Pulsed field ablation versus conventional radiofrequency catheter ablation for repeat pulmonary vein isolation in patients with paroxysmal atrial fibrillation

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Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON56980

Source
ToetsingOnline

Brief title
REPEAT-AF

Condition

- Cardiac arrhythmias

Synonym
Atrial fibrillation; catheter ablation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Boston Scientific,Boston Scientific Cooperation International

Intervention

Keyword: Atrial fibrillation, Implantable loop recorder, Pulsed field ablation, Redo ablation

Outcome measures

Primary outcome

The primary endpoint is freedom from AF/AT/AFl recurrence at 12 months follow-up defined as no documented AF recurrence of >30 seconds within 3 to 12 months of randomization (3-month blanking period).

Secondary outcome

- major secondary endpoint: The primary endpoint is freedom from AF/AT/AFl recurrence at 24 months follow-up defined as no documented AF recurrence of >30 seconds within 3 to 24 months of randomization (3-month blanking period).

- Freedom from AF/AFl/AT recurrence at 12 and 24 months follow-up (no blanking period)

- Repeat PVI within 12 and 24 months of AF ablation

- Acute outcome: 100% PV isolation post-repeat ablation

- AAD therapy initiated/re-initiated at 3, 6, 12 and 24 months of follow-up

- AF burden (proportion of cumulative time in AF divided by the total time accrued over follow-up)

- Delta AF burden (AF burden prior to repeat AF ablation minus AF burden post AF ablation)

- Quality-of-life (AFEQT and Eq-5D-5L questionnaires)

- Procedure time (initiation of venous access to venous access closure)

- Left atrial dwell time (sum of catheter entry-to-exit durations for the left atrium)

- Total ablation time (first ablation to last ablation)

- Fluoroscopy time (total duration of exposure)

- Duration of hospitalization for re-ablation procedure

- Progression to persistent AF

- heart failure hospitalization

- AF hospitalization or urgent visit

- ischemic stroke

- DCCV or iv chemical conversion

- QALYs (cost-effectiveness)

Study description

Background summary

Atrial fibrillation is a condition where the heart beats irregularly at times. Abnormal impulses originate in the pulmonary veins, and these can cause atrial fibrillation. Fortunately, there is a treatment that can help: an ablation. During an ablation, a thin tube, also called a catheter, is inserted through the groin into the heart. Using this catheter, a scar is created at the junction of the four pulmonary veins and the left atrium through heating, freezing, or an electrical pulse (ablation). This scar prevents any potential heart rhythm disturbances and other electrical signals from the pulmonary veins from reaching the heart.

Sometimes, atrial fibrillation can return. This can have various reasons. In most patients (around 85% of people), we observe that electrical conduction has reoccurred at the site of the previous ablation. This allows electrical signals to reach the heart again and cause atrial fibrillation once more.

During the execution of the second ablation, the cardiologist creates a

detailed map of the heart's electrical conduction and the pulmonary veins. If conduction from the pulmonary veins is detected again, the cardiologist will eliminate it using radiofrequency ablation. This involves heating the tip of the catheter, effectively burning away the connection.

For the past few years, another commonly used ablation technique called 'pulsed field ablation' has been available. With this technique, heart muscle cells are rendered inactive by a brief but strong electric shock. The corresponding catheter can investigate each pulmonary vein for new connections to the atrium without the need for an extensive map. If a new connection is discovered, the cardiologist can eliminate it with an electric shock. Pulsed field ablation is a fast technique that achieves the same goal with less information. However, it is currently unknown which technique produces the best results.

Study objective

In this study, we aim to compare two different techniques for the second ablation in patients who have previously undergone an unsuccessful ablation. The first technique is called "radiofrequency ablation," and the second technique is called "pulsed field ablation."

We want to determine which of these two techniques works best to reduce atrial fibrillation and prevent its recurrence after treatment. Both techniques have already been proven safe for this procedure, but we now want to investigate which of the two is most effective for individuals who have had a prior ablation. This has not been studied before.

