Calcium Role in the Excitation-Contraction and Excitation-Transcription Coupling Processes in Human Atrial Fibrillation.

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Objectives: 1/. To study the proarrhythmic effects of intracellular Ca2+ signaling alterations in AF.2/. To study the nuclear Ca2+ signaling in AF.3/. To study the Ca2+-dependent pathways activated in AF and the consequences of the inactivation of...

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

Summary

ID

NL-OMON38277

Source
ToetsingOnline

Brief title
Excitation-Contraction and Excitation-Transcription Coupling in AF.

Condition

- Cardiac arrhythmias

Synonym
Atrial arrhythmia., Atrial fibrillation

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Transatlantic Leducq network

Intervention

Keyword: Atrial fibrillation, Calcium, Excitation-Contraction Coupling, Excitation-Transcription Coupling

Outcome measures

Primary outcome

Main study parameters/endpoints:

1/. To identify new cellular proarrhythmic mechanisms.

2/. To identify new nuclear targets for therapy (i.e. important factors

involved in Ca2+-dependent transcription pathways).

Secondary outcome

The knowledge of the cellular mechanisms activated during persistent AF will

significantly enhance the chances of better treatment to not only cardioconvert

AF, but also to allow the atrial cells to recuperate their function after AF.

This is expected to reduce the thromboembolic risks and improve cardiac

function after cardioversion of AF.

Study description

Background summary

Rationale: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults with growing socio-economic burden. Although a significant progress has been made in understanding the pathophysiology of this arrhythmia, treatment of AF patients is still far from satisfactory. AF is characterized by an electrical remodeling inducing the reduction of the action potential duration (APD). Intracellular Ca2+ signaling is also altered in AF. Hypotheses: (1) Reduction of the APD in AF alters the intracellular Ca2+ signal which can be proarrhythmic; (2) The alterations in intracellular Ca2+ signaling affect the nuclear Ca2+ signaling which induces the activation specific Ca2+-dependent

transcription pathways in AF.

Study objective

Objectives:
1/. To study the proarrhythmic effects of intracellular Ca2+ signaling alterations in AF.
2/. To study the nuclear Ca2+ signaling in AF.
3/. To study the Ca2+-dependent pathways activated in AF and the consequences of the inactivation of these pathways on atrial electrical remodeling and contraction.

Study design

Study design: Right atrial appendages will be obtained from patients in SR, with paroxysmal and persistent AF. Sarcomere shortening will be measured in thin atrial trabeculae and/or isolated cells. Simultaneous recordings of cellular AP (or ionic currents) and Ca2+ signals will be performed in isolated atrial cells with the patch-clamp technique coupled to the dynamic confocal microscopy. Trabeculae or cells will be subjected to different pacing rates, Ca2+ concentrations, or drugs (i.e. inhibitors of transcription pathways). Structure and protein composition of the atria will also be studied. Finally, nuclei will be isolated from atria tissue to specifically study the nuclear Ca2+ signaling without the influence of the cytoplasmic Ca2+.

Study burden and risks

An informed consent will take place preoperatively. During the operation an atrial biopt will be prelevated. Biopsy prelevation will prolong the operation time by about 2 minutes.

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

Patients in sinus rythm and undergoing for openchest surgery.
Male and female patients over 18 years old.
Patients with paroxysmal AF and undergoing for openchest surgery.
Patients with persistent AF and undergoing for openchest surgery.
Patients who have given written consent.

Exclusion criteria

Patients who are scheduled for re-operation.
Male and female patients under 18 years old.
Patients who do not speak/understand Dutch.
Patients who are not will-competent.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-03-2011
Enrollment:	570
Type:	Actual

Ethics review

Approved WMO

Date:	15-06-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	06-06-2012
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	NL31236.068.10