Microfidelity (MIFI) Ablation Technology versus Standard Ablation Catheter for Atrioventricular Nodal Ablation

A Comparative Pilot Study of Time to Success

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NCT03114124 1/25/2021

Introduction

In some elderly patients with atrial fibrillation (AF), especially in combination with heart failure, a rate control strategy may be preferred. When pharmacological therapy is ineffective or not tolerated, it is reasonable to perform atrioventricular (AV) node ablation with ventricular pacing as a class IIA indication per current guidelines [1].

Usually, the procedure is simple and straightforward and complete heart block can be achieved without any difficulty. However, this "simple" procedure can sometimes prove to be a most difficult case. The most common reason for failure to achieve complete heart block is the inability to localize the compact AV node using the His signal with standard intracardiac electrograms. As these patients come to the laboratory in AF, the His signal may be obscured by AF waves. In some patients with a deeper intramyocardial location of the His bundle and compact AV node it becomes necessary to produce deeper ablation lesions using an irrigated catheter to achieve block.

In patients with AF, the target of ablation for the "ablate and pace" approach is the compact AV node, located at the apex of the triangle of Koch. Ideally, ablation is performed at the most proximal penetrating part of the His bundle in order to maintain a proximal automatic junctional rhythm and avoid pacemaker dependence.

Para Hisian pacing is most commonly used to reveal the presence of a septal accessory pathway. [2-3]

The His bundle is a deep insulated structure and it is difficult to capture it at usual energy outputs. Using a high- output pacing (usually 20 mA at 2 msec) it is possible to directly capture the deeply situated His bundle, which is confirmed by a narrower QRS complex on the paced electrograms. Thus, high-output pacing can be utilized to map the His bundle area in difficult situations.

By applying this electrophysiologic principle of differential tissue capture to help identify the location of the compact AV node, which is in close proximity to the His bundle. Ventricular pacing was performed initially at high output to capture both the basal right ventricular myocardium and the His bundle and the output was gradually lowered to lose His bundle capture. The QRS duration is relatively narrow with high output pacing and increases when the pacing output is lowered, representing ventricular myocardial capture alone. Finally, loss of ventricular capture is seen with further reduction of pacing output. This maneuver has been shown to aid in determining the proximity of the ablation catheter to compact AV node as was validated by successful ablation at this site. Parahisian pacing in conjunction with av nodal ablation has recently been described in the literature [4-5].

A novel catheter with three mini electrodes within the ablation tip (IntellaTip MiFi, Boston Scientific, Boston, MA) may enhance the available data for such a signal dependent technique. In this catheter, bipolar signals can be recorded between the three 0.8-mm-wide electrodes that

are arranged radially 1.3 mm from the end of the catheter alongside the standard distal and proximal bipolar recordings. Animal studies have already demonstrated that the mini electrodes in this novel catheter are more accurate in identifying conducting gaps in linear ablations than conventional electrode recordings [6].

Study Aims:

The aim of our study is to investigate the comparative efficacy of high fidelity multi electrode ablation catheters vs the standard bipolar configuration in success of AV nodal ablation. Both catheters are FDA approved and are being used as indicated on its label. For the purpose of this study, the standard bipolar catheter will be 8mm non-irrigated, and from the following list: Boston Scientific Blazer, Biosense Thermocool Non-Nav, and the St. Jude Sapphire. All of these catheters are currently used in ablation cases at the study site. This study will provide insights on the use of new technology where application may increase efficacy, promote patient and physician safety and decrease costs.

Primary and secondary objectives

Primary endpoints

1. Acute success of ablation identified by a junctional rhythm or complete heart block
2. Time from application of radiofrequency energy to acute success

Secondary endpoints include

1. Procedure time
2. Radiation time

3. Frequency of ablation application
4. Duration of ablation application

Research Plan

Inclusion Criterion

1. Patients with a diagnosis **of persistent or permanent atrial fibrillation** documented on electrocardiography
2. Patients must meet ACC/HRS guidelines for atrioventricular nodal ablation procedure
3. Patients have already been scheduled for their standard of care ablation
4. Patients must be available for at least 1 month post procedure
5. Patients must be greater than or equal to 18 years old.

Exclusion Criterion

1. Patients who do not meet ACC/HRS indications for av nodal ablation
2. Women who are pregnant

Research Design

The study will be performed at the University of Florida Health Science Center at UF Health, Jacksonville-Division of Cardiology. Patients will be recruited in the Cardiology Clinics of our institution and will be screened by Cardiology Research Staff, who will verify all

candidates meet inclusion and exclusion criteria.

