Permanent left ventricular septal pacing versus right ventricular pacing in patients with atrioventricular conduction disorders: a randomized trial: LEAP trial.

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

Summary

ID

NL-OMON54534

Source
ToetsingOnline

Brief title
LEAP trial.

Condition

- Cardiac arrhythmias

Synonym
left ventricular dyssynchrony, pacing induced cardiomyopathy

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW,Medtronic B.V.,Medtronic;Inc.

Intervention

Keyword: Cardiac pacing, Conduction system pacing, Left ventricular septal pacing, Randomized trial

Outcome measures

Primary outcome

The primary endpoint is a composite of all-cause mortality, hospitalization for heart failure, and a more than 10% point decrease in left ventricular ejection fraction (LVEF) leading to a LVEF below 50%, which as a binary combined endpoint will be determined at one year follow-up.

Secondary outcome

Secondary endpoints are:

- Time to first occurrence of all cause mortality or hospitalization for heart failure.

- Time to first occurrence of all cause mortality.

- Time to first occurrence of hospitalization for heart failure.

- Time to first occurrence of atrial fibrillation (AF) de novo.

- The echocardiographic changes in LVEF at one year.

- The echocardiographic changes in diastolic (dys-)function at one year.

- The occurrence of pacemaker related complications.

- Quality of life (QOL), cost-effectiveness analyses (CEA) and budget impact analysis (BIA).

The secondary endpoints (other than echocardiographic LVEF change) will be determined at the end of the follow-up period, when the last included patient

has reached one year follow-up. The individual follow-up time for patients at

this time point will vary with a minimum of one year.

Study description

Background summary

Permanent cardiac pacing is the only available therapy in patients with atrioventricular (AV) conduction disorders and can be life-saving. Right ventricular pacing (RVP), the routine clinical practice for decades in these patients, is non-physiologic, leads to dyssynchronous electrical and mechanical activation of the ventricles, and may cause pacing-induced heart failure and cardiomyopathy.
Left ventricular septal pacing (LVSP) is an emerging form of physiologic pacing that can possibly overcome the adverse effects of RVP.

Study objective

The primary objective of this study is to compare in a randomized trial the effects of permanent LVSP with RVP in patients with a pacemaker indication because of AV conduction disorders, with respect to a composite of all-cause mortality, hospitalization for heart failure, and a more than 10% point decrease in left ventricular ejection fraction (LVEF) leading to a LVEF below 50%. LVSP is anticipated to result in improved outcomes.
Pacemaker related complications are expected to be equal between groups.
Secondary objectives are to evaluate whether LVSP is cost-effective and associated with an improved quality of life (QOL) as compared to RVP. Quality of life is expected to improve with LVSP and reduced healthcare resource utilizations are expected to ensure lower costs in the LVSP group during follow-up, despite initial higher costs of the implantation.

Study design

The LEAP trial is a multi-center investigator-initiated, prospective, randomized controlled, open label, blinded endpoint evaluation (PROBE) study.

Intervention

LVSP vs. RVP.

Study burden and risks

LVSP is expected to be as safe as conventional RVP and procedure or lead related risks for the study subjects are expected to be comparable for both intervention groups. However, since LVSP is a relatively new implantation technique in which most implanting physicians need to get more routine, proper lead positioning may initially take longer: we estimate a mean procedure time prolongation with LVSP of around 20 minutes.
On the other hand, LVSP might be associated with better outcomes as compared to RVP, in terms of a reduction in the occurrence of pacing induced heart failure, as we hypothesize.
Besides baseline and follow-up examinations that are part of routine clinical care, all participants will undergo a baseline and 12 months follow-up study-related echocardiography, which contains no extra risk. Additionally, participants will be asked to fill in questionnaires (QOL, CEA, BIA) at baseline and every six months follow-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

Inclusion criteria:
- Age >=18 years with a life expectancy with good functional status of at least 1 year.
- Class I or class IIa permanent pacing indication owing to an AV conduction disorder with an expected ventricular pacing percentage of >= 20%. AV conduction disorders include:
- acquired third- or second-degree AV block.
- atrial arrhythmia with slow ventricular conduction.
- LVEF >= 40%.
- Signed and dated informed consent form prior to admission to the trial.

Exclusion criteria

Exclusion criteria:
- Heart failure NYHA class III-IV
- Class I indication for cardiac resynchronization therapy
- Class I indication for implantable cardioverter defibrillator
- Previous receipt of a cardiac implantable electronic device (except for implantable loop recorders)
- Atrial arrhythmia with planned AV junction ablation
- Unstable angina or acute myocardial infarction
- Percutaneous or surgical coronary intervention within 30 days before enrollment
- Valvular disease with an indication for valve repair or replacement
- Hypertrophic cardiomyopathy with septal wall diameter > 2 cm
- Renal insufficiency requiring hemodialysis
- Active infectious disease or malignancy
- Women who are pregnant

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-12-2020
Enrollment:	400
Type:	Actual

Medical products/devices used

Generic name:	Pacemaker
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	25-08-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-06-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-03-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-09-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-02-2023
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
ClinicalTrials.gov	NCT04595487
CCMO	NL72047.068.20