Dr. Healey concluded that the SIMPLE trial did not suggest that defibrillation testing improves the outcomes of patients undergoing ICD implantation.

Promising and Feasible: Leadless Cardiac Pacing

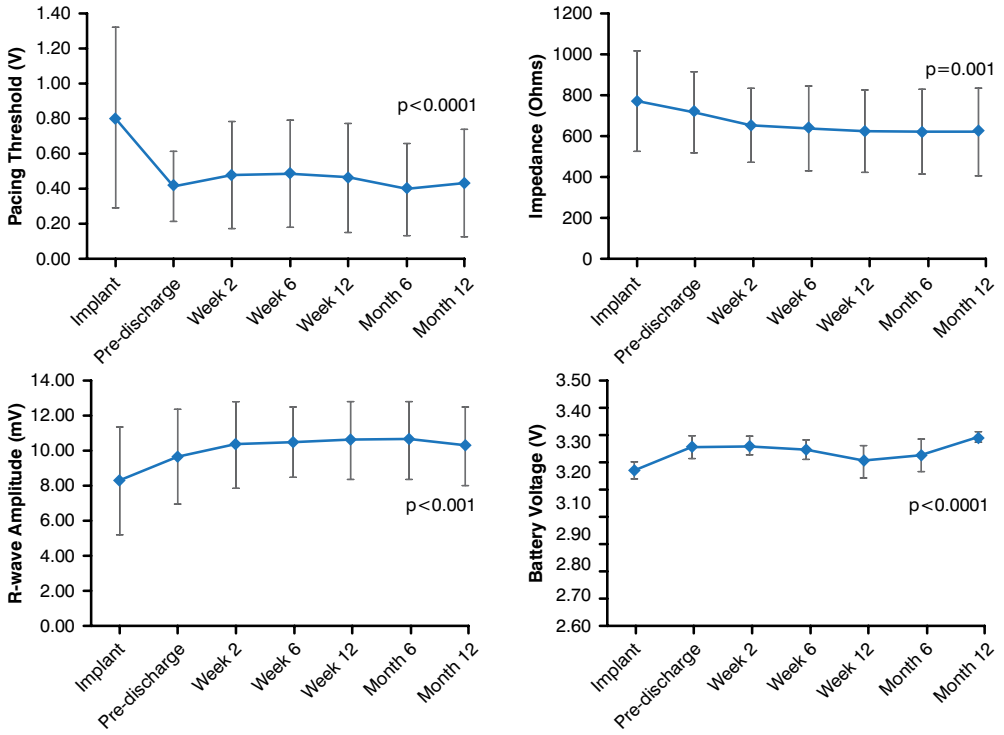
Written by Maria Vinall

Implantation of a leadless cardiac pacemaker (LCP) offers the potential to eliminate the need for the pocket, generator, and connections in most pacemaker systems—the transvenous lead subcutaneous pocket, subcutaneous pulse generator, and intra-system connections. Vivek Y. Reddy, MD, Mount Sinai School of Medicine, New York, New York, USA, reported that permanent leadless cardiac pacing is safe and feasible at 1 year after implantation in patients with an indication for single-chamber (ventricular) pacing. The leadless cardiac pacemaker contains a pulse generator and sensing or pacing electrodes within a single, miniaturized unit.

In this prospective, nonrandomized Evaluation of a New Cardiac Pacemaker study [LEADLESS; Reddy VY et al. *Circulation* 2014], 33 patients received the Nanostim LCP. The device was delivered to the right ventricle using a deflectable delivery catheter and affixed to the myocardium using a distal single-turn (screw-in) steroid-eluting helix. The mean age of the patients was 77±8 years, and 67% were male (n=22). Permanent atrial fibrillation with atrioventricular block was the most common reason for cardiac pacing (n=22; 67%). The mean procedure duration was 28±17 minutes, and the average time to hospital discharge was 31±20 hours. The overall complication-free rate was 94% (n=31). Five patients (15%) required the use of more than 1 leadless cardiac pacemaker during the procedure. One male patient sustained right ventricular perforation and cardiac tamponade during implantation; although this was successfully surgically repaired, he ultimately died approximately 1 week later from an AF-related stroke. The implant success rate was 97% (32/33).

After 1 year, the measures of pacing performance (sensing, impedance, and pacing threshold) either improved or were stable within the accepted range. Pacing threshold was 0.43±0.30 V (p<0.0001), R-wave amplitude was 10.32±2.23 mV (p=0.001), impedance was 627±209 ohms (p=0.001), and battery voltage was 3.29±0.02 V (p<0.0001). The p values were derived from a comparison between that measured at 12 months and at time of implantation (Figure 1).

