Rate Adaptive Atrial Pacing in Heart Failure Patients with Chronotropic Incompetence

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Primary Objective The primary objective of this pilot study is to assess the ability of MV sensor driven rate adaptive atrial stimulation to restore the quality of life in CI heart failure patients.Secondary Objective(s)The secondary objectives of...

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

Summary

ID

NL-OMON47907

Source
ToetsingOnline

Brief title
ADAPTION Trial

Condition

- Cardiac arrhythmias

Synonym
chronotropic incompetence; inability to increase the heart rate during exercise

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Boston Scientific

Intervention

Keyword: Chronotropic incompetence, Heart failure, ICD, Rate adaptive atrial pacing

Outcome measures

Primary outcome

The primary endpoint of the study is improvement of quality of life in CI heart failure patients. QoL questionnaire score with and without rate adaptive atrial pacing using the MV sensor will be compared. A 10% improvement in QoL score by rate responsive pacing is considered a significant improvement.

Please refer to chapter 6.1 of the protocol (study parameters/endpoints)

Secondary outcome

Secondary outcome of the study is:

1. Improvement of functional capacity in CI heart failure patients. 6MWT with and without rate adaptive atrial pacing using the MV sensor will be compared. A 10% improvement in 6MWT is considered a significant improvement.

2. Reversibility of CI by rate adaptive atrial pacing using a MV sensor will be assessed by comparison of the mHRS with and without rate adaptive pacing. The change in mHRS will be correlated to the change in functional capacity, activity level and quality of life.

3. Clinical status and daily activity level will be evaluated by assessment of NYHA score and activity score measured by the device*s accelerometer, and will be compared with and without rate adaptive pacing.

Please refer to chapter 6.1 of the protocol (study parameters/endpoints)

Study description

Background summary

Patients with congestive heart failure caused by systolic left ventricular (LV) dysfunction often suffer from chronotropic incompetence (CI). Prevalence rates vary from 24% up to 72% dependent on the degree of heart failure and the definition of CI, and seem independent of beta-blocker usage. While the normal heart increases both heart rate and stroke volume in response to increased demand, contractility reserve is largely lost in the failing heart thus rendering increases in cardiac output (CO) primarily dependent on cardio-acceleration. Insufficient cardio-acceleration due to CI is therefore considered to be a significant limiting factor in the exercise capacity of heart failure patients.
A substantial part of this patient population will be eligible for implantation of an ICD/CRT-D device, thus offering an unique opportunity to study heart rate by routinely recorded variables. Moreover, these devices offer the possibility of treatment of CI by rate adaptive (atrial) stimulation based on the incorporated activity sensor. Most ICD/CRT-D manufacturers include accelerometer sensors in their devices, which have known drawbacks since these sensors are insensitive for activity not related to body movements (e.g., isometric exercise, mental stress, or metabolic inadequacy consequent to pathologic conditions). Recently, however, Boston Scientific has incorporated a minute ventilation (MV) sensor in their ICD/CRT-D's. This sensor provides a superior index for metabolic demand, and has successfully been utilized in pacemakers. Although studies mentioned above suggest that CI in congestive heart failure affects a substantial portion of the heart failure population, literature on the subject as well as on its treatment by rate adaptive stimulation is scarce, and has drawn limited attention. Small scale studies have shown rate responsive pacing to be associated with improvement in walking distance and exercise tolerance especially in patients with severe CI. To date, the MV sensor has not been systematically evaluated in CI patients with congestive heart failure.

Please refer to chapter 1 of the protocol (introduction and rationale)

Study objective

Primary Objective
The primary objective of this pilot study is to assess the ability of MV sensor driven rate adaptive atrial stimulation to restore the quality of life in CI heart failure patients.

Secondary Objective(s)
The secondary objectives of this study are:
- Improvement of functional capacity in CI heart failure patients. 6MWT with and without rate adaptive atrial pacing using the MV sensor will be compared;
- Assessment of the reversibility of CI by rate adaptive atrial pacing using a MV sensor;
- Assessment of the effect of rate adaptive atrial pacing on clinical status and daily activity level.

