Cardiac sympathetic nervous system function and activity as a predictor for appropriate ICD therapy in patients with chronic heart failure

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The aim of this study is to identify CHF patients who are most likely to benefit from ICD therapy by the use of clinical patient characteristics related to CHF combined with a measure of myocardial sympathetic integrity/activity. This will enable to...

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

Summary

ID

NL-OMON33730

Source
ToetsingOnline

Brief title
123I-MIBG predicts appropriate ICD therapy in chronic heart failure

Condition

- Cardiac arrhythmias

Synonym
heart failure and fatal arrhytmias, sudden cardiac death

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,GE Healthcare

Intervention

Keyword: 123I-MIBG, cardiology, heart failure, sympathetic innervation

Outcome measures

Primary outcome

The primary endpoint of the trial will be appropriate ICD discharge or

anti-tachycardia pacing.

Secondary outcome

not applicable

Study description

Background summary

Motivation
Adequate risk stratification tools to identify patients with chronic heart failure who are most likely to benefit from implantable cardioverter defibrillators (ICD) are lacking.

Background
Chronic heart failure (CHF) is a complex clinical syndrome characterized by abnormal function of the ventricles and activation of neurohormonal compensation mechanisms which is accompanied by effort intolerance, fluid retention and reduced longevity. Especially activation of the sympathetic cardiac activity is detrimental in CHF.
In Europe, the prevalence of CHF is estimated as about 1% (approximately 4 million patients in Western Europe), while in the United States, the number of CHF patients is approximately 5 million.1-4 About $30 billion in costs, a million hospitalizations and 55,000 deaths are directly attributed to CHF in the United States of America (USA) annually. CHF is the only category of cardiovascular diseases for which the prevalence, incidence, hospitalization rate, mortality, and total burden of costs have increased in the past 25 years. This is related to the increasing number of elderly patients with an impaired left ventricular function. The incidence of CHF is approximately 1% of the population and increases to 8% after the age 65. Due to the aging of the population and the improved survival after acute myocardial infarction, it is

likely that the incidence of CHF and its impact on public health will continue to increase.
Although pharmacological therapies for CHF have been successful in reducing morbidity and mortality, sudden cardiac death (SCD) remains a leading cause of death among these patients. Especially patients with severely reduced left ventricular ejection fraction (LVEF) (<30-35%) are at risk. Implantable cardioverter-defibrillators (ICD) as a primary or secondary prevention reduce the relative risk for death by 20%. A rapid increase in the use of ICD therapy as primary treatment for this condition has been demonstrated. This results in an increasing burden on healthcare budgets in the USA and Europe. The MADIT II study, however, showed that the actual reduction of fatal events was 5.6 percentage points (from 19.8 to 14.2). In addition, the SCD-HeFT trial showed that the annual rate of ICD shock was 7.1% and of appropriate shock for rapid ventricular tachycardia or ventricular fibrillation was 5.1%, with a total of 21% patients receiving appropriate shocks over 5 years. Since the majority of patients in these studies remains without life-threatening arrhythmias, it is of the utmost importance to find risk stratification tools to identify patients most likely to benefit from ICD leading to higher cost-effectiveness.

Increased cardiac sympathetic activity, which is often present in patients with chronic heart failure, may play a role in the development of ventricular arrhythmias. High sympathetic activity has been demonstrated in CHF patients with ventricular arrhythmias. On the other hand, beta-adrenoceptorantagonists have shown to reduce the incidence of ventricular arrhythmias in CHF patients. Therefore, cardiac sympathetic nervous function and activity may serve as parameters that can be used to identify CHF patients who are at risk for life-threatening arrhythmias. Some small clinical studies have shown that cardiac sympathetic activity as assessed by the use of 123I-metaiodobenzylguanidine (123I-MIBG) scintigraphy is related to sudden cardiac death and appropriate ICD discharge.

Study objective

The aim of this study is to identify CHF patients who are most likely to benefit from ICD therapy by the use of clinical patient characteristics related to CHF combined with a measure of myocardial sympathetic integrity/activity. This will enable to discriminate responders from non-responders to ICD therapy in heart failure.

Study design

This is a non-randomized, dual centre, observational prospective study. Patients eligible for an ICD (both single-, dual chamber and biventricular ICDs are allowed to enter the study) according to the latest guidelines will be included. After implantation patients will be followed every six months for at least 2 years. Data from the ICD memory log will be regularly downloaded at

these visits. Inclusion of patients will be performed in the first 12 months after start of the study.

Study burden and risks

- The radiation burden is well within the international limits for participants as formulated by the ICRP (2.5 mSv).
- There are no known side-effects of MIBG in the concentration administered to the participants.

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

*Left ventricular dysfunction (LVEF *35%) due to prior MI (at least 40 days post MI)
*Left ventricular dysfunction (LVEF *35%) due to non-ischemic heart disease
*NYHA functional class II and III
*Receiving chronic optimal medical therapy
*Reasonable expectation of survival with a good functional status of more than 1 year

Exclusion criteria

*pregnancy
*Left ventricular ejection fraction >35%
*NYHA functional class I and IV
*Not receiving chronic optimal medical therapy
*Expected survival less than 1 year

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2010
Enrollment:	300
Type:	Actual

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	NL26293.018.08