Noninvasive electrocardiographic imaging for individuals at risk for apparently idiopathic ventricular fibrillation

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Primary Objective: To noninvasively obtain arrhythmogenic substrate mapping using ECGI in patients with polymorphic VT and/or idiopathic VF.Secondary Objectives: - To detect similar arrhythmogenic substrates in index patients of family cohorts with…

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

Summary

ID

NL-OMON56447

Source
ToetsingOnline

Brief title
VIGILANCE

Condition

- Cardiac arrhythmias
- Congenital and hereditary disorders NEC

Synonym
Idiopathic ventricular fibrillation, unexplained sudden cardiac arrest

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: ECGI, Genetic, Idiopathic, Ventricular Fibrillation

Outcome measures

Primary outcome

The study parameters are reconstructions of epicardial potentials, and electrocardiographic quantitative and qualitative measures based on body-surface potential maps. From these, relevant endpoints can be determined, i.e. *normal/abnormal activation or recovery patterns* and *increased dispersion of repolarization*.

Secondary outcome

At inclusion:

- Baseline: age, gender, ethnicity, index event, circumstances index event, medical history, family history

- Clinical data: ECG, blood chemistry (Na+, K+, Ca2+, Mg2+, cardiac enzymes, thyroid function), toxicology (drugs, intoxications), echocardiography, exercise stress test, Holter, CAG/CT-angiography, MRI, provocation tests (sodium channel blocker, ergonovine, epinephrine), EP study.

- Genetics: DNA stored, method of genetic analysis, family screening.

- Other/ if performed: SA-ECG, nuclear imaging, cardiac biopsy.

- ECGI: BSP mapping and a cardiac + low dose thoracic CT-scan

- Parameters acquired by strain echocardiography

Data used for the registry at follow up, part of routine standard care (in the

first year every six months, yearly control after one year):

- Clinical data: ECG, exercise test, echocardiography, Holter

- If patient received an ICD: appropriate shocks, inappropriate shocks, other

ICD complications during follow up

- Outcome: specific underlying diagnosis revealed during follow-up, death,

cause of death

Study description

Background summary

In the Western world, 20% of all deaths in adulthood is sudden, mostly because of Sudden Cardiac Death (SCD) caused by VF. VF can be induced by polymorphic VT. In some cases of VF, after extensive diagnostic workup, no cause can be found. This is called idiopathic VF. Causes of polymorphic VT can also be obscure. Current clinical expertise to define which patients are at risk for (recurrence of) polymorphic VT or idiopathic VF is insufficient with available diagnostic techniques. This also applies to the general knowledge of arrhythmogenic mechanisms of VF. This is where a new modality has proven to be of great potential value: ECG-imaging (ECGI). ECGI combines electrical body-surface mapping with 256 electrodes placed on the thorax with a CT-scan obtaining the anatomy of the heart and torso, hereby able to reconstruct local electrograms, activation and recovery times. In recent research, ECGI provided numerous extra insights into normal cardiac electrophysiology, but also electrophysiological disorders and disease. The results strongly suggest that ECGI can play a pivotal role in further characterizing arrhythmia mechanisms, therefore could do so for polymorphic VT or idiopathic VF leading to diagnosis and treatment improvement. Moreover, ECGI seems to have the potential to detect arrhythmogenic substrate in individuals before their first event, offering the possibility to diagnose and treat patients before SCA occurs.

By definition, patients with idiopathic ventricular fibrillation do not have any structural or functional abnormalities as seen with cardiac imaging. A novel technique named echocardiographic strain imaging allows quantification of global and regional myocardial mechanics with a high temporal resolution. This technique has shown to be of added diagnostic and prognostic value in various cardiac diseases.9,10 Interestingly, this technique can unmask a mechanical

substrate in subjects who for example are at risk of developing arrhythmogenic cardiomyopathy in which electrical and structural criteria of the disease are completely absent.11,12 Application of this technique in patients with idiopathic ventricular fibrillation is not done before, but may unravel a (subtle) mechanical substrate that is not seen with conventional imaging modalities.

Study objective

Primary Objective: To noninvasively obtain arrhythmogenic substrate mapping using ECGI in patients with polymorphic VT and/or idiopathic VF.

