Randall Lee, MD, PhD, University of California San Francisco, San Francisco, California, USA, presented the results of the Lasso Occlusion of the LAA trial [LARIAT] of LAA ligation with the LARIAT device in patients with AF.

The study objectives were to determine the efficacy of LAA closure with the LARIAT device and to assess procedural and 30-day periprocedural safety. The patient cohort consisted of 143 consecutive patients with nonvalvular AF with long-term contraindications for OAC therapy and ≥1 risk factor for embolic stroke ($CHADS_2$ score ≥1). The patients underwent attempted LAA ligation with the LARIAT device. Long-term end points were stroke or systemic embolism (SE) and the combined end point of stroke, SE, or all-cause death.

Four patients were excluded at the time of the procedure, and 139 were treated. Closure was successful in 138 patients (99.3%). At an average follow-up of 2.2 years, 4 strokes (1 embolic) had occurred in the total population (n=139), for an event rate of 1.3% per year, compared with an expected event rate of 6.2%. In comparison, the stroke rate in the National Registry of Atrial Fibrillation at 1.2 years was 3.9% per year [Gage BF et al. *JAMA* 2001].

Comparing event rates across clinical trials is problematic, since trials have different inclusion and exclusion criteria; nonetheless, for the LARIAT trial, the rate of stroke and SE was 1.3% per year, and the rate of combined stroke, SE, and death was 3.3% per year, similar to the event rates seen in other stroke prevention studies for patients with AF. The Aristotle study [Granger CB et al. *N Engl J Med* 2011] had a stroke and SE rate at 1.8 years of 1.27% per year in the apixaban arm and 1.6% in the warfarin arm and a stroke, SE, and death rate of 4.49% with apixaban and 5.04% with warfarin. The AVERROES study [Connolly SJ et al. *N Engl J Med* 2011] had a stroke and SE rate of 1.6% in the apixaban arm and 3.7% in the aspirin arm and a stroke, SE, and death rate of 4.2% with apixaban and 6.4% with aspirin.

Procedural adverse events included pericardial effusion (0.7%), pulmonary embolus resulting in death (0.7%), and cardiac perforation (1.4%). Other adverse events included pericarditis (5.8%), late hemopericardium (0.7%), late pericardial effusion (0.7%), and left atrial thrombus (1.4%).

Dr. Lee concluded that LAA ligation with the LARIAT device may be an option for high-risk patients with AF who have contraindications for anticoagulation therapy. Based on these results, prospective multicenter studies are being planned to better define the efficacy and safety of LAA ligation with the LARIAT device.

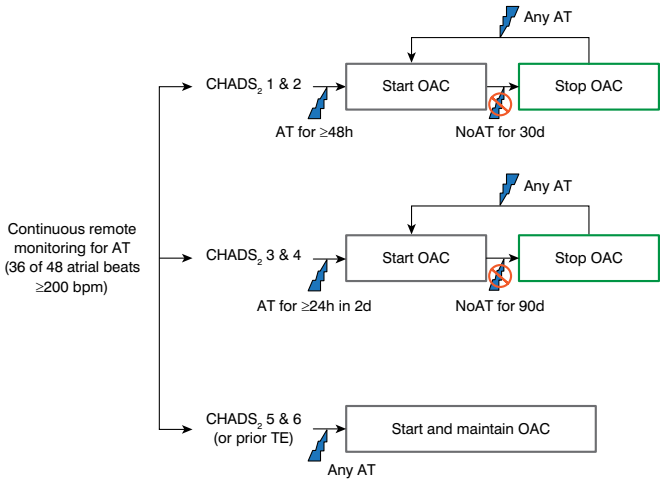
IMPACT Study: Rhythm-Guided Anticoagulation Therapy Did Not Improve Outcomes

Written by Toni Rizzo

Thromboembolism (TE) risk appears to be related to the burden of device-detected atrial tachyarrhythmias (AT) [Glotzer TV et al. *Circ Arrhythm Electrophysiol* 2009]. The investigators of the single-blinded Combined Use of BIOTRONIK Home Monitoring and Predefined Anticoagulation to Reduce Stroke Risk Trial [IMPACT; NCT00559988], presented by Jonathan L. Halperin, MD, Mount Sinai Medical Center, New York, New York, USA, hypothesized that a home monitoring–guided oral anticoagulation (OAC) strategy, including initiation early after AT detection and withdrawal after a prespecified window without AT, might reduce TE and hemorrhage in patients with an implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy defibrillator device.

In total 2718 patients with $CHADS_2$ risk scores ≥1 with ICD or CRT-D devices with home monitoring from 104 sites were randomized to home monitoring–guided OAC (n=1357) or physician-directed OAC without home monitoring (control; n=1361). The intervention group was assigned to remote monitoring for AT with a predefined plan for OAC based on the AT burden and $CHADS_2$ score (Figure 1), whereas the control group was treated on the basis of in-office identification of AT and current standards of care for OAC.

