The pathophysiology of ventricular arrhythmia: does inflammation increase the risk of ventricular arrhythmia through hyperthermia and/or inflammatory cytokines?

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

Summary

ID

NL-OMON32785

Source
ToetsingOnline

Brief title
The role of inflammation in the pathophysiology of ventricular arrhythmia

Condition

- Cardiac arrhythmias

Synonym
ventricular arrhythmia, ventricular fibrillation

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Arrhythmia, Cytokines, Hyperthermia, Inflammation

Outcome measures

Primary outcome

Proportion of VT/VF and/or ICD discharge episodes that occur during hyperthermia (body temperature >37.5°), and serum levels of interleukin-6, interleukin-8 and CRP during each episode of VT/VF and/or ICD discharge.

Secondary outcome

1. Proportion of patients with ECG changes during hyperthermia or when serum levels of interleukin-6, interleukin-8 and/or CRP are increased.

2. Changes in body temperature and serum levels of interleukin-6, interleukin-8 and CRP that occurs during each episode of VT/VF and/or ICD discharge.

3. Clinical variables (e.g., ischemia, heart failure, electrolyte imbalance, drug use) and cytokine gene variables that may determine the occurrence of VT/VF during inflammation.

Study description

Background summary

Sudden cardiac death (SCD) resulting from ventricular tachycardia/fibrillation (VT/VF) still has a high incidence, because its pathophysiologic basis is not fully resolved. While the substrate of VT/VF is based on reentrant excitation due to inherited or acquired ion channel dysfunction and structural abnormalities, its precipitating factors (triggers) are less clear. The

presence and severity of such factors may explain why some patients with acute myocardial infarction or inherited arrhythmia syndromes develop VT/VF, while other patients with the same disorder do not. We recently reported that fever may provoke ECG changes and VT/VF in patients with inherited arrhythmia syndromes, i.e., diseases linked to mutant ion channels. Experimental studies have indicated that these effects are consistent with the effects of hyperthermia on disrupted ion channels, i.e., ion channels whose function is modified by a mutation. However, while hyperthermia is linked to clinical and cellular cardiac electrophysiological changes, it is conceivable that the inflammatory cytokines, which underlie fever, also modulate cardiac electrophysiology. Accordingly, although systematic studies are lacking, anecdotal clinical reports indicate that fever may also be associated with increased VT/VF risk in common acquired cardiac disease (e.g., myocardial infarction, heart failure, and drug use). In this study, we aim to explore the association between inflammation , in particular hyperthermia and inflammatory cytokines, and the occurence of VT/VF.

Study objective

The primary objective is to establish whether patients are at increased risk for VT/VF during inflammation. The secondary objective is to establish whether increased risk during inflammation is mediated by hyperthermia and inflammatory cytokines. The third objective is to study whether cytokine gene variants that are associated with higher serum cytokine levels have an increased prevalence among patients with VT/VF.

Study design

We will conduct an observational study in which we collect data for at least 4 years of all patients with ICD to analyze whether ventricular arrhythmia is associated with inflammation. Most of the patients with ICD have common acquired cardiac disease, notably heart failure secondary to ischemic or non-ischemic cardiomyopathy.

Study burden and risks

Burden in group 1: blood samples are taken twice prior to and thrice after the ICD emplacement (every 2 hours 4 tubes of 4.5 ml; total of 5 x 20 = 100 ml blood). For this, a peripheral venous infusion line is used, which has been routinely placed for the sake of the ICD emplacement procedure. Thus, no extra burden of venipuncture is caused in this group of patients.
Burden in group 2: blood samples are taken twice (at presentation and at next routinely scheduled outpatient clinic visit; each time 20 ml). . Blood samples are taken through venipuncture. A questionnaire is filled in, which requires approximately 10 minutes.
Risk: no risks due to the study methods are expected.

Benefit: ICD-related infections might be diagnosed earlier due to frequent ECGs and body temperature measurements after ICD emplacement.

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

Adult patients, who are eligible for the emplacement of an implantable cardioverter defibrillator (ICD) according to current guidelines (group 1); and adult patient with an ICD, who present after an episode of VT/VF and/or ICD discharge (group 2).

Exclusion criteria

Patients using anti-pyretic or anti-inflammatory drugs.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2008
Enrollment:	200
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL25417.018.08