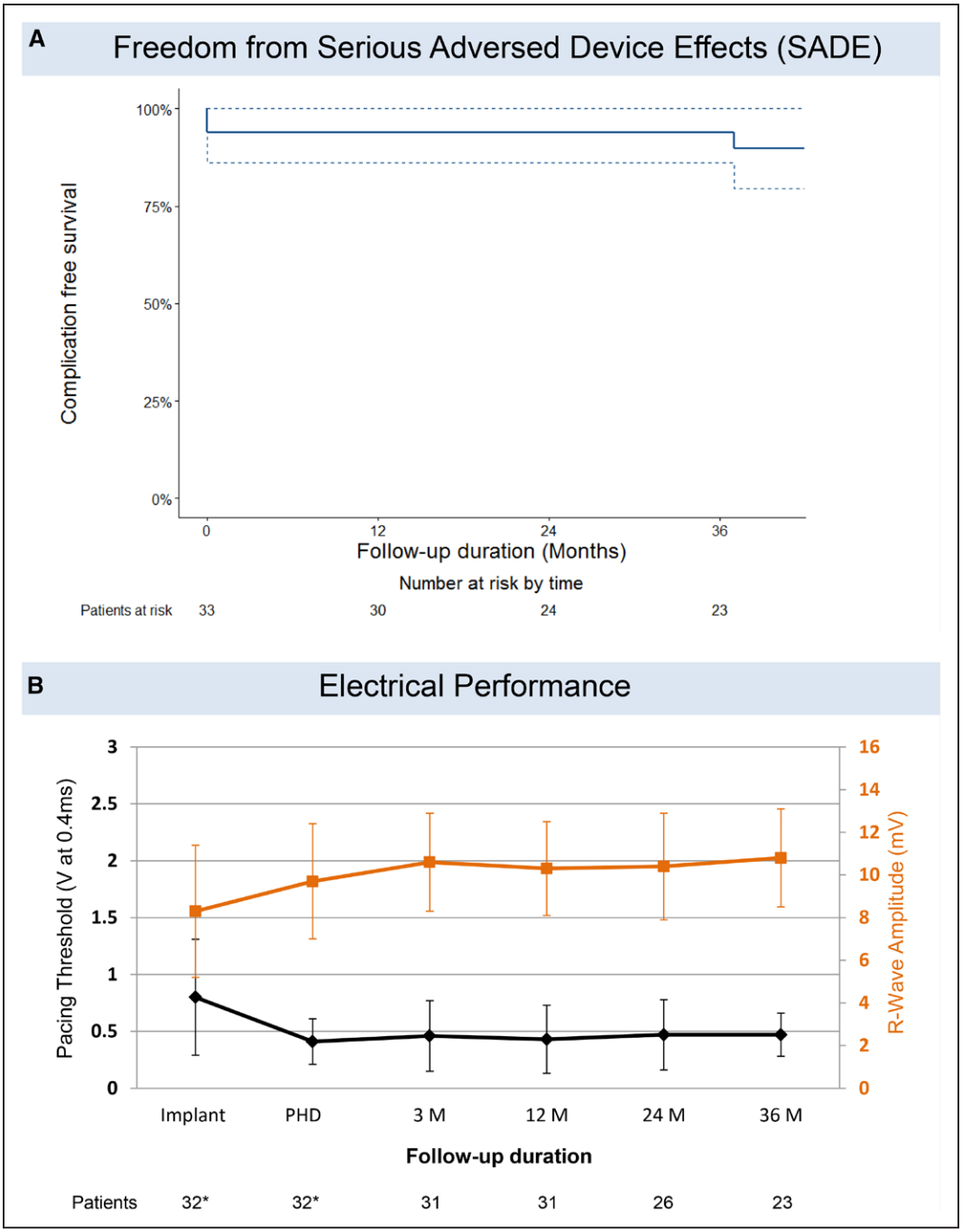

Figure. Safety and performance of leadless cardiac pacemaker at 3 years of follow-up.
A, Kaplan-Meier curve (with 95% confidence interval) displaying the freedom from serious adverse device effects (SADEs) during 40 months of follow-up. **B,** The electric performance (R-wave amplitude and pacing thresholds) of the leadless cardiac pacemaker during 36 months of follow-up. M indicates months. *One patient had an aborted implant procedure, and no implant/prehospital discharge (PHD) measurements were obtained.

24, and 36 months, respectively, 0.80±0.51, 0.41±0.20, 0.46±0.31, 0.43±0.30, 0.47±0.31, and 0.47±0.19 V at 0.4 ms pulse width. Similarly, the R-wave amplitudes were, respectively, 8.3±3.1, 9.7±2.7, 10.6±2.3, 10.3±2.2, 10.4±2.5, and 10.8±2.3 mV; and impedances were, respectively, 772±243, 719±196, 627±199, 627±209, 609±181, and 614±169 Ω. During follow-up in a substantial number of patients, the rate response feature was activated (61% at 12, 42% at 24, and 39% at 36 months).

This study is the first to report on 3-year outcomes in patients implanted with an LCP. The overall LCP complication rate of 10.1% is comparable to previous reports of transvenous pacemaker complications.[5] Two

acute, procedure-related complications were observed and warrant attention, in particular, during the learning curve of implanting operators. One battery issue–related complication occurred in the longer term, ultimately leading to the issuing of a battery advisory and redevelopment of battery components. This battery advisory is expected to involve more patients and could have a dominant effect on the overall complication rates of this generation of LCP. As with other pacemaker advisories, development of a new battery should resolve this issue. In 3 years of follow-up, the incremental rise in complications (attributable to pocket and leads), as observed for conventional transvenous pacemaker therapy, is absent in the present study. Despite the small size of this study, these intermediate-term results support the potential benefit of leadless pacing on long-term complications in comparison with transvenous pacemaker systems in which the lead is often the weakest link.[5] The electric performance was adequate and comparable to transvenous pacemaker systems. Because of the battery advisory, the estimations of device longevity were not reliable and are therefore not reported. LCP retrieval has been demonstrated to be feasible in this study, both (sub)acutely and chronically (>3 years). More data on the feasibility of long-term LCP retrieval is required to establish end-of-life replacement strategies.

This study has several important limitations, including the small number of patients, nonrandomized nature, and retrospective design. Furthermore, additional follow-up on the battery failure is not included in this analysis.

The adequate performance and freedom from SADEs at midterm follow-up in this first-in-humans patient cohort support the use of leadless pacing as an alternative to conventional transvenous pacing, especially considering the promise of decreasing long-term pacemaker complications. However, in addition to a solution for the battery issue, larger studies with long-term follow-up are required to assess the clinical safety and performance of this LCP and leadless pacing in general.

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FOOTNOTES

Requests to access the data that support the findings of this study may be sent to the corresponding author.

Clinical Trial Registration: URL: https://www.clinicaltrials.gov. Unique identifier: NCT01700244.

Circulation is available at http://circ.ahajournals.org.

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