LEADLESS II: Leadless Pacing Safe, Effective

Written by Emma Hitt Nichols, PhD

A leadless cardiac pacemaker (LCP) system was demonstrated to be safe and effective in patients who required single-chamber ventricular pacing. Vivek Y. Reddy, MD, Mount Sinai Hospital, New York, New York, USA, presented data from the study of percutaneous implantation of an entirely intracardiac leadless pacemaker [LEADLESS II; Reddy VY et al. *N Engl J Med*. 2015].

Current implantable cardiac defibrillators (ICDs) are associated with potential problems such as lead failure, device pocket infection, hematomas, discomfort, and complication rates up to 15% [Udo EO et al. *Heart Rhythm*. 2012]. The leadless pacemaker was developed as a strategy to avoid surgery and use of leads. The purpose of the LEADLESS II trial was to determine the safety and efficacy of the LCP system.

In the prospective, multicenter, nonrandomized LEADLESS II trial, patients indicated for VVI(R) pacemaker implantation received the LCP. The LCP is delivered percutaneously through the

Table 1. Device-Related Serious Adverse Events in the LEADLESS II Trial*

Event	Primary Cohort (N = 300)			Total Cohort (N = 526)		
	No. of Events	No. of Patients	Event Rate %	No. of Events	No. of Patients	Event Rate %
Total	22	20	6.7	40	34	6.5
Cardiac perforation						
Cardiac tamponade with intervention	1	1	0.3	5	5	1.0
Cardiac perforation requiring intervention	1	1	0.3	1	1	0.2
Pericardial effusion with no intervention	2	2	0.7	2	2	0.4
Vascular complication						
Bleeding	2	2	0.7	2	2	0.4
Arteriovenous fistula	1	1	0.3	1	1	0.2
Pseudoaneurysm	1	1	0.3	2	2	0.4
Failure of vascular closure device requiring intervention	0	0	0	1	1	0.2
Arrhythmia during device implantation						
Asystole	1	1	0.3	1	1	0.2
Ventricular tachycardia or ventricular fibrillation	1	1	0.3	2	2	0.4
Cardiopulmonary arrest during implantation procedure	0	0	0	1	1	0.2
Device dislodgement	5	5	1.7	6	6	1.1
Device migration during implantation owing to inadequate fixation	0	0	0	2	2	0.4
Pacing threshold elevation with retrieval and implantation of new device	4	4	1.3	4	4	0.8
Other						
Hemothorax	0	0	0	1	1	0.2
Angina pectoris	0	0	0	1	1	0.2
Pericarditis	1	1	0.3	1	1	0.2
Acute confusion and expressive aphasia	0	0	0	1	1	0.2
Dysarthria and lethargy after implantation	0	0	0	1	1	0.2
Contrast-induced nephropathy	0	0	0	1	1	0.2
Orthostatic hypotension with weakness	1	1	0.3	1	1	0.2
Left-leg weakness during implantation	0	0	0	1	1	0.2
Probable pulmonary embolism	1	1	0.3	1	1	0.2
Ischemic stroke	0	0	0	1	1	0.2

*Events were classified as device-related if they were considered by the clinical-events committee to be attributable to the investigational device or procedure. Some patients had more than one event, and therefore the number of patients is less than the number of events.

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femoral vein and is self-contained within the ventricle. The primary efficacy end point was acceptable pacing capture threshold and therapeutically acceptable sensing amplitude up to 6 months. The primary safety end point was freedom from device-related serious adverse events (SAEs) at 6 months. The primary cohort analysis was of the first 300 patients; safety and efficacy were analyzed in the intention-to-treat (ITT) population.

Patients were eligible for enrollment if they had chronic atrial fibrillation or normal sinus rhythm with secondary or tertiary atrioventricular or bifascicular bundle branch block, or sinus bradycardia with infrequent pauses or unexplained syncope. At baseline, the mean age in the primary cohort was 75.7, the mean body mass index was 29.2, 64.3% of patients were men, and 89.7% were white. In addition, coronary artery disease was present in 40.3%, hypertension in 84%, diabetes mellitus in 27.3%, and tricuspid valve disease with regurgitation or prolapse in 19.7%, and the mean left ventricular ejection fraction was 57.1%.