Patients found eligible, n=30 for this study will already have a diagnosis of atrial fibrillation and be indicated for an ablation per standard of care.After providing written informed consent, subjects will be randomized by random computer programming to receive an ablation with MIFI technology or standard ablation catheter for their procedure. Data will be collected prospectively (perioperatively and at follow up visit).

During the ablation each patient will have a 3D electroanatomical map of the his bundle region created in addition to pacing along the region of interest. The target will be where the HIS electrogram amplitude is greatest and where the QRS complex from pacing is narrowest. Data will be collected until the primary endpoint of success is achieved.

Subjects will return to UF Shands -Jacksonville on day 30(+/- 14 days) to assess underlying conduction. If conduction has returned they will be offered an additional av nodal ablation per standard of care. If they undergo additional ablation this data will be included

Statistics

Sample Size Justification

This is a pilot study in which the primary aim is to estimate the time until successful end point in each of the two study arms. Thirty patients will be randomized (15 in each study arm). Variable block sizes will be used to improve the blinding of the clinical team. This information will then be used to design a fully-powered randomized study to compare these two arms. Patients will be randomly assigned to study arms. The project biostatistician and team will generate a set of envelopes which contain the random assignments for each patient. Once a patient has consented to participate, the next envelope will be opened for that patient and the catheter assignment will be revealed. This will maintain the blinding of

the clinical team.

Statistical Analyses

The baseline demographic and clinical characteristics of the patients included in this study will be summarized by study arms. Frequencies and percentages will be summarized for categorical variables and means, standard deviations, medians, minima, and maxima will be summarized for numeric variables. For ordinal variables, the medians, minima, and maxima will be summarized. Based on the descriptive summaries and graphical summaries (e.g. box-and-whiskers plots), if there are individual baseline characteristics that differ between the study arms, these characteristics will be included a regression analysis to reduce the estimated variance of the difference between the study arms.

The primary analysis is the estimation of Kaplan-Meier median times to successful endpoints for each of the two study arms. Time zero is when the ablation procedure begins and the successful outcomes are either complete heart block or junctional rhythm. Patients in whom a successful endpoint is not reached will be censored at the time the procedure is stopped. A log-rank test will also be performed to compare these groups. If there are baseline characteristics that differ between the study arms based on the summaries described above, a Cox proportional hazards model will be fit that includes these baseline characteristics to adjust for these baseline differences in the study arms.

Additional Information

Subjects will be identified with a number and data collection sheets which will be stored in limited access areas, locked filing cabinets, and or in computers with security passwords. Data will be kept for 6 years after study completion to comply with UF and HIPAA regulations. Subjects will receive a hand out with names and phone numbers of the physicians and coordinators involved with the study.

Possible Discomforts and Risks

The most common risks associated with the procedure are per standard of care and include but are not limited to cardiac perforation, tamponade, vascular injury and pain. Possible serious adverse events may include cardiac tamponade, preforation and or death

Adverse Event

An adverse event is any unintended or undesirable experience that occurs during the course of the clinical investigation whether or not it is considered to be therapy related. This includes any newly occurring event or previous condition that has increased in severity or frequency since the initiation of study treatment. Adverse events will be followed until resolution while the patient remains on-study. Once the patient is removed from study, events thought to be related to the study therapy will be followed until resolution.

Serious Adverse Event

Serious Adverse Events (SAE): An adverse event occurring while on study and considered related (reasonable possibility that the study treatment caused the adverse experience) to the study treatment that results in any of the following outcomes:

- Death
- A life-threatening adverse experience.
- A persistent or significant disability, incapacity, or is a congenital anomaly, or birth defect.
- Requires inpatient hospitalization, or prolongation of existing hospitalization.

The definition of serious adverse event also includes 'important medical event'. Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening

or result in death or hospitalization but may jeopardize the patient and/or may require medical or surgical intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious. Example of such event is an intensive treatment in an emergency room.

Serious adverse events will be reported per Boston Scientific and UF policy & procedure.

Any clinical events described above will be recorded and if required reported.

The investigator is responsible for informing the IRB and/or the Regulatory Authority of the SAE as per local requirements.

Conflicts of Interest

Dr. Catanzaro does not have any conflicts of interest

Product

The PI is not requesting catheters be included. The catheter or product will be purchased separately as it is done with standard of care.

References

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