Reappraisal of Atrial Fibrillation: Interaction between HyperCoagulability, Electrical Remodeling, and Vascular Destabilisation in the Progression of AF (RACE V) - Workpackage 5

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1. find out the true time-in-AF per AF category and identify progression of AF,2. uncover genetic predisposing patterns for AF and AF progression,3. find out electrical basis of AF,4. investigate the relationship between genetic changes, electrical...

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

Summary

ID

NL-OMON53124

Source
ToetsingOnline

Brief title
RACE V WP5

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Nederlandse Hartstichting;CVON project 2014-09;EU network MAESTRIA (grant number: 965286)

Intervention

Keyword: Atrial fibrillation, Continuous rhythm monitoring, Hypercoagulability, Pathophysiology

Outcome measures

Primary outcome

Determining genetic, electrical, biochemical, molecular and structural factors

in atrial and ventricular biopsies and blood that contribute to AF initiation

and progression during 3 years after open heart surgery.

Secondary outcome

- AF incidence and duration,

- severe cardiovascular and cerebral consequences of AF,

- complexity of AF on digital EKG,

- AF biomarkers associated with AF progression,

- CT and ultrasound parameters predictive of AF progression and duration,

- genotyping of different AF types.

Study description

Background summary

Although the socio-economic burden of AF is growing steadily and significant progress has been made in understanding the pathophysiology of this arrhythmia, treatment of AF patients is still far from satisfactory. The success rate of cardioversion is still limited and anti-arrhythmic drugs are unable to prevent recurrences of AF. Prevention of thromboembolic events still requires

anticoagulation therapy with all the associated risks. Radio-frequency ablation, originally developed for treatment of paroxysmal AF, varies in its efficacy to cure persistent AF and is afflicted with a number of potentially serious side-effects.
AF is a progressive arrhythmia. With time, paroxysmal AF becomes persistent and the success rate of cardioversion declines. This progressive nature of AF is presumably related to a slow but steady process of structural remodeling in the atria characterized by hypertrophy, activation of fibroblasts and enhanced collagen deposition. Also the distribution and function of gap junctions undergoes changes, which are important for the development of intra-atrial conduction disturbances. Since these structural and electrophysiological alterations form the basis for initiation and perpetuation of AF, characterization of the atrial substrate is essential to develop better strategies for prevention and treatment of the arrhythmia.
Clearly, the mechanisms underlying the progression of AF are multifactorial. Atrial fibrosis, vascular rarefaction, inflammation, abnormalities in atrial Ca2+ handling and atrial adipose tissue infiltration as well as hypercoagulability appear to play a role in the progression of AF.
An area logically effected by AF seems to be the left and right ventricle. A well described pathology correlated to AF is tachycardia-induced myopathy where there is a significant decrease in left ventricular function. Recent evidence correlates atrial fibrillation to structural changes as well as overall loss of function of both ventricles.
Despite new insights on electrical mechanisms leading to AF initiation and progression, it is still unclear which electrical properties are associated with lower probability of successful ablation or poorer long-term outcomes. Detailed analysis of electrical conduction patterns using epicardial mapping in patients with and without a history of AF provides unique information about complexity and sources of AF. This information will be used to develop new ablation strategies in patients with AF.

Study objective

1. find out the true time-in-AF per AF category and identify progression of AF,
2. uncover genetic predisposing patterns for AF and AF progression,
3. find out electrical basis of AF,
4. investigate the relationship between genetic changes, electrical adaptations and structural properties in the atria,
5. to unravel the role of coagulation in AF progression,
6. uncover molecular mechanism in cardiac tissue and detect specific biomarkers to recognize the severity of AF or AF-prone patients.

Study design

Before the operation:
1. CT scan of the heart,

2. Taking questionnaires,
3. Blood collection,
4. Digital electrocardiogram (EKG),
5. OPTIONAL: MRI brain and neuropsychological testing.

During the operation
1. Taking small biopsies
2. OPTIONAL: Epicardial Mapping of the Atria
3. OPTIONAL: insertion of a rhythm monitor under the skin.

After 1 year on the control appointment
1. Physical examination,
2. Taking questionnaires,
3. Digital electrocardiogram (EKG),
4. Duplex carotides,
5. OPTIONAL: neuropsychological testing.

After 2.5 years at the control appointment
1. Sound examination (USG) of the heart,
2. Blood collection,
3. Digital electrocardiogram (EKG);
4. OPTIONAL: neuropsychological testing.
5. OPTIONAL: Remove the rhythm monitoring device

Study burden and risks

- Rhythm monitoring: this will no longer be done with implanted recorders, but with non-invasive techniques. This will reduce the burden on the patients. Patients will no longer have to return for a recorder explant and they will no longer have to make weekly transfers with their home monitors. Previous research has shown that non-invasive techniques are effective for detecting symptomatic AF that also plays a greater role with poorer long-term outcomes. Study subjects can easily and quickly make transfers with the non-invasive recorder, which means that these results will also be translated more quickly into future clinical practice.
- Epicardial mapping: in this study epicardial mapping electrodes will be used that will allow to map electrical conduction in the atria. An extensive analysis of the electrodes has taken place and they can be used safely in patients.

The important benefits for the understanding of AF pathophysiology and also for the patient themselves will certainly outweigh the above mentioned risks.

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

- Age > 18 years;
- Undergoing first elective open chest cardiac surgery;
- Able and willing to sign informed consent for the registry;
- Able and willing to undergo heart rhythm monitoring with noninvasive recorders.

Exclusion criteria

- Deemed unsuitable or not willing to undergo heart rhythm monitoring with noninvasive recorders or to attend follow-up visits;
- Pregnancy;

- Life expectancy of less than 2.5 years;
- History of prior cardiac surgery or ablation for AF.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-10-2016
Enrollment:	380
Type:	Actual

Medical products/devices used

Generic name:	Implantable loop recorder
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-07-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-10-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	31-01-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-09-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-03-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-12-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL56796.068.16