Comparative Effectiveness Research to Assess the Use of Primary ProphylacTic Implantable Cardioverter Defibrillators in Europe

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-To characterise total mortality risk in a prospective patient cohort of ICD candidates newly implanted for primary prophylaxis of malignant ventricular arrhythmias, compared to a non-randomised control group not implanted for primary prophylaxis.-...

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

Summary

ID

NL-OMON41346

Source
ToetsingOnline

Brief title
EU-CERT-ICD study

Condition

- Cardiac arrhythmias

Synonym
Sudden cardiac death; primary prophylactic ICD-therapy

Research involving
Human

Sponsors and support

Primary sponsor: University Medical Center Göttingen

Source(s) of monetary or material Support: Europese Unie Seventh Framework Programme

Intervention

Keyword: electrocardiography, implantable cardioverter-defibrillator, quality of life, sudden cardiac death

Outcome measures

Primary outcome

Primary study endpoint is all-cause mortality. Co-primary endpoint is the time

to first appropriate shock as defined as an ICD high voltage therapy delivered

appropriately for malignant ventricular arrhythmia (per judgement of the

investigator and the endpoint committee).

Secondary outcome

-ICD Electrical Shock Endpoints (including Inappropriate ICD Shock)

-Mortality Endpoints (SCD, Cardiac Death and Non-Cardiac Death)

-other Clinical Endpoints: Arrhythmogenic Syncope, Resuscitation, Any ICD

Shock, Atrial Fibrillation

-Quality of Life

-Device Revision/Replacement

-Costs and Cost-effectiveness

Study description

Background summary

An estimated 500.000 sudden cardiac deaths (SCD) occur in the European Union (EU) annually. Most SCDs are caused by malignant ventricular arrhythmias, which are life threatening especially for patients with cardiovascular diseases.
Patients who have survived a severe arrhythmic cardiac event unequivocally

receive treatment with an ICD today (so-called secondary prevention). Other patients may not yet have had a life-threatening event but have an increased risk of future malignant ventricular arrhythmias due to markedly reduced left ventricular (LV) function. According to two clinical trials, both published about 10 years ago, patients with an increased risk of malignant ventricular arrhythmias had a 31% and 23% survival benefit, respectively, if prophylactically implanted with an ICD (so-called primary prevention). Based on these two trials, implantation of an ICD device for primary prevention has become an integral part of international guidelines and is widely used in clinical routine. Today, an estimated > 100.000 ICDs are implanted in the EU annually with device costs alone exceeding ¤2 billion. Implantation rates, however, vary significantly between EU regions, reflecting considerable socio-economic and health-care inequality across the EU. In addition, experts disagree increasingly regarding the validity of the decade-old trial results as the basis for current medical practice. The reasons of this dissent are manifold:

(1) Randomised trials have shown no survival benefit from primary ICD prophylaxis.
(2) ICD candidates today exhibit lower rates of malignant arrhythmias and have better outcome without an ICD than the patients included in the seminal trials 10 years ago, most probably due to improvements in pharmacological and other non-ICD therapy.
(3) Less than one third of patients with a prophylactically implanted ICD device ever receive an appropriate shock from their device. The risk of death due to non-arrhythmic cause may presently outweigh the risk of death due to arrhythmia in these patients.
(4) Not every appropriate shock prevents SCD. Presumably less than 50% of appropriate shocks are truly life-saving.
(5) ICDs themselves may increase mortality by yet unidentified effects.
(6) Harm and side-effects of ICD treatment may have been underestimated in women.

To increase the effectiveness of prophylactic ICD implantation, expert consensus demands more accurate strategies for the selection of candidate patients. Randomised prospective trials on ICD therapy are not an option for ethical reasons. As implantation rates depend on medical decisions as well as on a country*s economic background, cost-effectiveness of ICD therapy has been assessed in Markov models, however, these models are subject to variability from the input parameters.

Study objective

-To characterise total mortality risk in a prospective patient cohort of ICD candidates newly implanted for primary prophylaxis of malignant ventricular arrhythmias, compared to a non-randomised control group not implanted for primary prophylaxis.

-To determine prespecified clinical baseline characteristics (confounding variables) contributing to the risk of the primary endpoints
-To assess simple and cost-effective electrocardiographic noninvasive risk stratification techniques
-To define subgroups within the cohort with a lower or higher benefit from ICD treatment
-To perform blood-sampling from each patient for analyses of biomarkers and genetic-information
-To provide outcome data as a basis for extensive health economic evaluation of ICD use including subgroups and country-specific differences

Study design

This prospective study is open, observational, non-invasive, non-interventional, outpatient, non-randomised, multi-centre, multi-national and includes one blood sampling per patient for later genetic testing. No therapeutic intervention is performed. No medicinal products, medical devices or drug substances are tested.
The study includes patients who are eligible for primary prophylactic ICD device implantation, whether they receive an ICD device or not. Patients who do receive an ICD device will be followed as part of the ICD Group, while patients who do not receive an ICD device will be followed as part of the Control Group.

Study burden and risks

Study participation includes a few additional diagnostic tests, which are part of standard diagnostics in other patients with heart diseases and bear no health risk. Blood sampling from one of your veins bears the risk of developing a haematoma (bruise). The bruise can hurt for a few days but does not require treatment, except in very rare cases. A theoretical residual risk remains of vessel- and nerve damage or infection through the transmission of germs, although this risk does not play a role in practical everyday life.

Contacts

Public
University Medical Center Göttingen

Robert-Koch-Str 40
Göttingen 37075
DE
Scientific
University Medical Center Göttingen

Robert-Koch-Str 40
Göttingen 37075
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Ischaemic or non-ischaemic (dilated) cardiomyopathy and recommendation for primary prophylactic ICD treatment following current international treatment guidelines
-Age * 18 years
-Written informed consent
-If ICD implantation is planned, enrolment and study baseline testing needs to be completed before de-novo ICD implantation

Exclusion criteria

-Persistent or permanent atrial fibrillation in the baseline ECG recordings in no more than 15% of such patients at a given time have been enrolled, thus atrial fibrillation is an exclusion criteria only if this percentage has been surpassed in the overall enrolled patient population
-Indication for other than above mentioned primary prophylactic ICD treatment
-Indication for secondary prophylactic ICD treatment
-Indication or candidate for cardiac resynchronisation therapy, i.e.: (1) QRS duration of *135 ms, left bundle branch block QRS morphology, and an LVEF *35% or (2) QRS duration *150 ms, irrespective of QRS morphology, and an EF *35%
-QRS duration of 120-130 msec, left bundle branch block QRS morphology, and an EF *35%, if the investigator deems cardiac reysnchronisation therapy indicated
-AV block II°-III° at resting heart rates
-Implanted pacemaker
-Unstable cardiac disease such as decompensated heart failure (NYHA functional class IV) or acute coronary syndrome

-Participation in other clinical trials which exclude enrolment in other trials

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-06-2015
Enrollment:	88
Type:	Actual

Ethics review

Approved WMO Date:	09-07-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	31-08-2017
Application type:	Amendment
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	NL47300.041.14