Mechanistic insight in left ventricular septal and left bundle branch pacing.

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To demonstrate superiority of left ventricular septal pacing over right ventricular pacing and to investigate the additional effect of capturing the left bundle branch in left ventricular septal pacing (LVsP). This will be done by studying...

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON49575

Source
ToetsingOnline

Brief title
MASTER-LV

Condition

- Cardiac arrhythmias

Synonym
bradycardia, heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Medtronic B.V.

Intervention

Keyword: Conduction system pacing, Left bundle branch pacing, LV septal pacing, Physiological pacing

Outcome measures

Primary outcome

Primary study parameters/endpoints:

• To show superiority in electrophysiological effect (standard deviation of activation times (SDAT) measured by the ECG-Belt) of LV septum pacing over RV septum pacing in patients indicated for permanent cardiac pacing.

Secondary outcome

Secondary study parameters/endpoints:

• Comparing vectorcardiographic characteristics (QRS area) during pacing at different depths within the IVS;

• Comparing electrocardiographic characteristics (QRS duration, QRS morphology) during pacing at different depths within the interventricular septum (IVS);

• Comparing systolic and diastolic blood pressure (invasively measured) during pacing at different depths within the IVS;

• Determine the ability to capture the left bundle in LVS pacing;

• Assess global and regional LV strain patterns measured by echocardiography during LVS pacing;

• Assess reverse remodelling after three months in patients undergoing deep LV septal pacing with a CRT indication.

Study description

Background summary

The efficiency of cardiac pump function depends on synchronous electrical activation of the ventricles. The normal, synchronous activation sequence is disturbed during conduction system disease like left bundle branch block (LBBB) and during artificial electrical stimulation (= pacing) of the right ventricle (RV). RV pacing is, despite the known detrimental effects, the common therapy to treat symptomatic slow heart rate. The RV pacing site has become the preferred site as it is easily accessible and because it yields chronically stable lead performance. However, as a consequence of disturbed electrical activation, RV pacing and LBBB reduce cardiac pump function and increase cardiac morbidity and mortality.(2, 3) RV pacing in combination with left ventricular (LV) pacing (RV + LV pacing = cardiac resynchronization therapy; CRT) is the common therapy to treat patients with RV pacing or LBBB who develop heart failure.
Under normal, physiological conditions the electrical impulse generated in the sinus node exits the fast-conducting Purkinje system at sites located at the LV endocardial surface of the septum.(4, 5) It was therefore hypothesized that pacing near these sites results in better systolic and diastolic function compared to RV pacing. Animal studies in our lab confirmed that LV function was maintained at normal level during ventricular septal pacing on the left side of the interventricular septum (LV septal pacing; LVsP).(6) In these experiments the LVsP lead was permanently implanted by introducing a adapted pacing lead transvenously into the RV and driving it from the RV side through the interventricular septum (IVS) to the left side of the septum. This was shown to be a feasible and safe procedure, and leads remained mechanically and electrically stable during 4-month follow-up.(7) Furthermore, cardiac pump function during LVsP was at least as good as during BiV pacing (BVP), indicating that LVsP could be applied in CRT. Subsequently a first-in-man study performed in our center demonstrated the feasibility of permanently implanting a LVsP lead in symptomatic sinus node disease patients using a transvenous approach through the interventricular septum.(8)

More recently, it was observed in a patient with heart failure and LBBB that in LVsP the left bundle branch (LBB) could be stimulated. In this patient, pacing the LBB completely resolved the conduction block.(9) At 1-year follow-up the left ventricular ejection fraction (LVEF) increased from 32% to 62% and LV end-diastolic volume decreased from 76 mm to 42 mm. These results were confirmed by Zhang and colleagues who demonstrated mechanical as well as electrical resynchronization in eleven consecutive patients with heart failure (HF), reduced LVEF and LBBB.(10) At a mean follow-up period of 7 months, NYHA functional class, BNP plasma level, LV end diastolic diameter, and LVEF were significantly improved. This new pacing technique has also been investigated in bradycardia patients without heart failure. In a study of 33 patients with

atrioventricular block (AVB), Li et al.(11) reported that LBB pacing had slightly improved cardiac function and left ventricular synchronization by 2-dimensional echocardiographic strain imaging at the 3-month follow-up compared with that at baseline. These results were confirmed in a larger study performed in 56 patients with normal cardiac function, where all patients survived without any symptoms of heart failure during a mean follow-up of 5*±*2* months. LVEF, LV end systolic diameter, and LV end diastolic diameter remained unchanged during follow-up.(12)
However, the LBB is not always captured and reported success rates range from 81%(13) to 93%(14). Despite the many recent publications regarding LBB pacing, there are still many unknowns that need to be investigated. Three main unknowns are 1) optimal septal lead depth , 2) the effect of additional LBB capture, and 3) long-term clinical benefits.

