Left ventricular septum pacing in patients by transvenous approach through the inter-ventricular septum - feasibility, long-term lead stability and safety

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Primary objectives: • To determine the feasibility of LV septum lead placement by transvenous approach through the inter-ventricular septum in patients with sinus node dysfunction (SND) and structurally normal hearts, as well as in patients with...

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

Summary

ID

NL-OMON39464

Source
ToetsingOnline

Brief title
Left ventricular septum pacing

Condition

- Other condition
- Heart failures

Synonym
Left ventricular dyssynchrony

Health condition

Hartaandoening: geleidingsstoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Het onderzoek wordt gefinancieerd door de industrie,Medtronic B.V.

Intervention

Keyword: Cardiac pacing, Feasibility, Lead stability, Left ventricular septum

Outcome measures

Primary outcome

• Successful LV septum lead placement. Placement is considered successful if the lead can be placed in the endocardial LV septum and adequate and stable sensing and pacing tresholds are achieved. Implantation is considered unsuccesfull if the lead cannot be placed due to inability to penetrate the interventricular septum due to anatomic reasons or if a suitable and acutely stable endocardial LV septal site cannot be found due to elevated pacing tresholds, persistent extra-cardiac stimulation or because of hemodynamic instability leading to the termination of the initial implant procedure.

• Maintenance of stable lead function using the electrical parameters: sensing value, pacing threshold and lead impedance at baseline versus 6 months follow-up.

• Adverse effects of the LV septum lead, with special attention given to the presence of perforation or rupture of the interventricular septum or free wall,

pericardial effusion, thrombosis, heart rhythm disturbances, conduction disturbances, lead-/screw dislocation/-fracture.

Secondary outcome

• Acute change in LV systolic function using the hemodynamic parameters LVdP/dtmax and Nexfin LV stroke volume, during LV septum pacing compared to:

- RVA pacing and baseline (atrial pacing / AAI mode) in patients with SND.

- RVA pacing, single LV epicardial lateral wall pacing, Bi-LV pacing (LV septum and LV lateral wall pacing) and BiV pacing (RV septum and LV lateral wall pacing) and baseline (atrial pacing / AAI mode) in heart failure patients who are candidates for CRT.

• Change in sequence of LV electrical activation during LV septum pacing compared to the other above mentioned pacing configurations using the electrocardiographic parameters QRS duration and 3 dimensional QRS vector direction.

• Change in regional myocardial deformation patterns during LV septum pacing compared to the other above mentioned pacing configurations using the echocardiographic parameter SPECKLE-tracking strain.

• Absolute change in cardiac function using the echocardiographic parameters LVEF (biplane Simpson method), LV End-Systolic Diameter (LVESD), LV End-Diastolic Diameter (LVEDD), LV End-Systolic Volume (LVESV) and LV End-Diastolic Volume (LVEDV) at baseline versus 4-6 weeks follow-up.

• Correlation between the non-invasively measured LV stroke volume using Nexfin

and the invasively determined LV dP/dtmax.

Study description

Background summary

In the Netherlands each year, approximately 8000 patients receive a pacemaker (PM) for bradycardia and 2000 patients receive a biventricular (BiV) PM for cardiac resynchronization therapy (CRT).

Cardiac pacing is the only effective treatment for symptomatic bradycardia. After the introduction of the implantable PM, the right ventricular apex (RVA) has become the most frequently used ventricular pacing site. However, clinical studies have shown that RVA pacing leads to left ventricular (LV) dyssynchrony, and on the long run to adverse structural changes (remodeling), a higher risk of developing atrial fibrillation and heart failure, and higher mortality.

CRT has become increasingly important for the treatment of heart failure when accompanied by intraventricular conduction delay. Large clinical trials have shown that CRT improves LV systolic pump function, reverses structural remodelling, improves quality of life and exercise tolerance, and decreases mortality. Unfortunately, problems encountered during positioning and fixation of the LV pacing lead in the coronary vein result in suboptimal or loss of CRT in at least a quarter of CRT candidates and require re-operation in 7% during follow up.

Over the last years alternate pacing sites have been investigated to overcome the adverse effects of RVA pacing and the limitations of BiV pacing. Recent studies in animals have shown that pacing at the LV septum induces significantly less ventricular dyssynchrony than RVA pacing and is able to improve LV function to a similar degree as BiV pacing. In the animal experiments the LV septum lead was permanently placed by introducing a custom pacing lead with extended screw (Medtronic 09066 lead) transvenously into the RV cavity and positioning it against the RV septum using a guiding catheter, and then driving it from the RV side through the inter-ventricular septum into the LV endocardial layer. This was shown to be a feasible and safe procedure and lead stability was shown during four months of follow-up.