In the LEADLESS II trial, the total duration of the procedure in the primary cohort was 50 minutes, with the insertion to removal of the delivery catheter lasting 30.4 minutes. Device repositioning was required once in 18.3% of patients and twice in 8.3% of patients. The final location of the LCP was within the apex in 48.4% of patients; in the outflow, septum, or other area in 49.8%; and in the apical septum in 1.7%.

The primary safety end point was achieved in 93.3% of patients (95% CI, 89.9 to 95.9; $P < .001$), and the efficacy end point was achieved in 90% (95% CI, 86 to 93.2; $P = .007$). LCP implantation was successful in 93.4% of patients (95% CI, 89.9 to 96; $P = .001$). Freedom from SAEs at 6 months was 97.5% in the primary cohort, with the most common device-related SAEs including cardiac perforation and vascular complications (Table 1). Dr Reddy pointed out that most SAEs occurred within the first several weeks after implantation.

Dr Reddy concluded that the safety and efficacy data from the LEADLESS II trial suggest that the LCP system is a feasible alternative to the standard implantable pacemakers in patients who require single-chamber ventricular pacing.

MANTRA-PAF: Ablation Beats Antiarrhythmic Drugs for Reducing AF Burden at 5 Years

Written by Emma Hitt Nichols, PhD

First-line treatment of symptomatic paroxysmal atrial fibrillation (AF) with radiofrequency ablation (RFA) resulted in reduced occurrence and burden of AF at 5 years compared with antiarrhythmic drug (AAD) therapy. Jens Cosedis Nielsen, MD, PhD, Aarhus University, Aarhus, Denmark, presented 5-year follow-up data from the MANTRA-PAF [NCT00133211].

Over a 2-year period, there was no significant difference in AF, and improvements in quality of life were similar in patients with paroxysmal AF who received either RFA or AAD therapy [Nielsen JC et al. *N Engl J Med*. 2012]. The purpose of this analysis of the MANTRA-PAF trial was to evaluate the 5-year outcomes among patients who received first-line treatment with either RFA or AAD.

In the multicenter MANTRA-PAF trial, 294 patients with symptomatic paroxysmal AF were randomly assigned to undergo RFA or receive AAD. A 5-year follow-up was preplanned and included a 7-day Holter monitoring, quality of life assessment, AAD use, and RFA since 2-year follow-up. The mean age at baseline was 55 years, and 32% of patients had hypertension, 5% had diabetes mellitus, and 3% had a prior stroke or transient ischemic attack. The $CHADS_2$ score was 0 in 144 patients, 1 in 75 patients, and ≥ 2 in 26 patients.

At 5 years, the burden of AF was significantly lower in patients who underwent RFA compared with patients who received AAD ($P = .003$). In addition, treatment of AF with RFA resulted in a greater proportion of patients achieving freedom from any AF, freedom from symptomatic AF, and lower rates of persistent AF (Table 1). Overall, the burden of AF was lower with both therapies compared with baseline. However, there was no significant difference in the physical or mental components of quality of life at 5 years.

Patients in the AAD arm were significantly more likely to be taking a class Ic AAD at 5 years compared with the RFA arm ($P = .001$). In addition, slightly more patients in the AAD arm were taking a calcium-channel blocker or digoxin at 5 years compared with patients who underwent RFA. The proportion of patients taking a class III agent was similar among both arms.

Table 1. AF by 7-Day Holter Monitoring at 5 Years of Follow-up

Parameter	n/N (%)	*P* Value
Freedom from AF		
RFA	126/146 (86)	.001
AAD	105/148 (71)	
Freedom from symptomatic AF		
RFA	137/146 (94)	.015
AAD	126/148 (85)	
Persistent AF		
RFA	5/146 (3)	
AAD	7/148 (5)	

AAD, antiarrhythmic drug; AF, atrial fibrillation; RFA, radiofrequency ablation.

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