During the research, we will examine various aspects. The main objective of this study is to discover which technique best ensures that atrial fibrillation remains absent in the two years following treatment. We will continuously monitor this using a small implantable heart rhythm monitor. Additionally, we will assess the patients' quality of life, whether any extra hospital admissions are required, the duration of both procedures, the need for a potential third ablation, and whether additional medication is necessary.

With the results of this study, we hope to make better decisions in the future for patients undergoing a second ablation for atrial fibrillation.

Study design

This multicentre, national, randomised, open-label, parallel group, phase 3 study aims to compare the effectiveness of two different techniques for the second ablation in patients who have previously undergone an unsuccessful ablation for atrial fibrillation (AF). The two techniques being compared are "radiofrequency ablation" (RF) and "pulsed field ablation" (PFA).

Patients will undergo screening evaluations, including a review of medical history, medication assessment, AF documentation, echocardiogram, and evaluation by a cardiac electrophysiologist. Eligible patients will provide written informed consent according to national regulations. Confidentiality measures will be implemented, using deidentified subject identification codes to secure data. Results reporting will be anonymised.

The trial will be conducted at 5 clinical centres in the Netherlands.
Additional sites may be added if needed. Enrolled patients meeting inclusion and exclusion criteria will be randomised 1:1 to either PFA or RF using a tool within the Netherlands Heart Registration (NHR) database. Randomization will occur 1 month prior to the ablation.

Patients will be evaluated for PV isolation at the start of the ablation. Those with isolated PVs will be withdrawn and followed in an observational registry.

Implantable heart rhythm monitor will be implanted in all randomised patients at least 1 month prior to repeat ablation and explanted at 24 months or earlier if needed. Patients will be on uninterrupted oral anticoagulation therapy before the procedure. Heparin will be administered during the procedure. OACs will continue post-procedure for at least 3 months.

The study aims to determine which technique better reduces and prevents atrial fibrillation recurrences. The primary endpoint is the absence of atrial fibrillation in the two years following treatment. Secondary endpoints include quality of life, hospitalization rates, procedure duration, need for a third ablation, and medication requirements. The results will guide treatment choices for future patients undergoing repeat ablation for atrial fibrillation.

Intervention

Patients will be randomised in a 1:1 ratio to RF ablation or PFA.

PFA ablation arm
All enrolled patients will be sedated either with general anaesthesia or (conscious) sedation according to institutional protocol. Intravenous heparin will be administered as boluses and continuous infusions to obtain activated clotting time 300 s prior to the first ablation lesion and throughout the procedure.
Femoral vein access will be obtained, and a single transseptal puncture will be performed with an 8.5-F sheath and exchanged for a 13-F sheath in the left atrium. A baseline electrophysiological assessment of PV connection will be made with the FARAWAVE catheter in each PV. If PV reconnection is detected in more than 1 PV with diagnostic catheters, then the patient will undergo PFA re-ablation, as per trial protocol. If PV reconnection is not detected in any PV with diagnostic catheters (100% PV isolation/ durable PVI), then the patient will be withdrawn from the study and followed in an observational registry.

Withdrawn patients will be treated according to treating EPs discretion (either with the FARAWAVE catheter or RF ablation) and will no longer adhere to the trial protocol.
Propofol boluses synchronized to PFA applications: a 0.035-inch, 180-cm extra-stiff, straight or j-shape guidewire will be used to cannulate each vein. A multielectrode FARAWAVE ablation catheter will be advanced over the guidewire to the left atrium. The guidewire will be advanced into the target PV, the catheter splines will be deployed to fit anatomy (retracting the deployment knob), and the deployed catheter will be advanced to the ostium of the target PV. Positioning of PFA ablation catheter in the ostium will be monitored with ICE imaging and/or fluoroscopy. An ablation dose of 2kv will be delivered in accordance with the guidelines for FARASTAR. All PVs, regardless of reconnection, will be re-ablated/re-isolated and re-antralized with PFA (i.e. repeat PVI). Number of pulses delivered, waveforms (monophasic/biphasic), output of generator, and number of applications (minimum 8 per PV) delivered with the FARAWAVE ablation catheter determined by individual investigator. Cavotricuspid isthmus (CTI) ablation may be performed with an RF ablation catheter, if warranted. Investigators are deterred from performing additional ablations lesions for non-PV triggers, unless necessary. Patients with atrial flutter and atrial tachycardia were excluded at baseline to minimize ablations of non-PV triggers.
Acute isolation of the treated PVs will be determined by mapping electrodes on each spline of the PFA catheter. In addition, pacing will be performed at each bipolar electrode pair (1-2 of spline 1 and 2, 2-3 of spline 2 and 3, etc). No waiting period is allowed.
Post-ablation testing for phrenic nerve injury is recommended using fluoroscopy detecting movement of the diaphragm.