LVsP/LBB pacing has great potential in future cardiac pacing therapy with possibly a wide application. It is, therefore, of importance to obtain more mechanistic insight in this therapy.

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Study objective

To demonstrate superiority of left ventricular septal pacing over right ventricular pacing and to investigate the additional effect of capturing the left bundle branch in left ventricular septal pacing (LVsP). This will be done by studying differences in electrophysiological effects, measured by electrocardiogram (ECG), vector cardiogram (VCG) and the ECG-Belt (Medtronic product), of different LV septal pacing lead penetration depths.

Study design

The study is a multicentre prospective interventional cohort study performed in the Maastricht UMC+ and Radboudumc to investigate the electrophysiological and hemodynamic effects of different LV septal lead penetration depths.
Forty consecutive patients referred for pacemaker implantation will be included. The aim is to include approximately 20 patients referred for pacemaker implantation with structurally normal heart and approximately 20 patients referred for pacemaker implantation with reduced LV ejection fraction.

Intervention

All patients eligible for study participation have a clinical indication for permanent cardiac pacing and will receive a standard (CRT-)pacemaker implantation whether they decide to participate in the study or not. Patients will be recruited from the outpatient pacemaker/ICD clinic and from the cardiology ward. Prior to implantation, they will be asked informed consent to

undergo extra measurements at the time of implantation.

Forty study participants referred for pacemaker implantation will be included. Participants will consist of patients with structurally normal hearts (bradycardia indication) and patients with heart failure and LBBB (CRT indication). In both patient groups the atrial lead is positioned in the right atrial appendage according to routine clinical practice. The LV septal pacing lead (Medtronic 3830 lead) is positioned via transvenous approach at the right side of the interventricular septum and advanced (screw-in) in on average 4 steps to the endocardial border of the left ventricular septum with the aim to obtain left bundle branch capture. Electrical and hemodynamic measurements are performed when pacing at different inter-ventricular septum penetration depths of the pacing electrode, starting at the RV side of the inter-ventricular septum (= baseline measurement) and advancing to mid-septum, left side of septum and finally near the left bundle branch.

Atrio-ventricular pacing will be performed with relative short AV-delay of 80 ms ensuring ventricular capture.
Left bundle branch capture will be defined as following: 1) paced right bundle branch block (RBBB) QRS morphology, 2) stable and short stimulus to LV activation time (LVAT; R in V5) at high and low pacing output and 3) recorded LBB potential.
Once the lead is positioned in an adequate stable position the lead will remain in position and is connected to the pacemaker.
When the implantation is completed, an echocardiogram will be performed evaluating the global and regional LV and RV contractions patterns during intrinsic rhythm and during LV septal pacing.
Patients will undergo a routine pacemaker follow-up at 2 weeks and 3 months to evaluate the sensing and pacing threshold values of the implanted LV septal pacing lead and echocardiography will be performed immediately after as well as 6 months after the implantation procedure to evaluate LV dimensions.

Study burden and risks

All study participants have a clinical indication for permanent cardiac pacing and will receive left ventricular septal pacemaker implantation as part of their routine medical care. The intra-procedural measurements with VCG, Verathon Heartscape system, and the invasive blood pressure measurements are not part of routine medical care. The burden and risks of these study procedures are described below:

1. Blood pressure is invasively measured via the femoral artery by connecting the femoral sheath directly to the standard blood pressure measurement system as is standard practice in coronary angiography (CAG) procedures. Local vascular complications of the arterial 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. Heparin will be administered as part of standard procedure.

2. VCGs are constructed post-procedure from the routine 12-lead ECGs using the Kors matrix and will therefore not require any additional action.

3. Verathon Heartscape system (*ECG-Belt)* measurements are performed using a 55-electrode body surface mapping system developed by Medtronic. The belt is placed prior to the procedure and the patient has to wear this belt during the procedure. Since the measurements are of non-invasive nature and that they are not diagnostic, they do not expose the patient to any risks.

Performing all measurements during the implantation including will lengthen procedure time by a maximum 30 minutes, this increasing the burden for the patient.

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

Indication for permanent cardiac pacing:

o pacing indication in structurally normal heart because of:
• sinus node dysfunction (SND)
• atrioventricular block (AVB)
• atrial tachyarrhythmia refractory to antiarrhythmic medications that required atrioventricular node ablation
o Pacing indication with reduced LV ejection fraction (LVEF)
• pacing indication with reduced LVEF and expected high percentage of ventricular pacing
• Heart failure with wide QRS and left bundle branch block (LBBB) and reduced LVEF

Exclusion criteria

• >2 premature ventricular complexes on standard 12-lead ECG on all ECG*s within 3 months prior to implantation.
• Age < 18 years
• Incapable of giving informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-05-2021
Enrollment:	40

Type:	Actual

Ethics review

Approved WMO Date:	15-01-2021
Application type:	First submission
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	NL74074.068.20