Better mechanistic understanding and risk stratification of ventricular arrhythmias through ECGI

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Main objectiveTo identify and describe the electrophysiological substrate and triggers in patients with (an increased risk of) VTAs using ECGI, in order to improve understanding of arrhythmic mechanisms and use these for arrhythmia risk...

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

Summary

ID

NL-OMON52499

Source
ToetsingOnline

Brief title
BREACH-ECGI

Condition

- Cardiac arrhythmias
- Cardiac and vascular disorders congenital

Synonym
sudden cardiac arrest, ventricular arrhythmogenesis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Combinatie collectebus/Hasselt

Intervention

Keyword: Arrhythmogenesis, ECGI, Mechanistic, Ventricular

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

As part of standard/routine care, if applicable:

o Baseline parameters: year of birth, ethnicity, gender, date and circumstances

index event

o Patient history: symptoms or medication preceding the ventricular

arrhythmias, family history

o Physical examination (blood pressure, saturation, body temperature)

o ECG parameters

o Blood chemistry

o Toxicological screening

o Echocardiography

o Exercise test/ Holter monitoring

o CAG/ CTA

o MRI

o Provocation tests

o Electrophysiological study

o Genetics

o Outcomes

o ICD parameters

o ICD and pacemaker therapy; appropriate, inappropriate and ICD complications

o Specific diseases that emerged during follow-up

o Extra diagnostic testing, if performed

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

cause of death

Study description

Background summary

Cardiovascular diseases are responsible for approximately 17 million deaths every year in the world, approximately 25% of which are sudden cardiac death (SCD). The annual incidence of out-of-hospital cardiac arrests (OHCAs) in Europe is 636,000 . Both are caused by ventricular tachyarrhythmias (VTAs), of which the incidence can be assumed to be significantly higher. Premature ventricular complexes (PVCs) can be the trigger to induce these VTAs and can be closely related to them. However, arrhythmogenic mechanisms of the PVCs and arrhythmia on a whole-heart level can be obscure.

The variety of patients that have or have a higher risk for VTAs and SCD is large, varying from patients with ischemic or non-ischemic cardiomyopathies, patients with non-structural heart disease, but also specific groups of patients with congenital heart disease are mentioned in literature to have a higher risk of VTAs and SCD. Moreover, even if the arrhythmogenic mechanisms precipitating to VTA are known for a specific patient, it remains a major challenge to predict the risk of recurrent episodes. This is clearly demonstrated by the fact that the implantation of an ICD is recommended for primary prevention of SCD (class I, level A) based on ejection fraction during rest, which is an inaccurate and hemodynamic parameter, unrelated to the electrophysiology of the patient.

For these reasons, an increased mechanistic understanding of VTAs and improved risk stratification for both VTAs and SCD are needed 8. Although still very important, the use of the 12-lead electrocardiogram is not sufficient, because of its low resolution, particularly regarding regional de- and repolarization characteristics. Catheter-based high-density electro-anatomical mapping during an electrophysiological study is of value, but time- consuming, costly and may lead to complications. This is where a new modality has proven to be of potential value: ECG-imaging (ECGI). ECGI combines electrical body-surface mapping with 256 electrodes placed on the thorax with a CT or MRI scan obtaining the anatomy of the heart and torso. By combining these techniques, a high-resolution three-dimensional epicardial electrophysiological map can be reconstructed using mathematical formulations, showing local electrograms and activation and recovery times. Within our team, Cluitmans et al. validated this method in-vivo in dogs, proving it gives a correct reconstruction of epicardial electrophysiology.

Other research groups also showed (epicardial) ECGI to be a non-invasive high-resolution alternative/addition that provides numerous extra insights into normal cardiac electrophysiology, but also electrophysiological disorders and disease, not (easily) detectable with current clinical techniques. ECGI highlighted the role of increased dispersion in several arrhythmogenic diseases. Furthermore, ECGI is able to show conduction block, areas of early repolarization, and steep electrical gradients, unidirectional conduction block, focal ectopy, and excitation in relation to a history of reentrant tachyarrhythmias. Several studies have highlighted to role of ECGI in detecting arrhythmogenic substrate that could not be detected with routine clinical tools. The results strongly suggest that ECGI can play a pivotal role in further characterizing arrhythmia mechanisms, and therefore could do so for ventricular arrhythmia diagnosis and treatment improvement. Moreover, this novel tool seems to have the potential to detect arrhythmogenic substrate in individuals at risk for (recurrent) VTAs, allowing preventive measures and possibly reducing morbidity and cardiac death. Lastly, better mechanistic understanding of VTAs through ECGI could aid in diagnosis and treatment, by i.e. guiding ablations.

Study objective

Main objective
To identify and describe the electrophysiological substrate and triggers in patients with (an increased risk of) VTAs using ECGI, in order to improve understanding of arrhythmic mechanisms and use these for arrhythmia risk stratification and management.

Secondary objectives
- To identify and describe the cardiac electropathology using ECGI in control subjects.
- To integrate information obtained by ECGI with other imaging modalities of

the heart, (for example CT, CMR, electro-anatomical mapping) for improved understanding of disease pathology. By combining the results, a more personal approach can be made in the future, which can potentially lead to better risk stratification and better guidance for treatment options.
- To identify and describe the cardiac electrophysiology using ECGI in patients who require an electrophysiological study (EP), to obtain knowledge about the comparison between endo- and epicardial activation and repolarization, learn about transmurality of the electrophysiological substrate, and potentially develop integrative modalities which in the future may guide such procedures.

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.

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, have a either a history or a risk of VTAs and have one of the following diagnoses:

- Ischemic cardiomyopathy
- Non-ischemic cardiomyopathy
- Non-structural heart disease
- Congenital heart disease (with a limitation to CCTGA and situs inversus)

Or: a subject must be >= 18 years old and have a structurally normal heart.

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.
• 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.
• In case of a CT scan: the subject has an estimated glomerular filtration rate (eGFR) of <30mL/min/1.73m2, using the MDRD calculation 14.
• In case of a CT scan: A known strong reaction against contrast agent.
• In case of an MRI scan: the subject is unsuitable to get an MRI scan (such as described in ODIN protocols *Voorbereiding klinische patiënten voor MRI onderzoek* and *Uitvoering van MRI onderzoek bij patiënten met een cardiaal implanteerbare elektronisch device, waaronder een pacemaker en ICD*):
o Non-MRI-compatible metallic implants (vascular clip, neuro-stimulator, cochlear implant etc.).
o Non-MRI-compatible pacemaker or implantable cardiac defibrillator (ICD).
o Claustrophobia.
• Being unable to give informed consent.

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):	10-06-2020
Enrollment:	270

Type:	Actual

Ethics review

Approved WMO Date:	12-02-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-05-2021
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	NL69831.068.19