Post*extrasystolic Potentiation as a Predictor of Ventricular Arrhythmias

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

Summary

ID

NL-OMON48836

Source
ToetsingOnline

Brief title
A PRIORY Study

Condition

- Cardiac arrhythmias

Synonym
Post-extrasystolic Potentiation; an temporarily increase in blood pressure after an extrasystolic beat

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Chronic Heart Failure, Implantable Cardioverter Defibrillator, Post-extrasystolic Potentiation, Sudden Cardiac Death

Outcome measures

Primary outcome

- Evoked PESP-BP (i.e. blood pressure differences between baseline, ESB and

post-ESB)

- Spontaneous PESP-BP (i.e. blood pressure differences between baseline, ESB

and post-ESB)

- Timing parameters (in ms): the basic cycle length interval; Extra-systolic

interval (ESI); Post-extrasystolic interval (PESI).

Secondary outcome

not applicable

Study description

Background summary

Patients at increased risk for sudden cardiac death (SCD) caused by lethal ventricular arrhythmias, may receive an implantable cardioverter defibrillator (ICD). The primary criterion for ICD implantation is a left ventricular ejection fraction (LVEF) *35%. Studies indicate that only 11-30% of ICD carriers receive appropriate device therapy (ADT). Therefore, patient selection for primary prevention ICD implantation needs refinement. Identification of new parameters associated with SCD might lead to improved selection of patients. Post-extrasystolic potentiation (PESP) may be a new risk marker for SCD. PESP is defined as a temporary increase in contractility that follows an extrasystolic beat (ESB) and is associated with myocardial calcium handling. In heart failure, changes in calcium homeostasis may lead to afterdepolarisations and thus predispose for SCD. PESP can be measured indirectly and non-invasively as post-extrasystolic blood pressure potentiation (PESP-BP). Abnormal PESP-BP, using spontaneous ESB, was found to be an independent predictor of increased mortality in post-myocardial infarction patients with a reduced LVEF. However,

it is unknown if this increased mortality in heart failure patients with abnormal PESP-BP is caused by SCD.
When using spontaneous ESB for assessment of PESP-BP, however, coupling intervals between the ESB and both previous and subsequent beats are not controlled and may vary substantially. These coupling intervals, as well as the basic cycle length, are known to influence changes in contractility significantly.
ICD patients offer the unique possibility to evoke atrial and ventricular ESB in a reproducible manner. Basic cycle length and coupling intervals can be controlled by cardiac stimulation using the ICD leads. Systolic BP change after an ESB can reliably be assessed with a non-invasive continuous finger arterial BP photoplethysmographic device. Using this reproducible assessment of PESP-BP, different stimulation protocols can be evaluated and compared with PESP-BP of spontaneous occurring ESB. This pilot study sets out to assess stimulation-evoked PESP-BP using various stimulation protocols and to compare outcomes with PESP-BP by spontaneous ESB. Moreover, we aim to derive a stimulation protocol for PESP-BP assessment, which can be used in a larger cohort of ICD patients to test PESP-BP as a new predictor for the occurrence of ventricular arrhythmias. Please refer to chapter 1 of the protocol (introduction and rationale)

Study objective

This pilot study sets out to assess stimulation-evoked PESP-BP using various stimulation protocols and to compare outcomes with PESP-BP by spontaneous ESB. Moreover, we aim to derive a stimulation protocol for PESP-BP assessment, which can be used in a larger cohort of ICD patients to test PESP-BP as a new predictor for the occurrence of ventricular arrhythmias.

Study design

This pilot study has a stratified design.
Patients: 30 patients who are scheduled for ICD replacement/reposition or pacemaker implantation/replacement/reposition will be included in this study; (1) 10 ICD patients with LVEF < 35% who previously received ADT; (2) 10 ICD patients with LVEF < 35% who are free from ADT and (3) 10 dual-chamber pacemaker patients with normal LVEF (control group).
Intervention: During scheduled device implantation/replacement, ESB with various extrasystolic and post-extrasystolic coupling intervals will be evoked by electrical stimulation via the right atrial and ventricular device leads of the patient. Throughout the stimulation study, blood pressure response will be measured continuously and non-invasively, and a continuous electrocardiogram will be recorded. Either before or after the procedure, patients will undergo a 30-minutes assessment of spontaneous ESB, again with blood pressure and ECG recordings.
Comparator: 10 dual-chamber pacemaker patients without heart failure (control

group).
Outcome: Evoked PESP-BP (blood pressure differences between baseline, ESB and post-ESB)
Time schedule: 15 minutes evoked PESP-BP assessment; 30 minutes spontaneous ESB assessment; no follow-up necessary.

Intervention

In this study, the intervention is the small EPS as previously described.

Study burden and risks

Subjects do not have a direct benefit from the study, as participation will not change treatment or prognosis. The study will cause no harm to the subjects* health. However, measurements will add a maximum of 15 minutes to the length of the procedure.

A provoked atrial or ventricular ESB might have a pro-arrhythmic effect. However, the chance that an ESB will provoke a ventricular arrhythmia very small. Recently, we performed comprehensive electrophysiological tests for the assessment of the excitability of VT/VF in 64 primary prevention ICD patients within the No RisC Study (METc studynumber NL19680.029.08) . This stimulation protocol consisted of a maximum 3 consecutive extrastimuli with different and very short cycle lengths provoked in the right ventricular apex. During these stimulation tests, 36 patients did not develop VT or VF, in 10 patients VT/VF occurred after 2 consecutive extrastimuli and in 18 patients VT/VF occurred after 3 consecutive extrastimuli. Furthermore, all VTs occurred after an ESI below 300 msec. None of the patients developed VA based on one extrastimulus [17]. Since the stimulation protocol of the A PRIORY STUDY will only provoke one extra stimulus per cycle, with an ESI *300 msec, the chance of a developed VA is very small. Furthermore, the study will be performed at the cardiac catheterization laboratory, with a highly trained professionals and a crash car directly available.

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 participate in this study, a subject must meet the following criteria:
- Implanted with a dual-chamber device;
- For patients with an ICD: LVEF *35%, measured both recently (< 12 months prior to inclusion) and prior to the original device implantation.
- For patients with a pacemaker: a LVEF > 50%, measured recently (<12 months prior to inclusion)
- An ICD device follow-up of at least one year must be available;
- An pacemaker can be a new implantation, replacement or reposition
- Optimal (stable) medical therapy;
- Sinus rhythm.

Exclusion criteria

Age <18 or incapacitated adult; Unknown left ventricular function prior to device implantation; Patients unwilling to participate; Documented chronic atrial fibrillation; Second or third degree AV-conduction disorders; Patients with a cardiac resynchronization therapy (CRT-D) or one-chamber device; Hypertrophic cardiomyopathy (CMP); Conditions with insufficient blood flow to the fingers, e.g. M. Raynaud or conditions with extreme vasoconstriction.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-11-2018
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	ICD lead or pacemaker lead
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	27-07-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-06-2019
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	NL62775.029.18