Safety and feasibility of leadless pacemaker in patients undergoing atrioventricular node ablation for atrial fibrillation

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BACKGROUND Atrioventricular node (AVN) ablation and permanent pacing is an established strategy for rate control in the management of symptomatic atrial fibrillation (AF). Leadless pacemakers (LPs) can overcome some of the short-term and long-term limitations of conventional transvenous pacemakers (CTPs).

OBJECTIVES The purpose of this study was to compare the feasibility and safety of LP with those of single-chamber CTP in patients with AF undergoing AVN ablation.

METHODS We conducted a multicenter observational study of patients undergoing AVN ablation and pacemaker implantation (LP vs single-chamber CTP) between February 1, 2014 and November 15, 2016. The primary efficacy end points were acceptable sensing (R wave amplitude $\geq$5.0 mV) and pacing thresholds ($\leq$2.0 V at 0.4 ms) at follow-up. Safety end points included device-related major and minor (early $<$1 month, late $>$1 month) adverse events.

RESULTS A total of 127 patients with LP (n = 60) and CTP (n = 67) were studied. The median follow-up was 12 months (interquartile range 12–18 months). Ninety-five percent of the LP group and 97% of the CTP group met the primary efficacy end point at follow-up (57 of 60 vs 65 of 67; $P = .66$). There was 1 major adverse event (loss of pacing and sensing) in the LP group and 2 (lead dislodgement) in the CTP group (1 of 60 vs 2 of 67; $P = 1.00$). There were 6 minor adverse events (5 early and 1 late) in the LP group and 3 (early) in the CTP group (6 of 60 vs 3 of 67; $P = .30$).

CONCLUSION Our results demonstrate the feasibility and safety of LP compared with CTP in patients undergoing AVN ablation for AF.

KEYWORDS Atrial fibrillation; AV node ablation; Leadless pacemakers; Nanostim; Transvenous pacemaker

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Introduction

Atrioventricular node (AVN) ablation and permanent pacing (ablate and pace) is an established strategy for rate control in symptomatic atrial fibrillation (AF) refractory to catheter ablation and medical management.[1–3] The current American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines have a class IIa recommendation for AVN ablation in the management of AF.[4] Although an ablate and pace approach does not affect survival, it alleviates symptoms, improves quality of life and exercise tolerance.[1–3] Most patients undergoing AVN ablation have long-standing persistent AF and receive a single-chamber conventional transvenous pacemaker (CTP) unless the left ventricular ejection fraction is $<$50% when a biventricular pacemaker is indicated.[5]

Traditional pacemakers are associated with complication rates of up to 10%.[6] The subcutaneous pocket created for the pulse generator is associated with pocket

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hematoma, infection, and erosion, while the transvenous leads are associated with endocarditis, dislodgement, cardiac perforation, valvular regurgitation, and venous occlusion.[7,8] Recently, leadless pacemakers (LPs) have become increasingly popular. They are self-contained devices that include a pulse generator, battery, and electrode in 1 device and overcome some of the shortcomings of CTPs.[9] LPs use a catheter-based delivery system and are directly implanted into the right ventricle, potentially minimizing the complications that are associated with CTPs.[10] Currently there are 2 self-contained LPs that have been investigated for single-chamber right ventricular pacing: Nanostim LP (Abbott, formerly St. Jude, Lake Bluff, IL) and Micra Transcatheter Pacing System (Medtronic, Minneapolis, MN). LPs have been proven to be safe and effective in single-chamber pacing in the initial feasibility clinical trials.[10,11] However, the Nanostim LP is currently out of the market because of a manufacturer-issued battery advisory for premature battery depletion and a detached docking button more recently.

With the advent of LP, patients undergoing AVN ablation and pacemaker implantation can theoretically minimize complications related to CTP. We performed an observational study, comparing the safety and efficacy of the Nanostim LP, before the battery advisory, with those of the single-chamber CTP in patients with AF undergoing AVN ablation during short-term follow-up.

