Substrate and mechanisms of ventricular arrhythmia in non-ischemic cardiomyopathy

Published: 19-10-2011
Last updated: 15-05-2024

1) To improve our understanding of the underlying pro-arrhythmic substrate and electrophysiologic mechanisms of VA in NICM, and to develop individualized treatment for VA based on the identified substrate. 2) To improve risk stratification for VA...

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

Summary

ID

NL-OMON38075

Source
ToetsingOnline

Brief title
Non-ischemic cardiomyopathy

Condition

- Cardiac arrhythmias

Synonym
dilated cardiomyopathy, heart muscle disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Non-ischemic cardiomyopathy, Substrate, Ventricular arrhythmia, Ventricular tachycardia

Outcome measures

Primary outcome

The main study parameters are extent, location and pattern of fibrosis in

biopsy specimens, in-vitro electrophysiological properties of biopsy specimens

and electroanatomical mapping results. The main study endpoints are

inducibility of VA, type of induced VA, spontaneous VA and type of spontaneous

VA.

Secondary outcome

Secondary study parameters:

- CE-MRI

- 123-I MIBG/MIBI imaging

- Collagen turnover markers

- Electroanatomical mapping findings: low voltage, late potentials,

fragmentation and progressive conduction delay during extrastimuli

- Fibrosis (e.g. percentage of fibrotic cells and extracellular matrix) in

biopsy specimens

Secondary study endpoints:

- Heart failure

- Cardiac mortality

- All-cause mortality.

- Disease progression (as assessed by 123-I MIBG/MIBI-scans and MRI-scans).

Study description

Background summary

Sudden cardiac death, mainly caused by ventricular arrhythmias (VA), is a major cause of morbidity and mortality in non-ischemic cardiomyopathy (NICM). Therapies that effectively prevent VA are lacking. Improved understanding of the substrate and mechanisms of VA in NICM may allow more effective, individualized and substrate-based therapies to be developed. In addition, risk stratification in NICM needs to be improved so that therapies can be allocated more efficiently.

Study objective

1) To improve our understanding of the underlying pro-arrhythmic substrate and electrophysiologic mechanisms of VA in NICM, and to develop individualized treatment for VA based on the identified substrate. 2) To improve risk stratification for VA and sudden cardiac death in NICM based on substrate characteristics. 3) To evaluate disease progression in non-ischemic cardiomyopathy.

Study design

A prospective cohort study. All patients will be evaluated according to current standards for patients with NICM. Evaluation will include 24h-Holter, echocardiography, coronary angiogram and contrast-enhanced MRI (CE-MRI). Additionally, blood samples (arterial, cardiac venous and peripheral venous) for collagen turnover markers will be taken from all patients. 123-iodine metaiodobenzylguadinine (123-I MIBG) and methoxyisobutylisonitrile (MIBI) imaging, electrophysiologic study and endomyocardial biopsy will be performed in group A and B. Intra-operative biopsy will be performed in group B and C. An overview of all procedures and clinical indications is provided in appendix A.

Study burden and risks

The majority of patients in group A will not be exposed to additional risks. Only a minority of patients in group A and B will be exposed to minor additional risks associated with femoral artery access for blood sampling, electrophysiologic study and endomyocardial biopsy. All patients in group A and B will be exposed to radiation during 123-I MIBG/MIBI imaging. All patients in group B will be exposed to additional risks of intra-operative mapping, ablation and biopsy. Patients in group C will all be exposed to additional

risks of CE-MRI and intra-operative biopsy. Details on risks are provided in appendix B and an overview of risks is provided in appendix C. Nevertheless, risks involved in this study are outweighed by substantial benefit that this study may provide for these, and future patients, which is outlined below.

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

A) NICM patients with
- documented VA or
- suspected VA (e.g. because of out-of-hospital cardiac arrest, palpitations or syncope) or
- high risk for VA (LVEF * 35% and NYHA functional class II or III*) or
- intermediate risk for VA (LVEF * 50%* and late enhancement on CE-MRI)
who are not admitted for cardiac surgery;B) NICM patients with

- documented VA or
- suspected VA (e.g. because of out-of-hospital cardiac arrest, palpitations or syncope) or
- high risk for VA (LVEF * 35% and NYHA functional class II or III*)
who are admitted for cardiac surgery (e.g., mitral valve annuloplasty or CorCap)

C) Non-NICM patients (controls) who are admitted for
- Coronary artery bypass graft surgery and who do not have prior myocardial infarction.
- Aortic valve replacement.

Exclusion criteria

Exclusion criteria are as follows:;- Age < 18 years or > 80 years
- Inadequate patient competence
- Pregnancy
- Inability to comply with the protocol due to haemodynamic instability
- Non-NICM (e.g., prior myocardial infarction, infiltrative cardiac disease such as sarciodosis, amyloidosis or Chagas cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy/dysplasia, hypertrophic cardiomyopathy, non-compaction cardiomyopathy and congenital heart disease);Exclusion criteria for CE-MRI:
- According to the safety guidelines for MR-imaging. These can be found on Albinusnet: MRI / Veiligheidsrichtlijnen voor MR-imaging, http://albinusnet.lumc.nl/home/reg/pro/1010/60711030322284).;Exclusion criteria for blood sampling:
- Haemoglobin < 6.0 mmol/L

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	01-12-2011
Enrollment:	220
Type:	Actual

Ethics review

Approved WMO Date:	19-10-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	21-08-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28325
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL37472.058.11
OMON	NL-OMON28325