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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Prof Nielsen concluded that the data from this 5-year follow-up of the MANTRA-PAF trial suggest that first-line treatment of AF with RFA led to improved outcomes with decreased occurrence and burden of symptomatic AF compared with patients who received AAD therapy. However, he acknowledged that there are currently no data that indicate RFA improves survival compared with AAD therapy, and the risk of severe complications associated with RFA must be considered when advising patients.

Education Program Fails to Improve Adherence to Apixaban: The AEGEAN Study

Written by Emma Hitt Nichols, PhD

The addition of an educational program to apixaban therapy did not improve patient adherence to therapy. Gilles Montalescot, MD, PhD, Pitié-Salpêtrière Hospital, Paris, France, presented data from the AEGEAN study [NCT01884350].

Vitamin K antagonists have multiple limitations, including regular laboratory monitoring to ensure that the INR is maintained within the narrow therapeutic window, frequent dose adjustments, multiple food and drug interactions, and the risk of bleeding [Mani H, Lindhoff-Last E. *Drug Des Devel Ther*. 2014]. In contrast, the novel (nonwarfarin) oral anticoagulants (NOACs) have fixed dosing, do not require laboratory monitoring, and have few food or drug interactions [Heidbuchel H et al. *Europace*. 2013]. However, patient adherence to NOAC therapy has been suboptimal because patients do not undergo frequent monitoring at an anticoagulation clinic. The purpose of the AEGEAN trial was to assess the efficacy of an education program in improving adherence to apixaban.

Adherence consists of 3 phases: (1) initiation, which occurs when the first dose is received, typically during hospitalization; (2) implementation, which refers to the patient's actual dosing relative to the prescribed dose; and (3) persistence, which is the time that a dose is omitted and no additional doses are taken.

In the open-label, phase 4 AEGEAN trial, patients with atrial fibrillation with a $CHADS_2$ score ≥1 were randomly assigned to receive apixaban with the standard of care or apixaban plus an educational program that consisted of an education booklet about atrial fibrillation and anticoagulation for stroke prevention, a key ring, a short message service alert via a mobile phone, a smartphone application, and access to a virtual clinic with staff from an existing anticoagulation clinic. The standard of care consisted of the usual information about apixaban treatment. After 24 weeks, patients who received the education program were randomly assigned to receive the standard of care or to continue the education program for an additional 24 weeks.

The primary end point was the effect of education on the implementation phase of adherence at 24 weeks. The secondary end points included the effect of education on the persistence phase of adherence at 24 weeks, the effect of an education program on efficacy and safety of apixaban, and identification of predictive risk factors for nonadherence. Patients were excluded if they were at a high risk of bleeding, could not self-administer apixaban, were hospitalized, or were in long-term residential care.

There was no significant difference in the implementation phase of adherence among the treatment arms at 24 weeks. Similarly, the rate of persistence at 24 weeks was 91.1% in the arm that received the education program compared with 90.5% in the standard-of-care arm. In addition, there was no significant difference in clinical outcomes at week 24 between the treatment arms.

In conclusion, Prof Montalescot stated that overall the data suggest that there is a high rate of adherence and persistence to apixaban during the first 6 months of therapy. However, the addition of an education program did not further improve adherence. The effect of the education program beyond 6 months will be evaluated in the second portion of the AEGEAN trial.

BELIEF Study: Left Atrial Appendage Ablation Improves Long-standing Persistent AF

Written by Emma Hitt Nichols, PhD

Empirical electrical isolation of the left atrial appendage (LAA) for the treatment of long-standing persistent (LSP) atrial fibrillation (AF) improved freedom from AF and atrial tachycardia (AT) without increasing complications compared with standard ablation. Luigi Di Biase, MD, PhD, Albert Einstein College of Medicine, Bronx, New York, USA, presented data from the BELIEF study [NCT01362738].

LSP AF is difficult to treat with catheter ablation [Tilz RR et al. *J Am Coll Cardiol*. 2012]. This is likely due to multiple origins of AF, including from the pulmonary vein and regions such as the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, left atrial posterior wall, and LAA [Di Biase L et al. *Circulation*. 2010]. The purpose of this study was to determine if the empirical electrical isolation of the LAA, in addition to pulmonary vein isolation and ablation of extrapulmonary triggers, would improve freedom from AF or AT.

The BELIEF trial was a randomized, open-label, parallel-group trial with 173 patients who had LSP AF that was