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The effect of optimization of the electrical synchronicity of both heart chambers on the blood flow and blood volumes in and around the heart, during and after a coronary bypass surgery, in patients with an impaired heart function based on asynchronous contraction of both heart chambers

Submission date 30/04/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 16/05/2014	**Overall study status** Completed	
Last Edited 29/05/2020	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Cardiac resynchronization therapy (CRT) synchronizes the contraction of the two heart chambers by pacing both chambers simultaneously. This differs from typical pacemakers, which pace only the right ventricle. This therapy increases the efficiency of the heart and reduces the amount of work the heart must do to pump blood. In many patients it improves exercise capacity (the maximum amount of physical exertion that a patient can sustain). The aim of this study is to find out if CRT during heart surgery can also improve blood flow and decrease pulmonary blood volume.

Who can participate?
Patients aged 18 and over who are scheduled for a coronary bypass operation.

What does the study involve?
All participants will receive the same treatment. Routine clinical practices are performed for the general anesthesia and coronary bypass surgery. Extra monitoring will be performed by insertion of an arterial line in the leg artery, which we routinely use in many operations and in intensive care. All patients undergo echocardiography during surgery. At least three times before and three times after the heart-lung machine (cardiopulmonary bypass) all patients will receive an injection of a small amount of ultrasound contrast agent with cold fluid to measure the pulmonary blood volume and other parameters like cardiac output. At the end of the surgery the

surgeon will place an extra pacemaker wire on the left chamber, next to the frequently placed right chamber wire and the upper-chamber wire. The pacemaker wires will be connected to a box, by which we can optimize the synchronicity of the contraction pattern of the heart.

What are the possible benefits and risks of participating?
Participants will not gain a direct benefit, except perhaps less use of medication to support the blood circulation. Echocardiography, inserting an arterial line in the leg artery and placing a right chamber pacemaker wire are procedures that are routinely carried out in cardiac surgery. Application of an additional left chamber wire will take no longer than one minute. It does not carry any extra risk than that of a right chamber pacemaker wire. The risk of an allergic reaction to the ultrasound contrast agent is very small.

When is study starting and how long is it expected to run for?
The study started in July 2009 and is expected to finish in January 2015.

Where is the study run from?
Catharina Hospital Eindhoven (Netherlands).

Who is funding the study?
Catharina Hospital Eindhoven (Netherlands).

Who is the main contact?
Mohamed Soliman (cardiac surgeon)

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
M07-1723

Study information

Scientific Title
Postoperative Hemodynamic Effects of Cardiac REsynchronization Therapy in cardiac surgery patients with impaired left ventricular function

Acronym

PHECRET II

Study objectives
The rationale of this study is to prove that biventricular pacing can improve the perioperative performance and reduce the intrathoracic blood volumes in patients with left ventricular dysfunction after cardiac surgery.
The study design will confirm accurately if biventricular pacing is superior to right ventricular pacing in treating asynchrony associated with conduction disturbance in patients with an ejection fraction of 35% or less.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethical Committee Catharina Hospital Eindhoven (Medisch Ethische Toetsings Commissie van het Catharina Ziekenhuis), 13/07/2009, M07-1723

Study design
Prospective mono-center pilot study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Heart failure patients with ventricular dyssynchrony in cardiac surgery; cardiovascular monitoring and contrast-enhanced echocardiography

Interventions
Medical history, physical examination, ECG, Echo-Doppler (see details), and preoperative laboratory data, which are included in the standard pre-operative care.

Echo-Doppler measurements:
1. Ejection fraction (EF %)
2. Left ventricular end systolic diameter (LVESD)
3. Left ventricular dyssynchrony (Tissue Doppler Imaging)
4. Mitral regurgitation

Surgical protocol
The main measurements take place during surgery after weaning from cardiopulmonary bypass.
At surgery (after cessation of CPB):
1. Temporary pacing wires are sutured to the right atrium and right ventricular free wall, according to the standard procedures. Similar to the right ventricle, additional temporary left ventricular leads are sutured to the basal obtuse marginal part of the left ventricle.
2. Pacing leads are connected to an external temporary pacing device.
3. LV dP/dtmax is measured by the Pulsiocath in the femoral artery
4. Pacing protocol:
4.1. Rate:
4.1.1. Atrial pacing: 10 beats above intrinsic rhythm.