Methods

Study group

This is a multicenter observational study including 127 patients (LP [n = 60] and single-chamber CTP [n = 67]) who underwent AVN ablation and permanent pacemaker implantation. Patients who received an LP as part of the LEADLESS II clinical trial (ClinicalTrials.gov identifier NCT02030418), which was a prospective international multicenter study that consisted of 56 centers in the United States, Canada, and Australia between February 1, 2014 and November 15, 2016, were included. This was compared with patients who underwent AVN ablation and received a single-chamber CTP during the same time periods. The study was approved by the institutional review board at each institution. Baseline characteristics, procedure reports, imaging, device interrogation, and adverse events were extracted in both groups.

Indications for AVN ablation included symptomatic AF refractory to medications and catheter ablation. Patients were excluded if younger than 18 years and had preexisting CTP, implantable cardioverter-defibrillator, subcutaneous implantable cardioverter-defibrillator, cardiac resynchronization therapy device, another implantable LP, implanted vena cava filter, pacemaker syndrome with retrograde ventriculoatrial conduction, mechanical tricuspid valve prosthesis, pulmonary arterial hypertension, and thrombosis in one of the veins used to gain access during the procedure. Patients requiring dual-chamber pacing and right-sided CTP were also excluded from the study.

Follow-up

Patients were followed up in 2 weeks, 6 weeks, and every 3 months thereafter. A complete device interrogation was performed at each of the follow-up appointments. Patients whose devices had remote monitoring capabilities were remotely monitored.

Clinical outcomes

The primary efficacy end point included acceptable sensing (R wave amplitude $\geq$5.0 mV) and pacing thresholds ($\leq$2.0 V at 0.4 ms) at follow-up. The primary safety end points are device- or procedure-related major and minor adverse events at follow-up. Major adverse events included procedure-related death, device/lead dislodgement, and other complications prompting immediate intervention such as pericardial effusion, cardiac perforation, large pneumothorax/hemothorax, pocket hematoma, device malfunction, diaphragmatic/phrenic stimulation, elevated pacing thresholds at implantation (>2.5 V at 0.4 ms) or between follow-up visits (an increase of $\geq$1.5 V at 0.4 ms), major bleeding, and other vascular complications. All device complications were adjudicated.

Complications not requiring immediate intervention were classified as minor adverse events. Minor adverse events were further classified as early ($\leq$1 month) and late (>1 month). Device malfunction not requiring immediate intervention (that could be managed by device reprogramming) was classified under minor adverse events. Immediate intervention was any procedure performed within 48 hours.

LP implantation

The LP was implanted before AVN ablation in all patients. Implantation of the Nanostim LP has been described in detail elsewhere.[10] Briefly, after placing an 18-F sheath through the right femoral vein, the delivery catheter with the LP was directed into the right ventricle under fluoroscopic guidance. Once positioned near the apex of the right ventricle, the retractable sleeve is withdrawn, exposing the fixation helix. The device is then screwed into the endocardium, and the delivery catheter is undocked from the pacemaker. A tethered connection remains to permit device measurements and assess the stability without the catheter. If the position and the pacemaker parameters are optimal on the basis of fluoroscopic imaging and device parameters of sensing (R wave amplitude $\geq$5.0 mV) and pacing threshold ($\leq$2.0 V at 0.4 ms), the tether is removed. The device was programmed at VVI at 40–50 beats/min in all patients before AVN ablation.

Transvenous single-chamber pacemaker implantation

All patients underwent single-chamber CTP implantation before AVN ablation. After obtaining vascular access via the left cephalic, axillary, or subclavian vein, a pacemaker lead was advanced into the heart under fluoroscopic guidance. Cephalic vein cutdown was the preferred approach, while axillary and subclavian veins were used when unable

