Electromechanical profiling of arrhythmogenic substrates and triggers in the long-QT syndrome

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To identify arrhythmogenic electromechanical risk profiles in LQTS patients; in baseline conditions and during provocation; the recognition of risk profiles will improve risk stratification for sudden cardiac death.

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

Summary

ID

NL-OMON54669

Source
ToetsingOnline

Brief title
EMLoQ study

Condition

- Cardiac arrhythmias
- Cardiac and vascular disorders congenital

Synonym
long-QT syndrome, Romano-Ward syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: NWO-ZonMw

Intervention

Keyword: Electromechanical mapping, Long-QT syndrome, Provocation, Ventricular tachyarrhythmias

Outcome measures

Primary outcome

Cardiac event risk prediction in LQTS patients using regional electromechanical dispersion.

Secondary outcome

Secondary study points consist of:

• difference in electromechanical dispersion (in ms) between symptomatic and asymptomatic genotyped LQTS patients and controls.

• comparison of electromechanical dispersion (in ms) between LQTS type 1, 2, and 3.

• relation between global electromechanical window vs regional electromechanical dispersion in LQTS.

• Comparison of mechanical dispersion using TPM-MRI and cine-MRI.

• Comparison of mechanical dispersion using TPM-MRI and speckle-tracking echocardiography.

Study description

Background summary

Sudden cardiac death (SCD) imposes a large socioeconomic and psychosocial burden, claiming almost a million deaths annually in Western societies. SCD is mostly caused by ventricular fibrillation (VF). In young patients, inherited arrhythmia syndromes including the long-QT syndrome (LQTS) account for 5-10% of victims. The LQTS is traditionally considered a primary electrical disease with

prolonged repolarization, and spatial and temporal repolarization heterogeneities. However, key publications claiming concomitant mechanical alterations in LQTS induced a paradigm shift: Therefore, some research-field leaders have now proposed LQTS as an electromechanical disease with mechano-electric triggers of arrhythmia.
For the purpose of this study protocol, we hypothesize that 1) Regional dispersion of repolarization and mechanical-strain patterns better depict the proarrhythmic substrate than global electrical parameters; 2) The extent of regional electromechanical heterogeneities and/or discordance of mechanical strain determine the site of abnormal electrical impulse formation prior to arrhythmia, whether or not through the emergence of local aftercontractions; 3) Electromechanical profiling in patients by smart provocation with catecholaminergic stimulation and pharmacological variation of atrioventricular (AV) relations will improve LQTS risk stratification.

Study objective

To identify arrhythmogenic electromechanical risk profiles in LQTS patients; in baseline conditions and during provocation; the recognition of risk profiles will improve risk stratification for sudden cardiac death.

Study design

Multicenter, case-control study

Intervention

Pharmacological (adenosine, epinephrine) provocation, ECG-imaging and tissue-phase mapping using magnetic resonance imaging (TPM-MRI).

Study burden and risks

LQTS patients:
Standard clinical workup: 12-lead ECG, lab tests, holter, echocardiogram and on indication contrast-enhanced MRI.
Study related: peripheral venous access, ECG-imaging, MRI (TPM-MRI) without contrast, pharmacological provocation.
A low dose CT scan will be performed in case of a contraindication for MRI is present.
The incidence of arrhythmias during smart provocation are expected to be small (<1%).

Control population:
Standard care: use of preexisting 12-lead ECG, Holter, echocardiogram and contrast-enhanced MRI.
Study related: peripheral venous access, lab tests, 12-lead ECG, Holter,

echocardiogram, ECG-imaging, MRI (TPM-MRI) without contrast, pharmacological provocation.

Using a one-stop-shop set-up, all clinical and study-related investigations will be performed sequentially within two days (no need for additional hospital visits).

Patient benefit resides in an improved risk prediction.

Outpatient visits for LQTS subjects include 12-lead ECG and Holter recording at 3, 12, and 24 months; control subjects will receive a phone call after 3 months.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

LQTS group (Group 1):
* Diagnosis of LQTS according to the ESC guidelines.
* Genetic testing either already performed or consent to genetic testing (at least 5 major LQTS-related genes tested: KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2).
Control group (Group 2):
* Control subjects with structurally normal hearts.

Exclusion criteria

* Pregnancy, nursing or planning to become pregnant.
* Known allergy or strong reaction to skin electrodes or contrast agent.
* Inability to give informed consent.
* Presence of metal objects in or attached to the body.
* Dialysis.
* Cardiomyopathy (LVEF < 50%).
* Second-degree heart block or higher degrees of block.
* Sick sinus syndrome.
* Asthma.
* Chronic obstructive pulmonary disease.
* Left-main coronary artery disease.
* Unstable coronary artery disease.
* Moderate to severe valvular disease.
* Inability to undergo MRI scan (control population).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-05-2021
Enrollment:	85
Type:	Actual

Ethics review

Approved WMO Date:	04-12-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-02-2022
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	NL70856.068.19
Other	NL70856.068.19