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PGY2

Comparison of Radiofrequency Catheter Ablation and Amiodarone in Patients with Paroxysmal Atrial Fibrillation

Background:

In the most recent AHA/ACC/EHA guidelines on atrial fibrillation, the recommendation for patient with recurrent paroxysmal atrial fibrillation (PAF) who fail first line antiarrhythmic therapy is to try either amiodarone or dofetilide as second line medications or to pursue a radiofrequency catheter ablation.(1)

Over the last twenty five years the pathophysiology and mechanism of atrial fibrillation has become clearer and the technique of radiofrequency catheter ablation has become increasingly utilized. This, in combination with increasing expertise and success with the procedure, as well as the well documented failure and high side effect profile of many antiarrhythmics has made ablations increasingly popular.

Amongst antiarrhythmics, amiodarone has been thought to be overall more effective in patients and this has been shown in the literature in a number of instances. Thus, despite a still relatively high toxicity profile, it has become somewhat more favored clinically (3-5)

Recent studies have began to assess antiarrhythmic medical regimens versus ablation in terms of various outcomes, most notably symptom relief. A most recent study, a multicenter RCT by Wilber et al, found a significant reduction in symptoms and arrhythmias at 1 year in patients with PAF, with no increase in adverse events. Prior studies, including RCTs, such as by Pappone et al. and Jais et al., have found similar data.

However, in the previously mentioned studies, amiodarone was either excluded, as in the study by Wilber et al, or not exclusively used, but rather the choice of antiarrhythmic was at the discretion of the investigator and often included other, perhaps less efficacious antiarrhythmics. Given the prior literature and data, our goal is to conduct a randomized controlled trial comparing radiofrequency catheter ablation to amiodarone, exclusively, in patients with symptomatic paroxysmal atrial fibrillation. The underlying hypothesis is that despite amiodarone's apparent effectiveness and superiority, radiofrequency catheter ablation will non inferior without increased adverse events.

Study Design and Analysis:

The study will be an unblinded, multicenter, randomized trial. Patients will be randomly assigned to the ablation group or the amiodarone group in a 1:1 fashion. Informed consent will be obtained prior to randomization. Data monitoring, including follow up

EKGs and telephonic monitoring analysis will be done by an independent, blinded, reader, but follow up appointments will be with unblinded physician.

The primary outcome measure will be absence of treatment failure at 1 year. Treatment failure would include symptomatic atrial fibrillation for either group, necessity for repeat ablation after 90 days in the ablation group, or need to discontinue amiodarone in the amiodarone group secondary to intolerability or toxicity. Secondary endpoints will include absence of any symptomatic atrial arrhythmias, absence of any atrial arrhythmia, symptomatic or asymptomatic, QOL of life outcome measures (AF frequency and severity checklist) as well as monitoring of adverse events.

This will be a non inferior study with an allowance of smallest clinical difference of 10% difference. In order to power the study for that difference, a total of 200 patients will be needed in each group, calculated using a Chi Square Test

Study Procedure:

Patients enrolled in the catheter ablation group will undergo ablation with attempt at pulmonary vein isolation. Additional ablation techniques will be permitted as per investigator discretion. If needed, recatheterization and ablation will be permitted with 90 days and not considered treatment failure. Use of anticoagulation during the first three months post procedure will be required and subsequent use will be as per current protocol. Evaluation of endpoints will begin after this 90 days period

Patient in the amiodarone group will receive amiodarone per the current standard recommendations by the AHA/AHA/ESC practice guidelines and evaluation will begin after completion of titration to proper dosing.

In both groups follow up will include EKGs at all follow up visits and telephonic monitoring which will include reporting of all symptomatic events. In addition, patients will have to provide transmissions routinely for the first 8 weeks and then monthly until the trial period was completed.

Study Drugs:
Amiodarone

Medical Devices:

Electrocardiograms at follow up visits
Telephonic monitoring devices

Study Questionnaire:

AF frequency and severity checklist

Study Subjects:

Inclusion Criteria:
Patients with symptomatic paroxysmal atrial fibrillation (at least one confirmed EKG with afib) who failed first line antiarrhythmic therapy

Exclusion Criteria:
Patients with prior use of amiodarone, prior catheter ablation, persistent atrial fibrillation, stage III-IV congestive heart failure, EF of <40%, MI within 3 months, CVA within last 3 months.

Recruitment of patients:
Patients will be primarily recruited from offices of cardiologists at centers of expertise or referred to these centers

Confidentiality of Study Data:
All study data will be confidential.

Potential Conflicts of interest:
None

Location of the Study:
The study will be conducted at multiple centers, across North America and South America, at which there are physicians with expertise and radiofrequency catheter ablation.

Potential Risks:
Potential risks in the amiodarone group include immediate and long term toxicity, most notably pulmonary and thyroid related. In the ablation group there is risk of death, venous thromboembolic event, bleeding, tamponade, access complications, and myocardial infarction.

Potential Benefits:
Potential benefits include relief of symptoms for atrial fibrillation or any atrial arrhythmia, relief of atrial arrhythmias, improved quality of life, and possible reduction in overall cardiac outcomes.

Compensation of subjects:
No compensation for patients and routine billing procedures will apply.

Costs to subjects:
None

References:

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6. Pappone C, Augello G, Sala S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. J Am Coll Cardiol. 2006 Dec 5;48(11):2340-7.

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