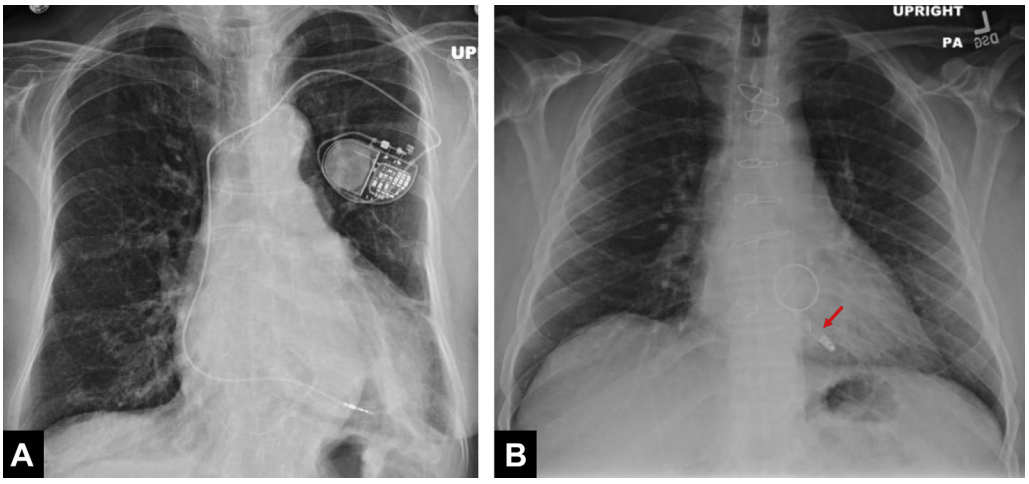

Figure 1 Chest radiographs with (**A**) conventional transvenous pacemaker and (**B**) leadless pacemaker (red arrow).

to access the cephalic vein. The right ventricular lead was then fixed to the apex or interventricular septum on the basis of physician discretion. The lead was then connected to the single-chamber pacemaker pulse generator, which was programmed to VVI at 40–50 beats/min. Appropriate device parameters during implantation included pacing ($\leq$2.0 V at 0.4 ms), sensing (R wave amplitude $\geq$5.0 mV), and impedance ($<$1200 Ω). Figure 1 shows chest radiographs with CTP and LP.

AVN ablation

Standard techniques used for AVN ablation has been previously described.[12,13] Because of the relative novelty and the uncertainty of device stability, all patients with LP underwent AVN ablation a minimum of 2 weeks after device implantation whereas all patients who received a conventional single-chamber pacemaker underwent AVN ablation at the same time as the pacemaker implantation. The safety of simultaneous AVN ablation with pacemaker implantation for conventional pacemakers has been well established.[14] An irrigated ablation catheter was introduced via the femoral vein access into the right atrium under fluoroscopic guidance. The position of the AVN was identified using fluoroscopy and electrograms, and radiofrequency ablation was performed. All pacemakers were programmed VVIR at 80 beats/min immediately after ablation for a duration of 4 weeks and subsequently reset to VVIR at 60–70 beats/min.

Statistical analysis

Continuous variables are expressed as mean ± SD if variables are normally distributed and median (interquartile range [IQR]) when deviations from normality were present. Categorical variables are expressed as counts and percentages. Categorical variables were compared between the groups using the χ^2 or Fisher exact test. Continuous variables were compared using the independent samples t test. A 2-tailed P value of $\leq$ .05 was considered statistically significant. Statistical analysis was performed using SPSS version 23.0 (IBM Corp, Armonk, NY).

Results

Patient characteristics

The mean age of the entire cohort was 74 ± 9 years. There was a significantly higher proportion of men in the LP group than in the CTP group (48% vs 24%; P = .005). There was no significant difference in age, comorbid conditions, or medications between the 2 groups (Table 1). The median follow-up was 12 months (IQR 12–18 months).

