Tissue, Blood and Biomarkers to Predict Future Atrial Fibrillation

Published: 03-12-2014
Last updated: 21-04-2024

The primary objective of this study is to identify atrial tissue miRNAs that are associated with the incidence of AF and histological alterations in a population of patients without documented AF. Secondarily, this study will validate AF associated...

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

Summary

ID

NL-OMON47800

Source
ToetsingOnline

Brief title
PREDICT AF

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation, heart rhythm disturbances

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO toekenning VIDI 2013 nr 016.146.310; t.n.v. J.R. De groot

Intervention

Keyword: atrial fibrillation, atrial remodeling, biomarkers, invasive treatment

Outcome measures

Primary outcome

Main study parameters are tissue miRNAs, atrial histopathology and blood biomarkers. Blood biomarkers will include miRNAs and markers of inflammation, oxidative stress, markers of fibrosis formation and circulating microRNAs. These will be correlated to the incidence of post-operative AF and the incidence of newly developed AF after 24 months follow-up. The study will be extended to five years.

Secondary outcome

Additional study parameters on the process of atrial remodeling and clinical data will be collected and include:

- Cardiac imaging data
- Clinical data on cardiac history
- Assessment of stroke-free status
- Epicardial mapping during thoracic surgery
- Experienced health

Study description

Background summary

Patients undergoing cardiac surgery are at risk of developing post-operative and recurrent atrial fibrillation (AF), which is related to an increased morbidity and mortality, but adequate risk prediction is currently impossible. Generally, patient follow-up in this population is insufficiently focussed on

the development of AF. The mechanisms leading to the development of AF are multifactorial and remain incompletely understood. MicroRNAs and circulating plasma biomarkers may elucidate the pathophysiological process underlying AF and are useful and promising tools for risk stratification, prognosis and future targets of therapy of AF. These biomarkers may identify those patients at risk for the development of AF.

Study objective

The primary objective of this study is to identify atrial tissue miRNAs that are associated with the incidence of AF and histological alterations in a population of patients without documented AF. Secondarily, this study will validate AF associated tissue miRNAs in plasma and will simultaneously correlate blood protein biomarkers with the incidence of AF. This will allow future risk stratification using circulating blood biomarkers.

Study design

This study will be an explorative study of a cohort of 150 cardiac surgery patients. Left atrial appendages will be removed and epicardial mapping will be performed during cardiac surgery at the beginning of the follow-up period. Atrial tissue and blood samples will be collected at baseline. MiRNA sequencing of atrial tissue will be performed a selection of patients. Potential disease related miRNAs will be correlated with histopathological alterations of atrial tissue and the expression of miRNAs will be validated in the patient*s plasma samples that were collected at baseline. The blood samples collected at baseline will in addition be used for determining plasma protein biomarkers. All data and biomaterial collected at baseline will be correlated to the incidence of AF. Patients will be followed for 24 months to detect post-operative and newly developed AF. In case of detection of new onset AF, patients will receive contemporary treatment conforming to the guidelines. The study period will be extended to a total follow-up of 5 years with one additional visit per year. The aim of the extended follow-up is to improve the sensitivity of the time-to follow-up analysis in order to discover more and different biomarkers.

Study burden and risks

Participants are estimated to have a 20% absolute risk of developing post-operative AF and a 10% risk of developing new AF within 2 years after surgery. These patients may therefore develop an indication for oral anticoagulation therapy and are likely to benefit from LAA excision for stroke prevention. LAA removal can be performed without additional risk. No adverse events have been reported in our thoracic surgery center (>313 procedures) over the past 5 years.
Follow-up of patients will be performed in our center at 1 month, 6 months, 12

months and 24 months with holter registration in order to detect atrial fibrillation.
The study will be extended to five years follow-up in total with 1 visit per year on 3, 4 and 5 years. Patients will be asked informed consent for the extended follow-up separately. The impact of the extended follow-up is limited as it includes only one visit per year and the preceding holter investigation may take place in the local referring hospital. If patients are capable to come to the AMC, they will be invited for a blood withdrawal. If patients are unable to attend to the AMC, patients will receive a telephone call.
Patients are asked to comply to additional physician attendance, but have potential benefit through the early detection of atrial fibrillation and start of oral anticoagulation therapy.

Atrial biopsy has been suggested as an alternative to LAA resection. However, when comparing LAA resection with LAA biopsy, it may be discussed whether the risk of atrial biopsy would not exceed the risk of atrial appendage resection due to the slender and fragile atrial wall. Lastly, participants may benefit from LAA resection, because that procedure will reduce the risk of AF related thromboembolic complications, whereas atrial biopsy does not carry any anticipated benefit for the study population.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- On-pump surgery
- Elective sternotomy for coronary artery bypass grafting or mitral valve surgery or aorta- or aortic valve surgery
- CHADS VASC score >= 2
- Sinusrhythm
- Age between 18 and 80 years

Exclusion criteria

- Documented or reported history atrial fibrillation, atrial flutter (duration > 5 minutes) or ventricular tachycardia.
- Emergency or redo of CABG or valvular surgery
- Endocarditis, pericarditis
- Active systemic inflammation
- active malignancy
- NYHA class IV heart failure symptoms
- Left ventricular ejection fracton < 30%
- Pregnancy
- History of previous radiation therapy of the thorax

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):	12-05-2015
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	03-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL50754.018.14