The Optimal Anti-Coagulation for Enhanced-Risk Patients Post–Catheter Ablation for Atrial Fibrillation (OCEAN) trial

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Background The optimal long-term antithrombotic regimen for patients after successful catheter-based atrial fibrillation (AF) ablation is not well defined. Presently, practice variation exists, and the benefits of oral anticoagulation over antiplatelet therapy across the entire spectrum of stroke risk profile remain undefined in the postablation population. To date, there are no randomized trials to inform clinicians on this therapeutic question.

Objective The objective was to assess whether rivaroxaban is superior to acetylsalicylic acid (ASA) in reducing the risk of clinically overt stroke, systemic embolism, or covert stroke among patients without apparent recurrent atrial arrhythmias for at least 1 year after their most recent AF ablation procedure.

Methods/design A prospective, multicenter, open-label, randomized trial with blinded assessment of outcomes is under way (NCT02168829). Atrial fibrillation patients with at least 1 stroke risk factor (as defined by the CHA2DS2-VASc score) and without known atrial arrhythmia recurrences for at least 12 months after ablation are randomized to rivaroxaban 15 mg or ASA 75-160 mg daily. The primary outcome is a composite of clinically overt stroke, systemic embolism, and covert stroke based on brain magnetic resonance imaging. Key secondary outcomes include major bleeding outcomes, intracranial hemorrhage, transient ischemic attack, neuropsychological testing, quality of life, and an economic analysis. Subjects will be followed for 3 years. The estimated overall sample size is 1,572 subjects (786 per arm).

Discussion The OCEAN trial is a multicenter randomized controlled trial evaluating 2 antithrombotic treatment strategies for patients with risk factors for stroke after apparently successful AF ablation. We hypothesize that rivaroxaban will reduce the occurrence of clinically overt stroke, systemic embolism, and covert stroke when compared with ASA alone. (Am Heart J 2018;197:124-132.)

Background Catheter-based atrial fibrillation (AF) ablation is a useful and effective rhythm-control therapy for patients with symptomatic AF. Multiple randomized trials have demonstrated that ablation is superior to antiarrhythmic drugs in reducing AF recurrence and improving quality of life, particularly for those in whom drugs are ineffective. Accordingly, ablation is an important therapy for patients with symptomatic AF, as reflected in current guidelines and by the considerable rise in procedural volumes over the past decade.

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The impact of AF ablation on stroke prevention is not well defined. Ongoing trials which address the prognostic impact of rhythm-control therapies including AF ablation, such as the Early Treatment of Atrial Fibrillation for Stroke Prevention trial (EAST; NCT01288352), Catheter Ablation vs. Anti-arrhythmic Drug Therapy for Atrial Fibrillation trial (CABANA; NCT00911508), and Rhythm Control–Catheter Ablation With or Without Anti-arrhythmic Drug Control of Maintaining Sinus Rhythm Versus Rate Control With Medical Therapy and/or Atrio-ventricular Junction Ablation and Pacemaker Treatment for Atrial Fibrillation (RAFT-AF; NCT01420393), will provide insight on this question. Yet, it is not uncommon for clinicians and/or patients to consider discontinuation of oral anticoagulation (OAC) after ablation. For many patients, the desire to stop anticoagulation is a prime motivation for ablation. Current guidelines, however, recommend continuation of OAC based on clinical risk scoring, irrespective of procedural outcome.2,3 Observational studies suggested that the risk of stroke or transient ischemic attack (TIA) among patients who discontinued OAC after “successful” AF ablation could be as low as 0.7% per year.8-17 Although this seems to support the notion that the embolic risk of AF patients with successful ablation may be low enough to justify discontinuation of OAC, these studies are limited by short follow-up periods and their retrospective, nonrandomized design which make them susceptible to confounding.8-17 As well, these studies had low event rates because they primarily included patients with few medical comorbidities.8-17 Presently, there are no randomized trials to inform clinicians on whether successful AF ablation sufficiently reduces patients’ risk of stroke to a point where long-term use of OAC is obviated, particularly at a time when non–vitamin K oral anticoagulants (NOACs) are widely used in clinical practice.

Current AF guidelines generally support continuation of OAC after apparently successful catheter ablation, but they reflect the paucity of high-quality data in inform practice. The Canadian guidelines recommend that OAC should be discontinued after ablation if the patient’s long-term risk of stroke is low and in the presence of sustained normal sinus rhythm.3 Recognizing the absence of randomized controlled data on this topic, European AF guidelines recommend that the decision to continue with OAC should follow general anticoagulation recommendations regardless of rhythm status.3 Similarly, the 2017 Heart Rhythm Society (HRS)/European Heart Rhythm Society/European Cardiac Arrhythmia Society/Asian Pacific Heart Rhythm Society/Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiología expert consensus statement on catheter and surgical ablation of AF stated that the decision to continue with OAC at more than 2 months postablation should be based on the patient’s stroke risk profile as opposed to the perceived success or failure of the procedure.4 Finally, performing catheter ablation to restore sinus rhythm for the “sole intent of obviating the need for anticoagulation” is a class III recommendation (level of evidence: C) in the 2014 American College of Cardiology Foundation/American Heart Association/HRS guidelines.5 The cautious wording of these recommendations underscores the lack of data to inform clinicians on the optimal long-term antithrombotic management for patients after AF ablation. In fact, the new 2017 HRS/European Heart Rhythm Society/European Cardiac Arrhythmia Society/Asia Pacific Heart Rhythm Society/Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología expert consensus statement on catheter and surgical ablation of AF lists the management of OAC post-AF ablation as the number 1 unknown question in our field.6 In the 2016 European Society of Cardiology AF guidelines and the Venice Chart international consensus statement on AF ablation, the optimal long-term management of OAC after ablation is a “key unresolved question.”5,18

The Optimal Anti-Coagulation for Enhanced-Risk Patients Post–Catheter Ablation for Atrial Fibrillation trial (OCEAN trial; NCT02168829) is a multicenter randomized controlled trial designed to examine the optimal method of stroke prevention for patients after successful AF ablation who are at risk for stroke based on their CHA2DS2-VASc (congestive heart failure, hypertension, age ≥ 75 years [2 points], diabetes mellitus, previous stroke/TIA [2 points], vascular disease, age 65-74 years, sex class [female]) score. Among patients without apparent atrial arrhythmia recurrences for at least 12 months after AF ablation, we hypothesize that the use of rivaroxaban will reduce the rate of stroke, systemic embolism, and covert embolic stroke (defined by cerebral magnetic resonance imaging [MRI]) when compared with acetylsalicylic acid (ASA).

Methods

Study design

The OCEAN trial is a multicenter, 2-arm randomized controlled trial with a prospective, randomized, blinded end point design. It is enrolling subjects at risk for stroke and who have not had clinically apparent atrial fibrillation, flutter, or tachycardia (AF/AFL/AT) recurrences for at least 12 months after their most recent paroxysmal, persistent, or longstanding persistent AF ablation procedure. Eligible and consenting subjects will be randomized in a 1:1 ratio to OAC therapy (rivaroxaban 15 mg daily) or single-antiplatelet therapy (ASA 75-160 mg daily). Randomization with concealed allocation will be performed using blocked cells of varying sizes using Web-based software (Dacima, Montreal, Québec, Canada). Outcomes will be adjudicated by personnel who are blinded to subjects’ randomization status. All sites will obtain approval from their respective ethics committees, and
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