Table 1 Comparison between demographic variables, comorbid conditions, and medications between the groups

Characteristic	Leadless pacemaker (n = 60)	Conventional pacemaker (n = 67)	*P*
Demographic characteristics			
Age (y)	74 ± 8.7	74 ± 9.6	.804
Sex: male	29 (48)	16 (24)	**.005**
Comorbidities			
Diabetes	15 (25)	12 (18)	.390
Hypertension	51 (85)	57 (85)	1.000
Hyperlipidemia	43 (72)	40 (60)	.192
Congestive heart failure	12 (25)	21 (31)	.161
Left ventricular ejection fraction (%)	57 ± 8.8	53 ± 12.8	.155
Coronary artery bypass surgery	9 (15)	6 (8)	.418
Percutaneous coronary intervention	9 (15)	9 (14.5)	1.000
Medications			
Antiarrhythmics	13 (22)	10 (16)	.489
Anticoagulants	51 (85)	58 (87)	.805
Antiplatelets	21 (35)	28 (42)	.469
ACE inhibitors/ARBs	21 (35)	22 (34)	1.000
β-Blockers	40 (67)	46 (69)	.850

Values are presented as mean ± SD or as n (%). Statistically significant differences are presented in boldface.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

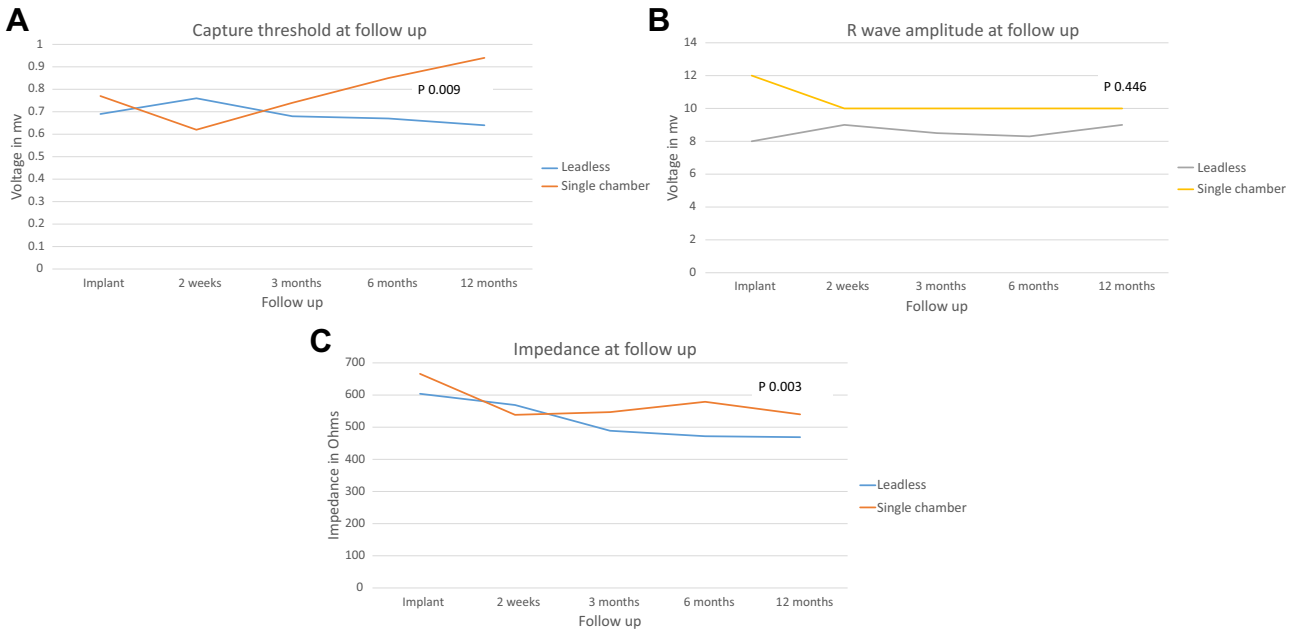

Figure 2 Comparison of device performance (ie, pacemaker parameters) between the groups at a median follow-up of 12 months: (**A**) capture threshold, (**B**) R-wave amplitude, and (**C**) impedance. *P* values are mentioned in the inset for each comparison.