Secondary Objectives:
- To detect similar arrhythmogenic substrates in index patients of family cohorts with a specific genetic mutation related to arrhythmogenesis, at high risk for polymorphic VT and/or idiopathic VF
- To evaluate the electrophysiology in this specific patient group and estimate their possible (increased) risk for polymorphic VT and/or idiopathic VF
- To translate the diagnostic potential of ECGI into an adapted flowchart for the *general* population of patients at risk for polymorphic VT and/or idiopathic VF; to apply ECGI in a diverse control group requiring CT as part of clinical care, as already approved in METC protocol ABR number 32128
- To compare (minimally invasive) electrophysiological (EP) study (in patients requiring this on medical indication, in Dutch: electrofysiologisch onderzoek: EFO), with ECGI.
- To noninvasively characterize the mechanical substrate of patients with unexplained polymorphic VT and VF, family members and control subjects using echo strain analysis.

Study design

Prospective (cohort) study

Study burden and risks

For the BSP procedure there is no substantial risk of physical or mental harm. The electrode system is passive and is electrically isolated from the recording components. Some skin irritation to the electrode attachment could occur in a small minority of patients. Application of the electrode strips is mildly uncomfortable, as the attached strips slightly reduce movement freedom and the patient is asked to move as little as possible. Furthermore, the patient*s torso is undressed during the whole procedure, but will be covered with blankets.

For the CT procedure , in which case an extended cardiac CT scan is performed, the radiation dose should be taken into consideration. Importantly, control

patients selected for the procedure would already receive a cardiac CT for medical reasons. The CT procedure for these patients is extended with a low-dose thoracic scan, to obtain the electrode positions. The radiation dose of the CT procedure consists of the cardiac CT (~5mSv) and the low-dose thoracic scan (~1mSv). We consider the radiation burden to be in balance with the major benefits that non-invasive reconstruction methods for electrical heart activity will bring to the patients. In comparison: the average yearly ionizing radiation background exposure is 2,6 mSv per person in the Netherlands. The optionel strain echocardiography does not contain any risk.

To perform the cardiac CT scan, an iodine-contrast agent is given intravenously. The patient could develop a mild allergic reaction to the contrast agent used during cardiac CT (incidence 1/20, only causing mild discomfort), with as very rare complication anaphylactic shock (incidence 1/3000-14.000) 15. Because the contrast is given intravenously, subjects could develop phlebitis at injection site.

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

In order to be eligible to participate in this study, a subject must be >= 18 years old and meet one of the following criteria:- All unexplained polymorphic VT or VF survivors in whom known structural myocardial, respiratory, metabolic and toxicological causes have been excluded through clinical evaluation*, with/without a genetic mutation.
NB. If results of a diagnostic tests show minor abnormalities but insufficient for a specific diagnosis, this is no exclusion criterion.
- Selected family members of these patients*
- Control subjects with structurally normal hearts with a clinical indication for a cardiac CT scan, as already approved in METC protocol NL32128.068.11 (ABR number 32128). *All 1st and 2nd degree family members being in contact with the cardiologist/treating physician as part of cascade screening will be contacted. Family members must be in adequate health to be able to travel to the hospital for research purposes. 3rd degree family members in contact with the cardiologist/treating physician can also be contacted if at least one of the following criteria is met:
• The family member has the same genetic mutation as index patient, or;
• The family member has demonstrated ventricular arrhythmias, or;
• The clinician has a very strong suspicion of ventricular arrhythmias in the family member.
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Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:- A known strong reaction against electrode attachment or contrast agent.
- Any serious medical condition, which in the opinion of the investigator, may adversely affect the safety and/or effectiveness of the participant or the study.
- Pregnancy, nursing or planning to be pregnant.
- Subject has an estimated glomerular filtration rate (eGFR) of <30mL/min/1.73m2, using the MDRD calculation.
- Unability to give informed consent.
- Family members of a patients with idiopathic unexplained polymorphic VT/VF , who have severe cardiac abnormalities and/or disease not related to the symptoms or phenotype of the index patients and which may have a negative influence on results of ECGI according to local investigators.

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Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-04-2019
Enrollment:	550
Type:	Actual

Ethics review

Approved WMO Date:	20-03-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-03-2020
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	NL67079.068.18