Connexin 40 polymorphism and protein expression in the right atrial appendix in patients without atrial fibrillation.

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The main objective of this study is to investigate the relation between Cx40 polymorphism and protein expression in the general population and patients without a history of AF.

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

Summary

ID

NL-OMON31871

Source
ToetsingOnline

Brief title
Cx40 gene polymorphism and in vivo protein expression

Condition

- Cardiac arrhythmias
- Chromosomal abnormalities, gene alterations and gene variants

Synonym
atrial fibrillation; heart rhythm disturbance

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: atrial fibrillation, connexin 40, polymorphism, protein expression

Outcome measures

Primary outcome

Indentifying the relation between Cx40 polymorphism and in vivo protein

expression in patients without a history of AF.

Secondary outcome

Not applicable.

Study description

Background summary

Connexin 40 (Cx40) protein is one of the most important connexins expressed in the atria which form the gap junctions. Gap junctions are clusters of transmembrane channels that link adjoining cells and mediate cell-to-cell electrical coupling and communication. The role thus of Cx40 on the propagation of the electrical stimulus in the heart is essential. Alterations in the organization of gap junctions and connexins expression are well established as a consistent feature of human heart disease and may lead to arrhythmias. On the other hand, studies in animals have also shown that heart arrhythmias, like atrial fibrillation (AF) can lead to changes in the distribution, intercellular orientation and expression of the connexin proteins. In patients with chronic AF quantitative and qualitative alterations in Cx40 expression of the right atrial appendix (RAA) have been shown and these changes could result in changes of the electrophysiologic properties of the atrial tissue, thereby increasing vulnerability to AF. Research from our department has shown that patients with idiopathic AF have a higher prevalence of Cx40 polymorphism (-44AA coupled with +71 allele). Cx40 polymorphism occurs in 7% of the general population. The direct relation however between Cx40 gene polymorphism and Cx40 protein expression in the atria has not yet been investigated.

Study objective

The main objective of this study is to investigate the relation between Cx40 polymorphism and protein expression in the general population and patients

without a history of AF.

Study design

This study was designed as a monocenter observational cross-sectional study. The participating center is the UMC Utrecht. Patients scheduled for cardiac surgery and free of AF will be asked to participate in this study. After informed consent patients will be included. During cardiac surgery the right atrium is incised at the base of the right atrial appendix (RAA) for the canulation of the heart- lung machine. The collection of a small part (0.5x0.5 cm) of the RAA does not do extra harm to the patient. This part of the RAA will be immediately snap frozen in liquid nitrogen and stored at -80 degrees and taken to the department of medical physiology for further analysis. Also, 5ml of blood will be obtained for genomic DNA extraction. First, the DNA samples will be genotyped for the Cx40 polymorphism at nucleotide position -44 (G*A), which is located within the regulatory region of the Cx40 gene. Sequencing will be performed on purified Polymerase Chain Reaction products and the samples will be run and analyzed on an ABI automated sequencer. Seven percent of the patients will be homozygote (group 1) for the polymorphisms. According to the Hardy-Weinberg equilibrium, 39% of the patients will be heterozygote (group 2) and the others will not carry the minor allele (group 3). An equal number of cardiac tissue samples from all these three groups will be used for further tissue analysis (Western-Blotting, reverse transcript PCR, immunohistology). We will look for differences in Cx40 protein expression among these three groups.

Study burden and risks

Participation in this study will have no additional risk to the patient. The excision of a small part of the right atrial appendix during surgery does not do extra harm to the patients. Approximately 5ml of extra blood will be drawn during a vena puncture which is a standard procedure for this type of operation.

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 planned for cardiac surgery.
Age *18 years.
Written informed consent.

Exclusion criteria

Permanent AF.
Mitral valve abnormalities (stenosis / regurgitation).
Left atrial size >50 mm (transthoracic echocadardiography).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-10-2008
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO

Date:	16-09-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL22229.041.08