Primary efficacy end points

Ninety-five percent of the LP group and 97% of the CTP group met the primary efficacy end point of stable device performance on follow-up (57 of 60 vs 65 of 67; $P = .66$). Two of the 3 patients in the LP group developed increasing capture thresholds: 1 underwent LP retrieval and upgrade to a dual-chamber device as rhythm control with an antiarrhythmic drug was attempted, and the other was monitored closely. One patient developed loss of pacing and telemetry at 1 year and underwent upgrade to a biventricular pacemaker. Both patients in the CTP group who did not meet the efficacy end point developed acute dislodgements and underwent revisions.

There was no statistically significant difference in the mean sensing amplitude between LP and CTP cohorts (8.9 ± 2.48 mV vs 9.8 ± 3.28 mV; $P = .45$) at 12 months (Figure 2). Patients with single-chamber CTP had a significantly higher mean capture threshold at 0.4 ms pulse width (0.94 ± 0.48 V vs 0.63 ± 0.45 V; $P = .009$) and impedance ($540 \pm 106.9\ \Omega$ vs $470 \pm 94.4\ \Omega$; $P = .003$) than did those with LP at 12 months of follow-up (Figure 2).

Primary safety end points

Major adverse events

There were 2 major adverse events in the CTP group and 1 in the LP group (2.9% [2 of 67] vs 1.6% [1 of 60]; $P = 1.00$) during the study period. There were 2 acute lead dislodgements in the CTP group: one patient had lead dislodgement with no symptoms within 12 hours of the index procedure, and the second patient had syncope secondary to lead dislodgement at 1 week postprocedure. There was 1 major adverse event in the LP group with loss of pacing and sensing at 1 year from the index procedure, requiring an upgrade to a biventricular pacemaker. There were no long-term major adverse events in the CTP group (Figure 3). Table 2 shows a comparison of safety and efficacy end points between the groups.

Mortality

There were no device- or procedure-related deaths in the study population. There was 1 (1.6%) cardiac death reported in the LP cohort. The cause of death was attributed to worsening heart failure and multiple comorbidities including advanced age, severe tricuspid and mitral regurgitation, and aortic valve replacement complicated by hemispheric stroke. In light of advanced heart failure, the patient was transitioned to comfort care and died subsequently.

There was 1 cardiac death (1.4%) in the CTP group during the study period. The cause of death was progressive right heart failure from pulmonary hypertension secondary to systemic sclerosis.

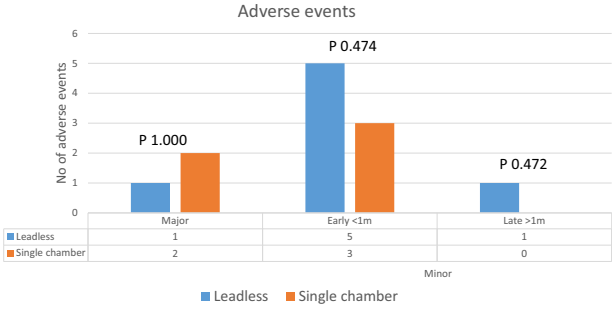

Figure 3 Bar diagram comparing the major and minor (early <1 month and late >1 month) adverse events between the groups. *P* values are mentioned in the inset for each comparison.

Table 2 Comparison of efficacy and safety end points between the groups at follow-up

Characteristic	Leadless pacemaker (n = 60)	Conventional pacemaker (n = 67)	*P*
Primary efficacy end points at a median follow-up of 12 mo			
Stable device performance (capture threshold ≤2.0 V at 0.4 ms, R-wave sensing amplitude ≥5.0 mV)	57 (95)	65 (97)	.66
Primary safety end points at a median follow-up of 12 mo			
Major adverse events			
Device/lead malfunction requiring immediate intervention	1 (1.6)	2 (2.9)	1.00
Minor adverse events			
Device malfunction requiring nonemergent intervention	2 (3.3)	0 (0)	.22
Device pocket complications	0 (0)	1 (1.4)	1.00
Vascular access complications	3 (5)	2 (2.9)	.66
Pericardial effusion not requiring intervention	1 (1.6)	0 (0)	.47

Values are presented as n (%).