Figure 1. Anticoagulation Protocol for the Intervention Group



AT=atrial tachyarrhythmia; OAC=oral anticoagulation.

Table 1. Clinical Outcomes in the IMPACT Study[a]

Outcome	Control Group (n=1361)		Intervention Group (n=1357)		Hazard Ratio	p Value
	n	Rate	n	Rate		
Primary endpoint	61	2.3	63	2.4	1.06	0.732
Mortality	140	5.1	147	5.4	1.07	0.662
Thromboembolism	37	1.4	32	1.2	0.88	0.586
Ischemic stroke	28	1.0	22	0.8	0.79	0.417
Systemic embolism	2		0		—	0.969
TIA	8		10		1.27	0.619
Hemorrhagic stroke	3	0.1	3	0.1	1.03	0.973
Other major bleed	32	1.2	43	1.6	1.39	0.145

IMPACT=Combined Use of BIOTRONIK Home Monitoring and Predefined Anticoagulation to Reduce Stroke Risk Trial; TIA=transient ischemic attack.

[a]Rates are expressed as the number of events per 100 patient-years.

The primary end point was the occurrence of the first stroke, systemic embolism, or major bleeding event. The secondary end points were all-cause mortality, all stroke, and AT burden.

The study was prematurely terminated on June 13, 2013, after the Data Monitoring Committee determined futility once 75% of expected events accrued. Cumulative follow-up included 5430 patient-years and median exposure of 701 days.

There were no differences in baseline characteristics except that 34.5% of the intervention group were taking antiplatelet therapy other than aspirin, compared with 30.7% of the control group (p=0.037). ATs were detected in 493 patients (36.3%) in the intervention group and 452 patients (33.2%) in the control group (p=0.0908). Of these, 126 patients in the intervention group and 115 in the control group had confirmed atrial fibrillation (AF) meeting the OAC criteria. The median $CHADS_2$ score was 2 (p=0.544), and 64% of patients in each group had ICDs.

Among patients with AF meeting OAC criteria, 91 (72.2%) in the intervention group and 69 (60.0%) in the control group started OAC therapy. Forty-six patients (36.5%) in the intervention group and 29 (25.2%) in the control group stopped OACs. Mean days on OACs were 409 in the intervention group and 450 in the control group. Adherence to the OAC protocol was observed in 126 patients, 45.2% started OAC within the specified time frame, and the time within the therapeutic range was 61.2% in patients taking vitamin K antagonists.

There were no significant differences between the groups for any endpoint. The rate of the primary end point was 2.4% in the intervention group and 2.3% in the control group (HR, 1.06; p=0.732; Table 1). There was no temporal relationship between the occurrence of device-detected AT and TE events, suggesting that an accelerated OAC strategy did not improve the prevention of TE, said Dr. Halperin

Limitations of this study include suboptimal adherence with the OAC protocol and greater use of antiplatelet therapy in the intervention group. The low event rate limited the power to detect between-group differences in outcomes.

Starting and stopping OAC on the basis of device-detected AF did not improve clinical outcomes in the IMPACT study. Dr. Halperin concluded that the decision to start OAC therapy for device-detected AF should be based on a comprehensive clinical assessment of risk and benefit and that the absence of device-detected AF should not lead to the discontinuation of OAC.

Edoxaban Noninferior to Warfarin for Stroke Prevention in AF

Written by Wayne Kuznar

Robert P. Giugliano, MD, SM, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented the results of the Global Study to Assess the Safety and Effectiveness of Edoxaban (DU-176b) Versus Standard Practice of Dosing With Warfarin in Patients With Atrial Fibrillation [ENGAGE-AF TIMI 48; Giugliano RP et al. *N Engl J Med* 2013] and new secondary analyses.

In ENGAGE-AF TIMI 48, the new oral anticoagulant (NOAC) edoxaban was studied in 21,105 patients who had atrial fibrillation (AF) and $CHADS_2$ scores ≥2. Patients were randomly assigned in a 1:1:1 double-blind, double-dummy fashion to warfarin (target international normalized ratio [INR] 2.0 to 3.0), high-dose edoxaban (60 mg/day), or low-dose edoxaban (30 mg/day). The objective of the study was to establish the noninferiority of once-daily edoxaban compared with warfarin.

The dose of edoxaban was reduced by half in about 25% of patients at randomization for creatinine clearance between 30 and 50 mL/min, if the patient weighed ≤60 kg, or in the presence of a strong P-glycoprotein inhibitor, and it was adjusted (increased or decreased) in 8.3% after randomization. After a median follow-up