Follow-up of patients with idiopathic ventricular fibrillation, the FU-IVF study.

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To phenotype and genotype the population of patients with IVF in our cohort, and to find alternative diagnoses as a cause of the event of VF.

Ethical review	Not approved
Status	Will not start
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON40680

Source
ToetsingOnline

Brief title
FU-IVF study

Condition

- Cardiac arrhythmias
- Cardiac and vascular disorders congenital

Synonym
life-threatening heart rythm disorder, ventricular fibrillation

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Follow-up, Idiopathic ventricular fibrillation

Outcome measures

Primary outcome

Alternative diagnoses discovered during follow-up in patients with IVF.

Secondary outcome

• Description of the population of our cohort (Prognosis, recurrence of arrhythmias, therapy, (in)appropriate shocks, presence of cardiac anomalies not sufficient for an alternative diagnosis)

• The detection of prognostic factors for IVF (family history, use of medication, gender, ECG features etc).

• Discovering new susceptibility genes for idiopathic VF

In patients who have no structural or electrical heart disease nor a known gene mutation responsible for ventricular fibrillation, we will pursue a *hypothesis-driven* approach and search for mutations in genes that are predicted to be of importance in IVF, based on existing gene networks and existing literature. When no susceptibility genes are discovered, sequencing will be extended to whole exome sequencing.

• Quality of life measurements of IVF patients, compared to the healthy population.

Study description

Background summary

Our cohort contains 95 patients diagnosed with idiopathic ventricular fibrillation, who experienced an OHCA because of VF between 1985 and present day and who were admitted to the University Medical Centre Utrecht. In order to confirm which patients have developed a structural heart disease and have had ventricular fibrillation as first symptom of an underlying heart disease, the missing investigations must be performed. This is all regular diagnostic work-up which is indicated by the consensus on the standardisation of clinical evaluation of IVF.

Our hypothesis is that idiopathic ventricular fibrillation is a non-existing diagnosis and that in every patient there is an underlying etiology either substrate that may give rise to VF. In order to detect this etiology, the first step is to define and phenotype the population in further detail, as documented in current consensus statements.
In a further stage of the study, all patients with idiopathic ventricular fibrillation will undergo further genetic testing, either targeted gene sequencing or whole exome sequencing in order to find novel genes that can give rise to arrhythmias such as VF. This may be of great clinical importance, as it has been for example in the case of finding the autosomal dominant DPP6 risk haplotype (which confers a greatly increased risk of sudden cardiac death between the ages of 20 and 60 years), that justifies life-saving primary prevention with an ICD.10 This finding has been of utmost importance, as genetic testing has proven to be the only way to identify the individuals at risk for sudden cardiac death in these families, as no way of functional cardiac testing can identify the individuals with the allele predisposing to sudden cardiac death at a young age.

Our cohort is the largest in the world and presently, no study with such a large group of IVF-patients has been published.

Study objective

To phenotype and genotype the population of patients with IVF in our cohort, and to find alternative diagnoses as a cause of the event of VF.

Study design

A retrospective cross-sectional study.

Study burden and risks

All patients have had diagnostic work-up after the event of VF and almost all patients received an ICD. These patients attend yearly or half yearly routine control, however a number of patients have missing data in their follow-up. To complete the work- and follow-up, extra procedures must be performed, such as echocardiography, or genetic testing. These procedures are all part of the

current regular diagnostic work-up, except for advanced genetic testing in the form of whole exome sequencing (WES) in a selected group of patients. In some patients not all procedures of the regular work-up have been performed and the event of IVF occurred many years ago. Nowadays, the insights on diagnostic work-up after an OHCA based on VF have been renewed and the protocol has been adjusted, therefore alternative diagnoses can be missed. In order to detect these alternative diagnoses, the missing procedures must be performed. Per patient, an analysis is made of which procedures are missing and which procedures are necessary. Procedures that could be additionally performed are: echocardiography, MRI/CT, ajmaline test, ergonovine test, adrenalin test, holter, coronary angiography, exercise-ECG and genetic testing. The risks and burden associated with participation are low, since all procedures are part of the regular work-up. The risks depend on what procedures need to be performed. The possible benefits are: Detection of a cause for the VF, improvement of treatment and, in a case of a pathogenic genetic mutation either a familial disease, the possibility of prophylactic treatment of affected family members. Per patient, the results will be carefully evaluated and per missing procedure will be determined if it is necessary and useful to perform the procedure.
In patients without any detectable cause for the VF, WES will be performed as an extension of the regular genetic testing, to take the first step in discovering new -genetic- etiologies and mechanisms of IVF.

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

All documented patients who had an OHCA, who were successfully resuscitated and had ventricular fibrillation as initial rhythm and were finally diagnosed as idiopathic VF.

Exclusion criteria

N/A

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	95
Type:	Anticipated

Ethics review

Not approved

Date:	30-04-2014
Application type:	First submission

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL47917.041.14