Minor adverse events

There were 6 (10%) minor adverse events in the LP group and 3 (4.4%) in the CTP group ($P = .305$) during the study period (Table 3).

There were 5 early and 1 late adverse events in the LP group. Early adverse events included access-related complications including groin hematoma (n = 1), pseudoaneurysm (n = 1), pericardial effusion (n = 1) not requiring intervention, and increasing pacing threshold (n = 2) requiring nonemergent device upgrade. Late adverse events included pseudoaneurysm (n = 1). All access-related complications in the LP cohort occurred at the time of LP implantation.

There were 3 early minor adverse events in the CTP group. Early adverse events included access-related complications including pseudoaneurysm and arteriovenous fistula (n = 1), groin hematoma (n = 1), and pocket hematoma (n = 1). Figure 4 shows Kaplan-Meier estimate of freedom from serious adverse events in both cohorts.

Table 3 Comparison of various adverse events between the 2 groups

Adverse event	Leadless pacemaker (n = 60)	Conventional pacemaker (n = 67)	*P*
Device malfunction requiring emergent intervention			
Loss of telemetry and pacing	1	0	.47
Lead/device dislodgement	0	2	.49
Hematoma/bleeding			
Pocket hematoma	0	1	1.00
Vascular access–related complication			
Pseudoaneurysm	2	1	.60
Groin hematoma	1	1	1.00
Pericardial effusion not requiring intervention	1	0	.47
Device malfunction requiring nonemergent intervention			
Increasing right ventricular pacing threshold	2	0	.22

Discussion

Main findings

Our study is the first study reporting on the feasibility of LPs in patients with AF undergoing AVN ablation. Our results demonstrate that LPs have similar safety and efficacy as single-chamber CTPs during short-term follow-up. Ninety-five percent of the LP group and 97% of the CTP group met the primary efficacy end point of stable device performance at a median follow-up of 12 months (IQR 12–18 months). Mean capture threshold and impedance were significantly higher in the single-chamber transvenous group at follow-up; however, this was not clinically relevant. Overall, adverse events were low in both groups. There were no statistically significant differences in the major or minor adverse events between the 2 groups during the study period.

LPs have come a long way since their inception. Earlier multicomponent leadless systems were associated with significant complications.[15] Newer self-contained systems include the pulse generator, battery, and electrode in 1 device and have overcome some of the complications of conventional pacemakers. The LEADLESS II clinical trial, which studied the safety of the Nanostim LP, showed complication-free survival in 94% of the patients at 90 days.[10] In the subsequent LEADLESS II trial, device-related complications occurred in 7% of the patients and included device dislodgements in 1.7%, elevated pacing thresholds requiring device repositioning in 1.3%, and cardiac perforation in 1.3%.[9] When the cumulative results of the LP studies were compared with those of the historical single-chamber pacemaker cohorts, LPs were found to be associated with a slightly higher (4.8% vs 4.0%) short-term complication rate.[16] This was thought to be secondary to the operator learning curve associated with LP implantation and underreporting of complications in the conventional pacemaker studies owing to lack of careful site level follow-up.

LPs had their shortcomings in recent times. In October 2016, the manufacturer issued a battery advisory for Nanostim LP devices. They reported pacemaker failures with loss of communication and pacing secondary to premature battery depletion. At the time of the advisory, 7 of the 1423

