non-responders of cardiac resynchronization therapy: the effect of left ventricular endocardial pacing and simulated exercise on acute hemodynamic response

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON32988

Source
ToetsingOnline

Brief title
non-responders in CRT

Condition

- Heart failures

Synonym
heart failure NYHA class III or IV; severe heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis
Source(s) of monetary or material Support: Stichting Cathrijne

Intervention

Keyword: cardiac resynchronization therapy, exercise, heart failure, left endocardial pacing

Outcome measures

Primary outcome

change in LV dP/dt max during left ventricular endocardial pacing OR during

simulated exercise with dobutamine (depening on subgroup)

Secondary outcome

change in NYHA functional class, quality of life determined by Minnesota Living

With Heart Failure Questionnaire, 6-minutes walking test, change in left

ventricular ejection fraction, change in left ventricular end-systolic and

diastolic diameter and volume.

Study description

Background summary

Cardiac resynchronisation therapy (CRT) with biventricular pacemakers and implantable cardiac defibrillators (ICD) has proven to be a valuable therapy in selected patients with systolic heart failure, ameliorating both morbidity and mortality. However, with current selection criteria and implant technique, about 20 tot 30 % of patients remain non-responders. Non-responders might be due to failing selection criteria or methodology in casu echocardiography. However, an important number of non-responders may result of sub-optimal positioning of the left ventricular lead, remote from the site of delayed activation. Endocardial left ventricular stimulation may ameliorate the shortcomings of epicardial stimulation. The advantage of an endocardial approach is the absence of phrenic nerve stimulation as limitation to position the lead, a more predictable pacing threshold and much less restriction to

position the lead in the area of interest.

Study objective

This study evaluates the difference in response to CRT between endocardial en epicardial left ventricular pacing. Secondly, we will evaluate the effect of simulated exercise by means of intravenous dobutamine on response to CRT and device optimization.

Study design

a prospective, single-centre, nonrandomized study, pilot phase

Intervention

all patients will undergo standard implantation of a CRT-device. During procedure the effect of CRT will be evaluated on-table by means of measurement of LV dP/dtmax according to the standard hospital protocol. In the subgroup of patients who do not show a response to CRT, temporary left ventricular endocardial pacing will be performed. In the subgroup of patients who do show response to CRT, the effect of simulated exercise will be evaluated by means of intravenous dobutamine.

Study burden and risks

at baseline a clinical examination, laboratory analysis, 6-minute walking test, echocardiography and cardiac magnetic resonance imaging will be performed. All of these examinations will be repeated at 6-months follow-up except for the cardiac magnetic resonance imaging. It is estimated that the investigations outlined above will require a maximum of three extra on-site visits. Two blood samples will be drawn. Two health questionnaires need to be completed by patient.
The echocardiography is a standard investigation needed to optimize the CRT device. However, some echocardiographic measurements will be performed after administration of an ultrasound contrast agent (SonoVue®). For this purpose an intravenous catheter is needed. When administered in a stable patient population, SonoVue® is considered a safe product. There is a low risk of allergic reactions (<0.1%); therefore patients with known allergies to sulphur will be excluded. Potentially unstable patients with recent hospitalized heart failure or acute ischemic syndrome will also be excluded.
A subgroup will undergo temporary left ventricular endocardial pacing, which will take place during routine implantation of the CRT-device. This procedure will lengthen the implantation with about 20 minutes.
Another subgroup will be administered intravenous dobutamine to simulate exercise. The standard procedure will be prolonged with about 20 minutes.

Administration of dobutamine can result in chest discomfort or palpitations.

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

The Class I ACC/AHA/HRS 2008 recommendations for CRT in patients with severe systolic heart failure are used as inclusion criteria. This means that patients who have a LVEF less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds with sinus rhythm and NYHA functional class III or ambulatory class IV heart failure symptoms despite optimal recommended medical therapy will be included. Optimal recommended medical therapy is defined as the use of angiotensin-converting-enzyme inhibitors or angiotensin-II-receptor blockers and beta-blockers (unless they are not tolerated or contra-indicated). Although a Class IIa recommendation, patients with atrial fibrillation will also be included.

Exclusion criteria

In case of following criteria patient will be excluded from our study: episode of acute heart failure within 3 months prior to inclusion, change in dosage of beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin-II receptor blocker within 3 months prior to inclusion; unstable angina pectoris, acute myocardial infarction, percutaneous intervention or coronary bypass surgery within 3 months prior to inclusion; chronic atrial arrhythmias other than atrial fibrillation; any mechanical or biological valve prosthesis, atrial septal defect, right-to-left shunt; severe pulmonary hypertension, uncontrolled arterial hypertension; known allergy to sulphur hexafluoride, end-stage renal or hepatic disease; pregnancy or child-bearing potential without the use of any birth control measurements; inability to provide a written informed consent; general contra-indications to magnetic resonance imaging.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-08-2010
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	gadolinium
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	dobutamine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-07-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-08-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-10-2009
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2009-011241-71-NL
CCMO	NL26963.060.09