The occurrence of cerebral embolism (CE) in catheter ablation of atrial fibrillation (AF) using three different ablation catheters

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1. To compare the induction of a procoagulant state between patients undergoing PVI using the PVAC catheter, the cryoballoon catheter or the cooled tip catheter.2. To compare the incidence of CE on diffusion weighted MRI between the three groups of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON35660

Source
ToetsingOnline

Brief title
Cerebral embolism in AF-ablation (CE-AF).

Condition

- Cardiac arrhythmias
- Central nervous system vascular disorders
- Cardiac therapeutic procedures

Synonym
palpitations, supraventricular tachycardias

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Medtronic B.V.

Intervention

Keyword: atrial fibrillation, catheter ablation, intracranial embolism

Outcome measures

Primary outcome

1. A rise in the procoagulant state, as measured with the following parameters:

markers of endothelial damage (VWF:Ag), markers of activated coagulation

(D-dimer, prothrombin fragment 1 and 2 (F1+2), and thrombin-antithrombin

complex (TAT)), markers of fibrinolysis (tissue plasminogen activator (tPA),

plasminogen activator inhibitor 1 (PAI-1), and plasmin-antiplasmin complexes

(PAP)), and by measurement of fibrinogen and thrombin generation.

2. New embolic lesions on diffusion weighted MRI

3. The succes rate of PVI. Success will be defined as symptom-free patients

with absence of > 30 sec AF on a 7-day holter recording 12 months after the

ablation,

Secondary outcome

1. New embolic lesions on diffusion weigthed MRI with neuro(psycho)logical

symptoms

Study description

Background summary

Catheter ablation induces a procoagulant state. The induction of a procoagulant

state has been studied separately in radiofrequency (RF) ablation of localised supra-ventricular tachycardia (SVT) and in non-cooled pulmonary vein electrical isolation (PVI), the cornerstone of catheter ablation of atrial fibrillation (AF). The induction of a procoagulant state in ablation of AF using cooled-tip RF catheters or using cryo catheters has never been studied. Due to the avoidance of high endocardial temperatures, it may be expected that these procedures induce a lower level of procoagulation than non-cooled RF ablation of AF.
AF increases the long-term risk for cerebral embolism (CE). In addition, catheter ablation of AF, even with modern, cooled tip catheters, poses an acute risk for symptomatic CE of approximately 1%. Although this incidence of acute CE is too low for single-centre research, recently a 11% incidence (6 out of 53) of CE was found with diffusion weighted MRI of the brain (DW-MRI) in patients undergoing cooled-tip catheter ablation of AF, including one patient with neurological symptoms.
Due to the amount of skill, training and time required to perform catheter ablation of AF, new catheters have been developed to simplify these procedures. In the LUMC, we currently use the classic cooled-tip catheter, the PVAC catheter as well as the cryoballoon catheter for PVI. The PVAC catheter is equipped with non-cooled RF electrodes, with the increased risk of endocardial charring and subsequent local thrombosis and CE. In contrast, the cryoballoon might even decrease the risk of CE, due to the different energy source.
Apart from the type of ablation procedure performed, the amount of pre-ablation left atrial fibrosis is a strong predictor of procedural success. Left atrial fibrosis can be detected with integrated backscatter echocardiography (IBS) or delayed-enhancement MRI (DE-MRI) of the left atrium. In addition, a biochemical marker of collagen degradation rate (ICTP) has been shown to differ among different types of AF (paroxysmal, persistent, permanent). The type of AF by itself is also a strong predictor of ablation success.

Study objective

1. To compare the induction of a procoagulant state between patients undergoing PVI using the PVAC catheter, the cryoballoon catheter or the cooled tip catheter.
2. To compare the incidence of CE on diffusion weighted MRI between the three groups of patients.
3. To quantify the proportion of CE with neuropsychological or neurological abnormalities detected by a neuro(psycho)logical questionnaire.
4. To assess the influence of left atrial fibrosis and cardiac collagen metabolism on the success rate of PVI after 12 months.

Study design

1. 270 patients scheduled for a first ablation of paroxysmal AF will be 1:1:1 randomised to PVI using the PVAC catheter, the cryoballoon catheter or the

cooled tip catheter. In these patients the procoagulant state will be assessed before, during and after the procedure by markers of endothelial damage, markers of activated coagulation, markers of fibrinolysis and by measurement of fibrinogen and thrombin generation. In addition, markers of collagen metabolism will be measured before and three months after the procedure.
2. In all patients a neuro(psycho)logical questionnaire will be taken and DW-MRI of the brain will be performed before and after ablation to document CE.
3. In all patients DE-MRI and IBS of the left atrium will be performed before and three months after the procedure to quantify left atrial fibrosis.
4. The induction of a pro-coagulant state and the incidence of CE will be compared between the three groups.
5. The influence of left atrial fibrosis and of collagen metabolism on the success rate of PVI will be determined

Intervention

Pre-treatment with clopidogrel or placebo from 7 days before the procedure until the second day after the procedure.

Study burden and risks

Burden:
Day -1: collection of blood sample, neuro(psycho)logical questionnaire, echocardiography with IBS analysis, DE-MRI of the heart (standard clinical care) and DW-MRI of the brain
Day 0: collection of two blood samples during the procedure
Day 1: collection of blood sample, neuro(psycho)logical questionnaire and DW-MRI of the brain
Dag 91: echocardiography with IBS analysis, DE-MRI of the heart (standard clinical care) and DW-MRI of the brain if the second MRI scan showed a new diffusion abnormality
Day 359-365 (approximately): 7-day holter recording. This recording is part of the standard clinical care.

Risks:
Other: Hematomas caused by the collection of blood samples, psychological distress due to the discovery of asymptomatic CE or neuropsychological dysfunction.

Possible Benefits:
Early discovery of neuropsychological dysfunctioning with the possibility of professional neuropsychological rehabilitation

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

Any patient scheduled for a first ablation of paroxysmal atrial fibrillation

Exclusion criteria

Any patient unwilling or unable to give informed consent
Minors and incapacitated adults
Any patient with contra-indications to DW-MRI of the brain or DE-MRI of the left atrium
Any patient unable to undergo neuropsychological testing due to mental retardation

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-03-2015
Enrollment:	270
Type:	Actual

Ethics review

Approved WMO Date:	30-03-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-03-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL26166.058.10