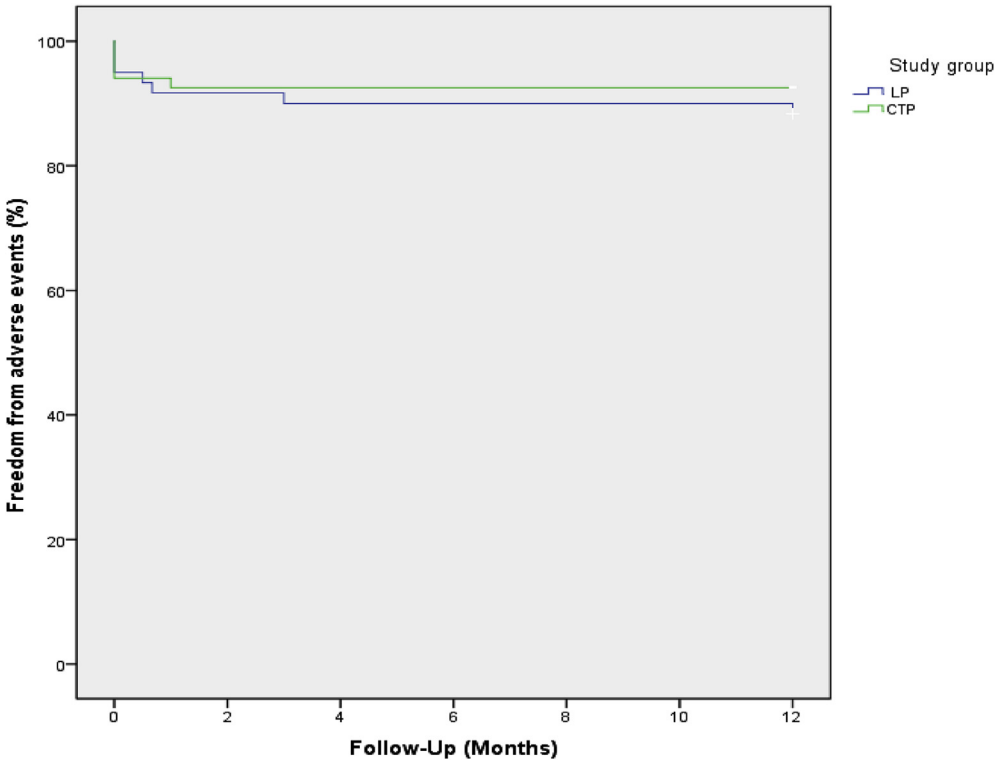

Figure 4 Kaplan-Meier curves comparing the freedom from adverse events between the leadless pacemaker (LP) and conventional transvenous pacemaker (CTP) groups at a median follow-up of 12 months.

devices (0.5%) were affected. Symptomatic bradycardia was reported in 1 patient, while the remaining 6 were asymptomatic. This was an unanticipated complication of the Nanostim LP, and it underlines the fact that electronic devices are prone to failures and their durability should be assessed over a long period of time. However, the medical community believes in the significant promise offered by the LPs in abating some of the major complications caused by CTP and investigations into the short-term and long-term durability should continue.

All patients included in the study had successful AVN ablation and device implantation. Most patients in both groups met the primary efficacy end point of stable device performance at a median follow-up of 12 months (95% in the LP group vs 97% in the CTP group; $P = .66$).

Both groups had similar safety profiles during the study period. There was 1 major adverse event (loss of pacing and sensing) in the LP group and 2 (lead dislodgement) in the CTP group (2 of 60 vs 1 of 67; $P = 1.00$). Even though minor adverse event rates were slightly higher in the study group, there was no statistically significant difference in major or minor adverse events between the groups. After the battery advisory, the manufacturer recommended device replacement in all pacemaker-dependent patients. Of the 60 patients with LP in our study, none had any serious adverse events due to premature battery depletion. Thirty patients underwent elective device replacement and the rest were monitored closely, despite being pacemaker dependent, without any significant adverse events to date.

Unfortunately, the battery advisory did not allow for long-term event analysis in our study. One would expect LPs to be an attractive option compared with CTPs when complications related to the device pocket or lead malfunction might ensue. Moreover, device- or procedure-specific complications such as tricuspid regurgitation and hemothorax are less likely to develop in the LP group. Further large randomized controlled trials are needed to validate our short-term findings and study the long-term safety and efficacy of LPs in comparison with CTPs.

Study limitations

Our main limitations are the observational nature of the study, small study population, and relatively low event rates. Moreover, long-term follow-up information was not available for the study group because of the battery advisory and outcomes could not be compared. Despite these limitations, this is the first proof-of-concept study that demonstrates comparable safety and efficacy of leadless pacing in patients with AF undergoing AVN ablation.

