Advanced Image Supported Left Ventricular Lead Placement in Cardiac Resynchronization Therapy III

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To establish the efficacy of targeted LV lead delivery in a sufficiently powered randomized, multicentre study. Efficacy is determined based on the distance of the LV-lead to the targeted cardiac segment, as determined pre-implantation by CARTBox.

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

Summary

ID

NL-OMON54061

Source
ToetsingOnline

Brief title
ADVISE-III

Condition

- Heart failures
- Cardiac therapeutic procedures

Synonym
Cardiomyopathy, heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW,CART-Tech

B.V.

Intervention

Keyword: Cardiac resynchronization therapy, CRT, Image guided intervention

Outcome measures

Primary outcome

The primary endpoint is the distance of the ultimateley selected electrode of a quadripolar LV-lead to a pre-defined target. This will be determined on the basis of a categorical variable and is based on fluroscopic images (LAO 40, RAO 30). As a consequence, lead location will be scored as residing within, adjacent to or remote from a pre-defined target, as determined on a 32- and 16-segment *bulls eye" plot. In addition, LV leads position will be judged for whether it is implanted in scar region (yes/no) and or implanted in a dyssynchronous region (yes/no).

Secondary outcome

1. Short term efficacy after 6 months: 1) differences in echocardiographic LV dimensions (end-systolic volume) and function (ejection fraction); 2) proportion of pattients with a structural response, defined as a relative reduction in LV end systolic volume >= 15%.

2. Short term functional response after 6 months: 1) differences in quality of Life as determined by the Kansas City Cardiomyopathy Questionnaire; 2) New York Heart Association (NYHA) classification and 3) EQ-5D.

3. Long term efficacy after one and two years: 1) all-cause mortality or heart

failure related hospitalisation; 2) clinical composite endpoint of death, transplantation and LV assisting device; 3) functional response determined by a Quality of Life questionnaire; 4) CRT response score.

4. Total cost of procedure and healthcare costs, using a Health Technology Assessment (HTA) approach.

Study description

Background summary

Chronic heart failure is a major cause of morbidity and mortality in the Netherlands. Heart failure accompanied by ventricular dyssynchrony, determined by a wide QRS complex on het electrocardiogram (ECG), is a predictor for worse prognosis. A wide QRS complex (>120ms) is present in about 25-50% of patients with chronic heart failure. Cardiac resynchronization therapy (CRT) is an important therapy for patients with dyssynchronized heart failure (ventricular dyssynchrony). With a CRT device, a special pacemaker, the heart can be electrically stimulated (via 3 pacemaker leads in the heart) in order to achieve synchronized contraction once more.

Unfortunately up to 30-40% of patients do not benefit from CRT. Suboptimal (left ventricular) lead positions are an imporant determinant for CRT non-response. To place the CRT device the implanting cardiologist currently uses fluoroscopic projections (2D X-ray images) of the heart. With this approach, the optimal pacing site for the pacemaker leads, unfortunately, is not visible. This is concerning, since multiple studies have addressed optimal pacing sites for LV stimulation that result in improved response rates and prognosis. Optimal pacing sites are charactarised by pacing in a targeted area of latest mechanical contraction, while pacing in or near an area of myocardial infarction reduces response to CRT. LV lead delivery to these optimal pacing site however is challenging due to restrictions caused by the coronary venous anatomy, areas with fibrosis (e.g. due to myocardial infarction) areas with phrenic nerve stimulation and high pacing thresholds.

For improving CRT response, optimizing the final LV lead position is of major importance. Unfortunately, the implanting physician currently has no information on the optimal position. This is because, during CRT implantation, fluoroscopic imaging provides no tissue characteristics. Consequently, and

despite already broad implementation of CRT during the past 20 years, LV-lead placement is still most often solely based on empirical placement somewhere on the LV lateral wall. Real-time visualisation of both infarct location and latest contracting area during implantation could therefore improve final LV lead position.

With a new techniqe we can merge MRI images of the heart (on which myocardial scar tissue and mechanical contraction timing can be identified) with the fluoroscopic 2D-projection made routinely during conventional CRT implantations. Tthis technique potentially allows the physician to perform the therapy much more accurate than before at the optimal pacing location in the heart. Using this patient tailored approach we believe that response to CRT can be augmented. Previous research already demonstrated that targeted therapy (away from scar and toward the latest mechanical contraction) improves patients' symptoms and prognosis.