Please refer to chapter 2 of the protocol (objectives)

Study design

This is a prospective randomized, double-blind, crossover trial in a multi-center setting. Prior to initiating a full scale study, this pilot study will be performed in the Vrije Universiteit Medical Center (VUMC), Noordwest Ziekenhuisgroep location Alkmaar (NWZ) and University Medical Center Utrecht (UMCU). All HF patients who received a Boston Scientific dual chamber ICD/CRT-D equipped with MV sensor for metabolic-demand driven rate adaptive pacing can be evaluated for the study. At least one month after implantation, CI patients will be identified using the modified heart rate score (mHRS) or the Age Predicted Maximal Heart Rate (APMHR). The mHRS can be calculated from the rate histogram provided by the ICD/CRT-D; the APMHR cal be calculated based on an exercise test(see chapter 6.2.1). Patients diagnosed with CI will be included in the study after receiving written informed consent. Study subjects will undergo a set of evaluations at baseline: New York Heart Association (NYHA) functional class assessment, quality-of-life evaluation (QoL) using the Minnesota Living with Heart Failure Questionaire, six-minute walking test (6MWT) and interrogation of the ICD/CRT-D (heart rate histograms and activity level). Subsequently, all patients enter the double blind randomized cross-over study. In the cross-over study, patients will be randomized in a 1:1 fashion to either rate responsive (MV only) function ON (AAIR-50) or OFF (DDI-50). MV sensor optimization will be performed with the Sensor replay in Rightrate technology using the intrinsic heart rate (HR) curve obtained during the latest 6MWT (same day). The MV sensor activity will be used to aim at achieving an maximum heart rate (upper rate) based on the derived equation [119 + 0.5(resting HR) * 0.5(age)] for heart failure patients during exercise. The pacing mode set by the pacemaker technician will not be disclosed to either patients or the study physician. After one week the patient will send a homemonitoring rapport, so the pacemaker technician can evaluate MV sensor optimalization. After 3-4 months all CI patients will again undergo the test set including NYHA assessment, QoL scoring, 6MWT and interrogation of the ICD/CRT-D. Subsequently, the pacing mode will be switched to the opposite mode (AAIR-50 to DDI-50 and vice versa). After one week, the patient will send a new home monitoring rapport for the pacemaker technician. After another 3-4 months all CI patients will undergo their final test set.

Please refer to chapter 3 of the protocol (study design)

Intervention

In this study, the intervention is MV sensor driven rate adaptive atrial stimulation as previously described.

Study burden and risks

Presently, the MV sensor driven rate adaptive atrial pacing function is widely used in patients implanted with a pacemaker. More recently, Boston Scientific also incorporated this function in their latest generation ICD/CRT-D*s. Since this function aims to adapt heart rate to exercise, patients who are unable to tolerate increased pacing rates will be excluded (for example patients with severe ischemic heart disease). Furthermore rate adaptive pacing might have a pro-arrhythmic effect. In case potentially dangerous ventricular arrhythmias are initiated the ICD will act appropriately by anti-tachycardia pacing or defibrillation. Risk for these severe cardiac arrhythmias, however, is very small since rate adaptive pacing is performed by the atrial lead only. MV driven rate adaptive pacing might be hazardous in patients with respiratory rate abnormalities (hyperventilation) or use of a mechanical ventilator as this may lead to inappropriate atrial overdrive pacing, therefore these patients are excluded from the present study.
Subjects may have a direct benefit from the study as participation will result in treatment of their CI. Small studies suggest that this leads to improvement in functional capacity but large scale studies are lacking, therefore the benefit of participation is described as *potential*.

Please refer to chapter 9.3 of the protocol (risk and benefit for the study subject)

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

- Chronotropic Incompetence
- Implanted with a Boston Scientific dual chamber ICD or CRT-D equipped with Minute Ventilation sensor
- Symptomatic congestive heart failure (NYHA class II-III)
- Left ventricular systolic dysfunction (Ejection Fraction <40%)
- Optimal (stable) medical therapy
- Sinus rhythm
- Subjects should be able to perform normal daily activities

Exclusion criteria

- Age <18 or incapacitated adult
- Documented atrial fibrillation >5% per month in the last 3 months prior to inclusion
- Indication for pacing (Sick Sinus Syndrome, atrioventricular conduction abnormalities requiring pacing)
- Respiratory rate abnormalities (hyperventilation) or use of a mechanical ventilator
- Patients who are unable to tolerate increased pacing rates
- Beta-blokker / ivabradine / amiodarone therapy is not an exclusion criterion

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-09-2017
Enrollment:	65
Type:	Actual

Medical products/devices used

Generic name:	Implantable Cardiac Defibrillator
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	11-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2019
Application type:	Amendment
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
Other	ISROTH20232
CCMO	NL58518.029.16