The Medtronic 09066 lead is derived from the market released Medtronic Select Secure lead model 3830 and is placed by standard transvenous right ventricular approach using a standard market released guiding catheter. The lead is designed to provide the handling characteristics needed to screw the distal

portion of the lead into the LV septal wall starting from the RV side. For this application the standard 3830 lead has been modified by extending the screw tip of the lead from 2 to 4 mm. The further composition of the lead has been left unchanged. In the animal study, 09066 leads were implanted in 11 canines as described above. Trans-septal lead placement at the desired LV septal location was shown to be a feasible and safe procedure. Except for insufficient lead tip penetration in only one case, no other procedure- or lead related complications (e.g. septum perforation/-rupture or lead-/screw dislocation/-fracture) were observed during 16 weeks follow-up or at the post-mortem evaluation. Furthermore, the leads remained mechanically and electrically stable during the follow-up period in otherwise healthy and active canines. In addition, it was shown that the 4 mm long screw has much better fixation than the standard 3830 2mm screw of which 4 out of 7 implanted dislocated within the first week of follow-up.

The abovementioned adverse effects of RVA pacing, the limitations of BiV pacing and the promising effects of LV septum pacing in preclinical studies have led to the idea that LV septum pacing is an attractive alternative for treating patients with a standard ventricular pacing indication, as well as patients with an indication for BiV pacing. In the latter category, CRT could then be performed using a single ventricular pacing lead, thus limiting the number of lead implantations, and thereby reducing complication rate and implantation costs as well as avoiding the difficult access route through the coronary vein.

It is the aim of this study to translate the findings from preclinical studies to the clinical situation by investigating in an initial phase 1 study the feasibility, long-term lead stability and safety of LV septum pacing by transvenous approach through the inter-ventricular septum in patients with a PM indication.The results may have a large impact on future pacing therapy. The LV septum may become the universal pacing site, being preferred for anti-bradycardia therapy, and being an equal alternative for BiV pacing, but easier to apply, less invasive and more cost-effective.

Study objective

Primary objectives:
• To determine the feasibility of LV septum lead placement by transvenous approach through the inter-ventricular septum in patients with sinus node dysfunction (SND) and structurally normal hearts, as well as in patients with heart failure and LBBB who are candidates for CRT.
• To determine the long-term (6 months) stability of the LV septum lead in these patients.
• To evaluate the safety of the LV septum lead in these patients.

Secondary objectives:
• To investigate the acute hemodynamic effect of LV septum pacing on LV

systolic function, assessed by invasive quantitative LVdP/dtmax measurement and non-invasive quantitative LV stroke volume measurement using Nexfin, as compared to:
- RVA pacing and intrinsic ventricular activation in patients with SND.
- RVA pacing, LV only pacing, BiV pacing and intrinsic ventricular activation in heart failure patients who are candidates for CRT.
• To investigate the effect of LV septum pacing on the sequence of LV electrical activation assessed by ECG and 3-dimensional vectorcardiogaphy (VCG).
• To investigate the effect of LV septum pacing on distribution of myocardial strains, assessed by SPECKLE-tracking echocardiography.
• To correlate the non-invasively measured LV stroke volume using Nexfin and the invasively determined LV dP/dt|max.

Study design

The present study is a prospective cohort study to investigate the feasibility, long-term lead stability and safety of LV septum pacing by transvenous approach through the inter-ventricular septum in patients with SND and CRT candidates. In addition, the effects of LV septum pacing on LV systolic function, sequence of LV electrical activation and distribution of myocardial strains in these patients is evaluated.

Intervention

Every patient who is enrolled in the study has a PM indication. Patients with SND receive a standard dual chamber PM and CRT candidates receive a BiV PM. Pacing leads are placed via standard transvenous approach by cephalic cut down and/or subclavian puncture. The atrial lead and the LV lead used for BiV pacing in CRT candidates are placed in the conventional positions. Subsequently, the implantation procedure differs from a standard (BiV) PM implantation in the following way: Instead of placing a pacing lead in the conventional RVA position, a lead will be placed in the LV septum by driving a lead from the RV to the LV side of the interventricular septum. For this purpose, we will use the newly developped Medtronic lead model 09066, which is derived from the market released Medtronic 3830 Select Secure lead. This lead which is fit with a tip with an extended screw is positioned against the RV side of the interventricular septum using a commercially available ventricular septum delivery catheter which is inserted transvenously. Subsequently the pacing electrode is advanced to the LV endocardial layer of the septum by driving the lead through the inter-ventricular septum. Intracardiac echocardiography (ICE) is used to guide LV septum lead placement. Proper position within the inner 1 mm of the septum is secured by fluoroscopy and by advancing the screw forward until pacing thresholds increase, indicating that the electrode is entering the LV cavity. Then the lead is slowly withdrawn until normal pacing thresholds are achieved. After achieving adequate sensing values and pacing thresholds, the

