# Cardiac sympathetic nervous system function and activity as a predictor for appropriate implantable cardioverter defibrillator (ICD) therapy in patients with chronic heart failure.

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruiting |
| **Health condition type** | - |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON21166

**Source**
Nationaal Trial Register

**Brief title**
SYMPATHETIC

**Health condition**

chronic heart failure, sympathetic cardiac activity, 123I-MIBG

### Sponsors and support

**Primary sponsor:** Academic Medical Center, University of Amsterdam, the Netherlands
**Source(s) of monetary or material Support:** GE Healthcare will kindly provide 123I-MIBG for the total number of included patients.

### Intervention

## Outcome measures

### Primary outcome

Increased cardiac sympathetic activity and decreased sympathetic neuronal function as assessed by cardiac 123I-MIBG scintigraphy is associated with increased ICD discharge and anti-tachycardia pacing in patients with CHF and can therefore be used to identify patients who will most likely benefit from ICD implantation.

### Secondary outcome

N/A

# Study description

### Background summary

Background:

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, 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.

Objective of the study:

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 objective**

Increased cardiac sympathetic activity is highly prevalent among patienst with chronic heart failure. The increased cardiac sympathetic activity as assessed with 123I-metaiodobenzylguanidine (MIBG) is a usefull tool to discriminate responders (i.e. appropriate ICD discharge) from non-responders (i.e. appropriate ICD discharge).

**Study design**

The primary endpoint of the trial will be appropriate ICD discharge or anti-tachycardia pacing. 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 three months for at least 2 years.
The data collected at the investigational sites will be presented to a Clinical Endpoint Adjudication Committee (CEAC) for review. The CEAC, composed of three cardiologists who are experienced in the assessment of Heart Failure (HF) patients, will review subject clinical data for the 24 months following the 123I-MIBG examination but are blinded to the 123I-MIBG imaging results. The remit of the CEAC is to determine if an appropriate ICD discharge or anti-tachycardia pacing has occurred. Furthermore the remit of the CEAC is to determine if a major cardiac event (MACE) has occurred. A MACE is defined as either: Cardiac death due to all causes, including myocardial infarction (MI), progressive heart failure, and SCD; Cardiac transplantation; resuscitated cardiac arrest. If the supporting data provided are insufficient to confirm occurrence of an event as reported by the investigator, the CEAC will classify the subject in the “no event” category.

**Intervention**

This is a prospective observational multicenter study.
Multivariate Cox proportional hazard regression analysis will be used to identify and evaluate risk factors associated with first occurrence of appropriate ICD discharge and those risk factors associated with no ICD discharge. Freedom from arrhythmia (i.e. no ICD discharge) will be evaluated by Kaplan-Meier analysis.

# Contacts

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# Eligibility criteria

## Inclusion criteria

1. Left ventricular dysfunction (LVEF ≤35%) due to prior MI;

2. Left ventricular dysfunction (LVEF ≤35%) due to non-ischemic heart disease;

3. NYHA functional class II and III;

4. Receiving chronic optimal medical therapy;

5. Reasonable expectation of survival with a good functional status of more than 1 year.

## Exclusion criteria

1. NYHA functional class IV at enrollment;

2. Coronary revascularization within the preceding three months;

3. Myocardial infarction within 40 days prior to enrollment, as evidenced by measurement of cardiac-enzyme levels;

4. Advanced cerebrovascular disease;

5. Childbearing age and not using medically prescribed contraceptive measures;

6. Any condition other than cardiac disease that is associated with a high likelihood of death during the trial;

7. Unwilling to sign the consent form for participation.

# Study design

## Design

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|---|---|
| Study type: | Observational non invasive |
| Intervention model: | Parallel |
| Allocation: | Non controlled trial |

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|---|---|
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 01-10-2010 |
| Enrollment: | 300 |
| Type: | Anticipated |

## Ethics review

Positive opinion

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|---|---|
| Date: | 04-02-2011 |
| Application type: | First submission |

## 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 |
|---|---|
| NTR-new | NL2607 |
| NTR-old | NTR2735 |
| Other | MEC AMC : MEC 08/367 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Study results

**Summary results**
N/A