We have recently demonstrated in a small pilot study that using the CARTBox software, developed by CART-Tech B.V., the optimal location for LV lead delivery can be visualized during CRT implantation (METC number 16/242). In the ADVISE-CRT II study with 30 patients (METC number 19/443), the software behind the technique has been improved. Moreover, 2D-imagefusion has been validated in 5 patients. To this end, no additional 3D rotational scan has to be performed in the ADVISE III study. The ADVISE-III study will be a randomised controlled trial with multiple centers (3 or more centers) in 130 patients. We therefore hope to be able to draw more firm conclusions about the efficacy and feasibiliy of real-time image-guided CRT implantations.

Study objective

To establish the efficacy of targeted LV lead delivery in a sufficiently powered randomized, multicentre study. Efficacy is determined based on the distance of the LV-lead to the targeted cardiac segment, as determined pre-implantation by CARTBox.

Study design

The ADVISE-III trial is a multicentre, interventional, blinded, randomised controlled trial. Patients will be stratified according to ethology of HF, to assure equal distribution of patients with ischemic cardiomyopathy (ICM) and non-ICM patients in both groups. We will use the CARTBox software during CRT implantation for targeting the LV-lead implantation towards predefined optimal pacing sites. Both the patient and the sonographer will be blinded from treatment outcome.

Intervention

CRT procedure (conventional), but carried out under guidance of CARTBox software (new) in the interventiongroup.

Study burden and risks

All patients will undergo an MRI scan. In rare cases (<1/1000) an allergic reaction can occur, such as an itch, nausea or small bumps on the skin. In the vast majority of cases these symptoms pass quickly. In extremely rare cases acute allergic reactions can occur, usually in subjects with known contrast allergies. Therefore, these subjects are excluded from participation in this study. Recently nephrogenic systemic fibrosis (NFS) has been linked to administration of gadolinium-based contrast agents in subjects with renal failure. Therefore, subjects with renal failure are excluded from an MRI scan. No cases of NFS have been documented in patients without renal failure.

The benefit of the Cardiac MRI is the knowledge of scar tissue, detailed description of LV function, and visualization of the LV region with late contraction where the LV lead has to be placed. For the patient, the additional burden of the MRI is the extra visit to the hospital and claustrophobic patients may not be able to undergo the assessment. The risk and/or complications of the CRT implantation itself are not additional to the study, as the CRT implantation with a quadripolar lead is a standard procedure in the UMC Utrecht. Cardiac MRI scan will be performed before CRT implantation.

During implantation, a 2D registration method for fusing MRI with fluoroscopy wll be used. Therefore, since no additional 3D rotational scan is made, total radiation burden is similar to conventional procedures.

The study can increase the response of patients to CRT. By fusing MRI images with fluoroscopy during LV lead positioning, the implanting physician can choose the most optimal position (out of scar and towards delayed contraction) for implanting the CRT device. A lead position away from the infarct area, and closest to or in the latest activated area will improve LV pump function. An improved response to CRT can improve quality of life and prognosis of heart failure patients. Especially patients with myocardial infarction and/or coronary artery stenosis (ischemic cardiomyopathy), since these patients are more often non-responders to CRT. The study may also improve the procedure itself. With increased knowledge of an optimal lead position during implantation, future procedures can be conducted more easily. The implanting physician can choose a target vessel for optimal lead position. It can therefore shorten the procedure and prevent potential complications of prolonged procedures.

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

An indication for cardiac resynchronization therapy according to the current international evidence based guidelines for CRT (the 2016 European Society of Cardiology Guidelines for Acute and Chronic Heart Failure:
- Chronic heart failure;
- New York Heart Association functional class II, III, IV (ambulatory);
- QRS duration >=130ms;
- Optimal pharmacological therapy;
- Left ventricular ejection fraction <=35%;
- Either a QRS duration >=130ms with left-bundle branch block OR a QRS duration >=150ms without left-bundle branch block.

Exclusion criteria

Contraindications for implantation of a CRT device;
- Age <18 years or incapacitated adult;
- Pregnancy; if there is anamnestic doubt regarding postmenopausal state (<1 year since last menstruation), a urine hCG test (Alere) will be performed.
- Lactation;
- Subjects with impaired renal function (severe renal insufficiency, GFR < 30 ml/min/1.73m2);
- Atrial fibrillation or atrial fibrillation during MRI
- Documented allergic reaction to gadolinium;
- Impossibility to undergo a MRI scan (determined by using the standard contraindications for MR imaging as used for clinical purposes).
- Participation in another clinical study that prohibits or influences any procedures other than standard.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-02-2021
Enrollment:	130
Type:	Actual

Medical products/devices used

Generic name:	CARTBox
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	20-08-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-10-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 29327
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL73416.041.20
OMON	NL-OMON29327