Conclusion

The results of our study demonstrate comparable safety and efficacy of LPs compared with traditional single-chamber transvenous pacemakers in patients with AF undergoing AVN ablation during short-term follow-up.

References

1. Kay GN, Ellenbogen KA, Giudici M, Redfield MM, Jenkins LS, Mianulli M, Wilkoff B; APT Investigators. The Ablate and Pace Trial: a prospective study of catheter ablation of the AV conduction system and permanent pacemaker

implantation for treatment of atrial fibrillation. J Interv Card Electrophysiol 1998; 2:121–135.
2. Wood MA, Brown-Mahoney C, Kay GN, Ellenbogen KA. Clinical outcomes after ablation and pacing therapy for atrial fibrillation: a meta-analysis. Circulation 2000;101:1138–1144.
3. Brignole M, Menozzi C, Gianfranchi L, Musso G, Mureddu R, Bottoni N, Lolli G. Assessment of atrioventricular junction ablation and VVIR pacemaker versus pharmacological treatment in patients with heart failure and chronic atrial fibrillation: a randomized, controlled study. Circulation 1998; 98:953–960.
4. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1–e76.
5. Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfesee L, Shinn T, Sutton MS. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013;368:1585–1593.
6. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, Moons KG. Incidence and predictors of short- and long-term complications in pacemaker therapy: the FOLLOWPACE study. Heart Rhythm 2012;9:728–735.
7. Tobin K, Stewart J, Westveer D, Frumin H. Acute complications of permanent pacemaker implantation: their financial implication and relation to volume and operator experience. Am J Cardiol 2000;85:774–776. A779.
8. Tarakji KG, Wazni OM, Harb S, Hsu A, Saliba W, Wilkoff BL. Risk factors for 1-year mortality among patients with cardiac implantable electronic device infection undergoing transvenous lead extraction: the impact of the infection type and the presence of vegetation on survival. Europace 2014;16:1490–1495.
9. Reddy VY, Exner DV, Cantillon DJ, et al. Percutaneous implantation of an entirely intracardiac leadless pacemaker. N Engl J Med 2015;373:1125–1135.
10. Reddy VY, Knops RE, Sperzel J, et al. Permanent leadless cardiac pacing: results of the LEADLESS trial. Circulation 2014;129:1466–1471.
11. Reynolds D, Duray GZ, Omar R, et al. A leadless intracardiac transcatheter pacing system. N Engl J Med 2016;374:533–541.
12. Lee SH, Chen SA, Tai CT, Chiang CE, Wen ZC, Cheng JJ, Ding YA, Chang MS. Comparisons of quality of life and cardiac performance after complete atrioventricular junction ablation and atrioventricular junction modification in patients with medically refractory atrial fibrillation. J Am Coll Cardiol 1998;31:637–644.
13. Ueng KC, Tsai TP, Tsai CF, Wu DJ, Lin CS, Lee SH, Chen SA. Acute and long-term effects of atrioventricular junction ablation and VVIR pacemaker in symptomatic patients with chronic lone atrial fibrillation and normal ventricular response. J Cardiovasc Electrophysiol 2001;12:303–309.
14. Issa ZF. An approach to ablate and pace: AV junction ablation and pacemaker implantation performed concurrently from the same venous access site. Pacing Clin Electrophysiol 2007;30:1116–1120.
15. Auricchio A, Delnoy PP, Butter C, Brachmann J, Van Erven L, Spitzer S, Moccetti T, Seifert M, Markou T, Laszo K, Regoli F. Feasibility, safety, and short-term outcome of leadless ultrasound-based endocardial left ventricular resynchronization in heart failure patients: results of the Wireless Stimulation Endocardially for CRT (WiSE-CRT) study. Europace 2014;16:681–688.
16. Tjong FVY, Reddy VY. Permanent leadless cardiac pacemaker therapy. Circulation 2017;135:1458.