PFA catheter system
Two components from the PFA system will be used for this study: custom PFA generator (Farastar, Farapulse, Menlo Park, California), over-the-wire 12-F multielectrode PFA catheter (Farawave, Farapulse; and the 13-F steerable sheath (Faradrive, Farapulse)
The Farawave *single-shot* multielectrode PFA catheter is the primary ablation catheter used for PV isolation in this trial. It consists of 5 splines with 4 electrodes per spline and 1 electrode available for electroanatomic visualization. In this trial, both diameter sizes of the fully deployed *flower* configuration of the Farawave ablation catheter, 31 or 35 mm, can be used based on physician preference.

RF point-by-point ablation arm (control)
All enrolled patients will be sedated either with general anaesthesia or (conscious) sedation according to institutional protocol. Intravenous heparin will be administered as boluses and continuous infusions to obtain activated clotting time of 300 s prior to the first ablation lesion and throughout the procedure.
Repeat PVI with RF ablation will be performed according to standard practice.

Following double transseptal puncture, a detailed activation map of the left atrium will be performed with a multipolar high density mapping catheter. All commercially available mapping systems are allowed. RF ablation will be performed with contact force sensing cooled tip RF ablation catheters. The PV reconnection site will be identified, and focal RF ablation lesions will be delivered at sites of PV reconnection. Figure 2 indicates the sites for re-ablation in the point-by-point RF arm. Ablation lesions should be targeted to the PVs. Low voltage areas in the carina and ostia may also be re-isolated. CTI ablation may be performed, if warranted. Investigators are deterred from performing additional ablations lesions for non-PV triggers, unless necessary. Patients with atrial flutter and atrial tachycardia were excluded at baseline to minimize ablations of non-PV triggers. If atypical flutter or AT occurs during the procedure, it is recommended not to ablate these arrhythmias. Post-ablation testing for phrenic nerve injury is recommended using fluoroscopy detecting movement of the diaphragm.

Implantable loop recorder (ILR) implants and explants
ILRs will be implanted in all randomised patients at least 1 month prior to repeat ablation. ILRs will be implanted in the EP lab and will be implanted according to standard procedures.
ILR explantation will occur at 24-months follow-up according to standard practice. Earlier explantation may occur in the case of infection or adverse event and will be based on treating clinician*s discretion.

Study burden and risks

The only additional risk that this study entails compared to a regular ablation is the placement of the implantable heart rhythm monitor. The complications that may arise from this are low and consist of temporary sensitivity around the injection site after placement or a local infection. The latter is rare (<1%), but does require the removal of the IHM and treatment with antibiotics.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patient had 1 previous PVI with either PFA, cryoballoon or RF ablation in past 5 years
- Recurrent, symptomatic, paroxysmal AF
- Age 18-80 years

Exclusion criteria

- Persistent AF (by diagnosis of duration >7 days)
- Underwent additional ablations outside the pulmonary veins during previous AF ablation
- Left ventricular ejection fraction (LVEF) <30% as documented by TTE (within <3 months prior)
- Left atrial volume index >60 ml/m2 or left atrial anteroposterior diameter >5.5 cm
- NYHA Class III or IV
- Intramural thrombus, tumor or other abnormality that precludes safe catheter introduction or manipulation
- BMI >35 kg/m2

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2024
Enrollment:	154
Type:	Anticipated

Medical products/devices used

Generic name:	FARAPULSE Pulsed Field Ablation System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	29-08-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT06199180
CCMO	NL85119.042.24