leads are connected to a dual chamber PM in SND patients and a BiV PM in CRT candidates, which is placed subcutaneously. Feasability of this implantation method using the lead model 09066 has been previously demonstrated in canine hearts. After implantation, the leads remained mechanically and electrically stable in healthy and active animals during the follow-up period of 16 weeks.

Study burden and risks

This is the first application of this pacing method in patients. Therefore, the risk of certain complications like inter-ventricular septum perforation or -rupture or screw fracture is still unknown. However, the feasibility, long-term lead stability and safety of trans-septal LV septum pacing has been demonstrated in animal experiments and was comparable to conventional pacing methods. Therefore, additional procedure- or lead related risks are not expected for the study subjects.

Intracardiac echocardiography (ICE) will be used as an extra visualization tool to guide lead implantation. Cardiac complications due to ICE have never been reported. Therefore ICE by itself is not known to carry any risks for the patients. The 8 F ICE catheter is introduced into the right ventricular (RV) cavity via the femoral vein. Before femoral vein puncture, local anaesthetics will be administered which may cause a burning sensation. Local vascular complications due to femoral vein puncture like bleeding or infection may occur but are very rare. Complication rates have never been published.

Following trans-septal LV septum lead placement, acute invasive hemodynamic measurements are performed by inserting a RADI pressure wire via the femoral artery into the LV cavity to determine maximal rate of LV pressure rise (LV dP/dt|max) as a measure of LV systolic function2 during various pacing configurations. Cardiac complications of the RADI pressure wire have never been reported. Therefore the wire by itself is not known to carry any risks for the patients. Local vascular complications of femoral artery puncture like bleeding, infection or damage to the vessel wall may occur but are rare. Complication rates have never been published, but will likely not exceed the complication rate of 1.6% observed after diagnostic cardiac catheterization. The LVdP/dtmax measurements by themselves are not harmful for the patient.

Subsequently, LV stroke volume measurements will be performed non-invasively during the same pacing configurations using the Nexfin technique. Nexfin uses an inflatable cuff that is placed around the mid-phalanx of the middle finger to measure finger blood pressure in combination with calibrated volume-clamp photoplethysmography. There are no risks involved with this procedure.

LV septum lead placement and all following invasive and non-invasive hemodynamic measurements will increase the total PM implantation time by a maximum of 1 hour.

ECG recordings, 3- dimensional QRS vector diagrams (VCG) and echocardiograms are performed at 4-6 weeks follow-up during various pacing configurations. These evaluations do not involve any risks for the patients, but require one extra visit to the hospital.

PM check-ups to evaluate lead stability will be performed the first day after implantation, 10 days (window: 5 - 15 days) after implantation, and 3 months (window: 10 - 14 weeks) as well as 6 months (22 - 26 weeks) after implantation. After 6 months, pacemaker check-up will be performed every 6 months, until study closure. The PM check-up at 3 months post implantation is not part of routine care and requires an extra visit to the hospital. Patients are not exposed to any risks during the PM check-up.

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

• Cardiac pacing indication for sinus node dysfunction (2-chamber pacemaker) or indication for a CRT-pacemaker as determined by the treating cardiologist
• Greater than 18 years of age
• Willing and capable of giving informed consent

Exclusion criteria

• Ventricular pacing dependent
• High degree AV block
• Previous septal myocardial infarction
• Previously implanted pacing device
• Abnormal venous anatomy
• LV septum wall thickness >10 mm determined by echocardiography
• Presence of severe valvular disease
• Presence of an ongoing progressive terminal disease associated with a reduced likelihood of survival for the duration of the study

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2012
Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	Pacemaker lead

Registration:	No

Ethics review

Approved WMO Date:	26-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-10-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL37648.068.11

Study results

Date completed:	24-02-2015
Actual enrolment:	12

Summary results
Trial is onging in other countries