Predictors of need for Repeat Ablation after Pulmonary Vein Isolation.

IRB Proposal
Jessica Fleitman MD, PGY1
Internal Medicine

A. Study Purpose and rationale:

In patients with atrial fibrillation (AF) who continue to be symptomatic or not adequately controlled on medical management, radiofrequency catheter ablation is a tool that can be used to put patients back into sinus rhythm. After Haissaguerre et al showed that pulmonary veins play a role in initiating AF[i], ablation techniques have evolved to electrically isolate the pulmonary veins – pulmonary vein isolation (PVI).

Despite this tool, patients frequently require a second ablation for either recurrent AF, or induced AFL. Efficacy of PVI has been studied in two small randomized trials. One showed that at 6 months 88% of patients with paroxysmal AF were asymptomatic off antiarrhythmic drugs.[ii] Another trial (in patients with both paroxysmal and persistent AF) assessed patients with 7 days of Holter monitoring at 6 months post procedure which showed 46% of patients had recurrence of symptoms and 58% had atrial arrhythmias on Holter monitoring.[iii] In a review of unpublished data from Columbia Presbyterian, the median time between ablations was 7 months with 90% of patients having a second ablation within 2.2 years, so the follow up times in these trials may have underestimated the need for repeated ablation in these populations. In this database, 196 patients required at least 2 repeat ablations while only 70 had follow up to 6 months and were symptom free (26%).

It would be useful to predict whether or not patients will require a second ablation or will continue to stay in sinus after a first ablation. Moreover if the class of arrhythmia developed subsequent to the PVI is predictive of developing that arrhythmia clinically, further interventions could be performed prior to the patient leaving his/her first ablation. A study by Elayi et al has already looked at patients with persistent AF who come in for a first ablation, and determined what rhythm the patients broke into after PVI (AF to sinus rhythm (SR) vs. macroreentrant AFL vs. atrial tachycardia) to determine if this was predictive of long term SR maintenance. In this study 69% maintained long-term SR at 2 years. Organization of the rhythm during AF termination was predictive of long-term SR (termination to SR> AT>AF) with ablation of focal AT correlated with higher long-term success rates than termination of macroreentrant AT (83% vs. 57% in SR at 2 years). [iv]

Given that despite ablation after PVI of resulting arrhythmias, these arrhythmias were predictive of decreased success in long term maintenance of SR, as well as the mode of recurrence. It has not yet been studied whether patients who are converted to SR during ablation, but then develop AT or AF on electric stimulation done post PVI have a similar higher rate of recurrence. The purpose of this study is to determine whether patients with SR during the study who develop an arrhythmia post stimulation are similarly more likely to need repeat ablation.

A. Study design and Statistical Analysis

This is a case controlled retrospective study of patients who have had pulmonary vein isolation (PVI) for atrial fibrillation and need a repeat ablation for either recurrent atrial fibrillation or for atrial flutter vs. those who do not require repeat ablation.

The total population will be patients who have undergone a first PVI between 2007 and 2012 for atrial fibrillation. The cases will be patients who underwent a PVI and then returned for a repeat ablation for either clinical AF or AFL. The controls will be patients who had a PVI without needing a repeat ablation.

The controls will have had clinical follow up for at least 1.6 years (1 year 7 months). This number was calculated given that the distribution of time between first and second ablations for patients requiring repeat ablation fit a skewed right curve with 80% of patients having their second ablation within 1.6 years, an 90% within 2.2 years (median time to second ablation was 7 months). Given that many patients in the case population will have had more than 2 years of follow up (90% percentile), using 1.6 years will increase the yield of patients, while ensuring that the control population would not cross-over into the case population if there were a longer follow up period.

All of the patients' charts will be assessed to see if there were any arrhythmias either spontaneous or induced subsequent to the PVI being completed. Patients who were in sinus rhythm subsequent to the PVI who did not have a stimulation after will be excluded as there is no way to extrapolate whether or not these patients would have had a post ablation inducible arrhythmia. Sub-group analysis may be necessary to compare patients who had post PVI arrhythmias only with and without stimulation, as well as to compare patients who had post PVI arrhythmias that were terminated by further ablation to those who had arrhythmias that either self-terminated or were cardioverted. Finally subgroup analysis may be used to compare patients who had post PVI atrial fibrillation with those with atrial flutters.

<u>Statistical Analysis:</u>

Sample Size:

- Given an alpha of 0.05 and a Power of 80%,
- Assuming ratio of patients not requiring repeat ablation/patients requiring repeat ablation of 0.36 as preliminary data suggests
- Assuming the proportion of patients who had an inducible arrhythmia is approximately 0.85 (preliminary data),
- Using chi-square test to determine a 15% difference, the study population would need to be 327 patients (240 patients with recurrent arrhythmia and 87 without).
- With the current data base (196 patients with recurrent arrhythmia and 70 without) we could only show a significant difference if only 67% of patients without recurrence had an inducible arrhythmia.

B. Study Procedure

This is a retrospective chart review, so the patients will have all undergone a PVI as clinically indicated, with no additional treatment specific to being included in the study.

C. Study Drugs

Given that this is a retrospective chart review there will be no study drugs used that were not used as a part of a routine PVI.

D. Medical Device

Given that this is a retrospective study, no investigational medical devices will be used.

E. Study Questionnaires

No study questionnaires will be used.

F. Study Subjects

Subjects will be patients who came in for a first PVI between 2007-2011 to CUMC and had either a repeat ablation or at least 1 year and 7 months of follow up after their first ablation.

Exclusion criteria include:

- Patients who had ablations prior to 2007, (as this is when the current software used for PVI at CUMC was instituted)
- Patients who had no repeat ablation, and follow up of less than 1 year 7 months. The median time between ablations for those requiring repeat ablation was 7 months. Median was used because the time length was not normally distributed (right skewed) with the vast majority of patients having repeat ablations within 1 year (3rd quartile is at 1.1 years) with 80% of patients having a repeat ablation before 1.6 years (1 year 7 months).
- Patients in sinus rhythm subsequent to PVI who did not have any programmed stimulation done subsequent to the PVI.
- Patients who had congenital heart disease, cardiac surgery, or ablations prior to first PVI.

G. Recruitment of Subjects

The study will be retrospective, with data pulled from the patients' paper charts and electronic medical records.

H. Confidentiality of Study Data

Data will be secured by a unique code and stored on a hospital computer that is password protected and only accessible to study personnel.

I. Potential Conflict of Interest

There are no conflicts of interest.

J. Location of the Study

The study is a retrospective chart review of patients at CUMC

K. Potential Risks

No potential added risks to patients, as this is a chart review.

L. Potential Benefits

No potential added benefits to patients, as this is a chart review.

M. Alternative Therapies

This study does not involve an experimental therapy.

N. Compensation of Subjects
There will be no compensation to subjects.

O. Costs to Subjects
There will be no added costs to subjects

P. Minors as Research Subjects
This study will not involve any minors.

Q. Radiation or Radioactive Substances
This study is a retrospective chart review and will not add any radiation or radioactive exposure to patients involved.

---

[i] M. Haissaguerre, P. Jais, D.C. Shah *et al.* Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med, 339 (1998), pp. 659–666

[ii] Oral H, Scharf C, et al. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. Circulation. 2003;108(19):2355.

[iii] Karch MR, Zrenner B, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation: a randomized comparison between 2 current ablation strategies. Circulation. 2005;111(22):2875.

[iv] Elayi CS, Di Biase L, et al. Atrial fibrillation termination as a procedural endpoint during ablation in long-standing persistent atrial fibrillation. Heart Rhythm. 2010 Sep;7(9):1216-23.