(123I-mIBG And Defibrillation for Atrial Fibrillation): Enhanced sympathetic activity as a mechanism of Atrial Fibrillation recurrence

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Patients with novel onset or recurrent atrial fibrillation have an altered myocardial sympathetic activity. The quantification of sympathetic activity with 123I-mIBG scintigraphy, as well as its change over time after restoration of sinus rhythm,...

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

Summary

ID

NL-OMON48497

Source
ToetsingOnline

Brief title
MAD-AF

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation, supravertricular arrhythmia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: VIDI beurs: 106.146.310

Intervention

Keyword: Atrial fibrillation, Cardioversion, Defibrillation, MIBG, Sympathetic activity

Outcome measures

Primary outcome

Documented recurrence of atrial fibrillation (or other atrial arrhythmias

lasting longer than 30 seconds as per HRS/EHRA/ECAS consensus document

definition) within the first 6 months after cardioversion.

Secondary outcome

AF recurrence within the first year after cardioversion (documented as stated

above)

Quality of life (SF-36) before and at 6 and 12 months after cardioversion

Hospitalization for atrial arrhythmias

Hospitalization for heart failure

Study description

Background summary

AF is the most common arrhythmia; its incidence and prevalence will increase more than twofold over the coming years. The role of the autonomic nervous system (ANS) in onset and perpetuation of AF remains incompletely understood. Indeed, the ANS plays a role in the at least in some, but probably in many patients. There are patients that specifically experience AF during high vagal tone, or, conversely during exercise. This notion, however, has had modest impact on the clinical care of patients.
We recently showed that stimulation of the ganglionated plexi resulted in a disparate response on activation time and conduction velocity, indicating that there is a direct electrophysiological effect of the ANS that may facilitate AF8. Similarly, stimulation of the ganglionated plexi during AF changes the complexity of the arrhythmia, conduction velocity, number of epicardial

breakthroughs and fractionation index in particular.

We do harm by subjecting a considerable number of patients to rhythm control strategies who will eventually fail, which puts a burden on the individual patient and the health care budget. On the other hand, there are patients with an unfavourable baseline profile who do unexpectedly well upon cardioversion, and these patients may be currently undertreated.

123I-mIBG scintigraphy allows non-invasive quantification of the sympathetic activity in the heart and has been shown a valuable tool for assessing prognosis for example in patients after myocardial infarction and patients with heart failure. The data on atrial fibrillation are limited, but there are reports that support 123I-mIBG scintigraphy for risk stratification for the development of atrial fibrillation. The time course of the sympathetic activity in the heart, and, more importantly the cause of increased sympathetic activity in the heart is unknown. It may very well be that the increased sympathetic activity observed in patients with atrial fibrillation is the result of the ongoing arrhythmia, rather than an independent phenomenon that causes the arrhythmia. This is a relevant distinction, because it will heavily impact on the targeted clinical strategy to prevent recurrence of atrial fibrillation in these patients.

Study objective

Patients with novel onset or recurrent atrial fibrillation have an altered myocardial sympathetic activity. The quantification of sympathetic activity with 123I-mIBG scintigraphy, as well as its change over time after restoration of sinus rhythm, can be used to target therapy and predict AF recurrence. The extent of sympathetic activity and its change over time are correlated with markers of electrical, structural and autonomic remodeling, as assessed by circulating biomarkers.

Study design

Patients with novel onset or recurrent atrial fibrillation, scheduled for elective electrical cardioversion are eligible for this study. Patients should be adequately anticoagulated according to the current guidelines2. Patients with rhythm disturbances other than atrial fibrillation or a history of catheter or surgical ablation will be excluded. Patients with an emergency indication for cardioversion will be excluded.
Patients will undergo 123I-mIBG scintigraphy within 7 days before the elective cardioversion is performed, and a questionnaire on the occurrence of AF and AF related complaints in the past months will be filled out. Blood samples will be collected during the cardioversion procedure. Rate/rhythm control management will be performed according to clinical protocols and at the discretion of the treating cardiologist, but will preferably remain unchanged during follow-up.

Six weeks after the cardioversion, the patients will be seen at the Cardiology outpatient clinic (as is standard clinical care), a second 123I-mIBG scan will be performed and blood samples will be collected again. The rhythm at that time will be confirmed. Additional visits to the outpatient clinic will be planned 6 and 12 months after cardioversion. At those visits, cardiac rhythm will be confirmed, blood samples will be collected, and a questionnaire on the occurrence of AF and AF related complaints over the past months will be filled out.

Intervention

123I-mIBG scan

Study burden and risks

1 maal inclusiegesprek met onderzoeker
2 maal 123I-mIBG scans (voor cardioversie, 6wk na cardioversie)
4 maal bloedafname
4 maal SF-36 questionnaire
2 maal extra polikliniek bezoek (6 en 12 maanden)

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

- Elective cardioversion is planned
- Adequate anticoagulation with vitamin K antagonists or NOACs for at least 3 weeks prior to the procedure
- Beta-blocker use at baseline, at least continued up to the second 123I-mIBG scintigraphy
- Age between 18 and 80 years
- Legally competent and willing and able to sign informed consent
- Willing and able to conform to the study protocol

Exclusion criteria

- Unable or unwilling to comply with study procedures
- Discontinuing of beta-blockers during follow-up period up to the second 123I-mIBG scintigraphy
- Discontinuing or switch of antiarrhythmic drugs during follow-up period up to the second 123I-mIBG scintigraphy
- Arrhythmia other than atrial fibrillation as the indication for cardioversion
- Emergency electrical cardioversion
- Overt heart failure symptoms (i.e. edema, pulmonary rales, orthopnea), NYHA class>=2 and/or left ventricular ejection fraction < 35%
- Known significant coronary artery disease (>50% stenosis)
- Myocardial infarction or acute coronary syndrome within 3 months prior to the cardioversion
- History of catheter or surgical ablation for any arrhythmia
- CVA within 6 months prior to the cardioversion
- Active malignant disease
- History of neurosecretory tumors
- Pregnancy or of childbearing potential without adequate contraception
- History of previous radiation therapy of the thorax
- Circumstances that prevent follow-up (no permanent home or address, transient, etc.)
- Life expectancy <2 years.

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	31-12-2020
Enrollment:	35
Type:	Anticipated

Ethics review

Approved WMO

Date:	23-09-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	03-02-2020
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	NL69420.018.19