Figure 1. Pacing and Sensing Parameters



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There were no device migration or dislodgements, no infections, no mechanical failure or early battery depletion, and no pro-arrhythmias detected after 1 year.

A completely self-contained, single-chamber, leadless cardiac pacemaker is stable and highly reliable over a 1-year time frame, with few safety issues. This small study suggests the leadless pacemaker could represent a paradigm shift in cardiac pacing. Future studies include a USA multicenter, prospective, single-arm FDA study of ~667 patients indicated for ventricular pacing and rate-adaptive therapy, as well as a European observational study (both studies are in progress). Also in development is an atrial LCP that will perform dual- or multi-chamber pacing.

Evidence of Added Benefit With Edoxaban in Patients With Paroxysmal AF

Written by Maria Vinall

Among patients with atrial fibrillation (AF) treated with anticoagulants, differences in baseline characteristics only partially account for the differences in outcome by AF subtype. Robert P. Giugliano, MD, SM, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented results of a secondary data analysis from the Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48 trial [ENGAGE AF-TIMI 48; NCT00781391]. These results showed that therapies that reduce bleeding while maintaining efficacy in the prevention of stroke (as compared with warfarin) may be especially beneficial in patients with paroxysmal AF.

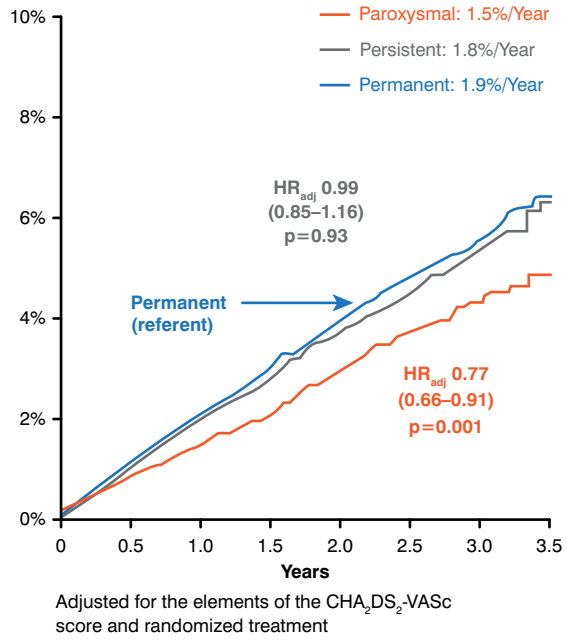
Edoxaban is a direct, oral, once-daily Factor Xa inhibitor. In the ENGAGE AF-TIMI 48 trial, both high and low doses of edoxaban were at least as effective as warfarin in preventing stroke and systemic embolic events (SEE) in patients with AF at moderate to high risk of stroke and caused less bleeding [Giugliano RP et al. *N Engl J Med* 2013].

The objective of the secondary analysis was to compare the baseline characteristics by AF subtype at presentation and compare the efficacy and safety of edoxaban by subtype during the 2.8 years median follow-up using the primary efficacy and safety outcomes from the main trial (efficacy=stroke or SEE; safety=ISTH major bleeding). Additional key secondary trial end points were also considered. For the ENGAGE AF-TIMI 48 trial, 21,105 patients with documented AF of any duration during the prior 12 months and a $CHADS_2$ score of greater than or equal to 2 were enrolled. For this secondary analysis, patients were categorized as having paroxysmal (n=5366 patients), persistent (n=4868), or permanent (n=10,865) AF based on the randomization ECG.

Patients with paroxysmal AF were more likely to be younger and female, to have a higher rate of diabetes, a lower $CHADS_2$ score, to have a history of coronary artery disease or dyslipidemia, and to be receiving antiarrhythmic therapy. Patients with permanent AF were slightly older and more were likely to have a higher $CHADS_2$ score and heart failure, as well as a higher incidence of prior stroke. They were also less likely to be vitamin K antagonist therapy-naïve.

The rate of stroke or SEE adjusted for elements of the CHA_2DS_2-VASc score, the group with paroxysmal AF was 23% lower in patients with paroxysmal AF as compared to permanent AF (adjusted HR, 0.77; 95% CI, 0.66–0.91; p=0.001); there was no difference in the rate of stroke or SEE between the permanent and persistent groups (Figure 1). Regarding the primary safety outcome, the adjusted rates for major bleeding were similar across all three groups.

Figure 1. Primary Efficacy Outcome by AF Subtype



SEE=systemic embolic events.

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Compared with subjects with permanent AF, subjects in the paroxysmal group had a lower risk for the key combined secondary outcome of stroke plus SEE plus cardiovascular death after adjusting for the CHA_2DS_2-VASc score (adjusted HR, 0.77; 95% CI, 0.70–0.86; p<0.001).