4.1.2. In the absence of atrial activity: at 80 beats /min.
4.2. AV interval
4.2.1. Fixed at 75% of intrinsic AV interval.
4.2.2. In the absence of AV conduction: 120 ms.
4.3. Pacing modes: AAI, DDD right ventricular pacing; left ventricular pacing and biventricular pacing.
4.4. Pacing sequence:
4.4.1. AV conduction present: AAI - DDD RV AAI - DDD LV AAI DDD BIV AAI
4.4.2. AV conduction absence: DDD RV DDD LV DDD RV - DDDBIV DDD RV
4.5. After switching pacing modes, 10 seconds is allowed to reach stability.
4.6. Data are obtained for a period of 20 seconds and thereafter the collected data will be averaged. Baseline is defined as the average of either AAI or DDD RV pacing preceding and following each pacing mode.
5. Pressure measurements (intra-operative):
6. LV pressure: systolic and end diastolic pressure
7. LV dP/dt max: maximum rate of pressure rise in the left ventricle during isovolumetric contraction (first derivate of LV pressure; mmHg/s)
8. LVEDP: left ventricular end diastolic pressure (mmHg).
9. Arterial blood pressure: systolic, diastolic and mean.

Echocardiographic measurements and transpulmonary thermodilution measurements; pulmonary blood volume (PBV) and intrathoracic blood volume (ITBV):
A Pulsiocath 5 F thermistor tipped catheter (Pulsion Medical Systems, Munich, Germany) is placed in the femoral artery instead of a radial artery catheter. To determine cardiac output (CO), PBV and ITBV; 20 ml of cooled saline (0-6°C) is injected into a central venous catheter.

Echocardiographically, the velocity time integral (VTI) is recorded from a deep transgastric view of the LV outflow tract; its diameter is measured by using a midesophageal long axis view. Cross-sectional area multiplied by VTI and heart rate yields cardiac output.
PBV and TCBV are measured before CPB, directly after implementation of CRT and before extubation.
Blood volume measurements are performed by injecting an UCA bolus of 0, 2 ml Sonovue® (Bracco, s.p.a Milan Italy) in 20 ml ice-cold saline intravenously. this enables a simultaneous measurement of the blood volumes with the Pulsiocath in the femoral artery as with echocardiography.
The ultrasound scanner was set in harmonics general at 2.4-4.8 MHz and a low driving pressure (mechanical index 0,1). For 180 sec after injection multiple digital loops of RV outflow tract view are recorded for the measurement of the RV and LA UCA indicator dilution curves (IDCs). Measurement of acoustic intensity for the IDCs are performed in a region of interest using Qlab software (Philips Medical Eindhoven Netherlands) placed in the RV and LA. These IDCs are fitted by the local density random walk model and analyzed. The ÄMTT is estimated from the IDCs and multiplied times CO to obtain PBV estimate. The recirculation curve fit is estimated in ROI placed in the RV in order to assess the Total Circulating Blood Volume.

Definition of responders:
Responders will be qualified by an increase of > 10% in LV dP/dtmax compared to baseline.

Postoperative protocol (standard care):
1. Patients will be paced with the pacing sequence with optimal LV dP/dtmax provided an increase of at least 10% to baseline, otherwise no pacing is advised.
2. Hemodynamic measurements are obtained using echocardiography by measuring PBV and TCBV

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Changes in left ventricular pressures, pulmonary blood volume, intrathoracic blood volume and total circulating blood volume after biventricular pacing in comparison with the patients own rhythm and right ventricular pacing.

Key secondary outcome(s))
Perioperative changes in hemodynamic performance after biventricular pacing.

Completion date
01/01/2015

Eligibility

Key inclusion criteria
1. Age 18 years or over
2. Patients scheduled for coronary artery bypass grafting surgery (CABG) and/or valve surgery
3. Left ventricular ejection fraction of 35% or less
4. Sinus rhythm with one of the following criteria:
4.1. QRS duration of > 130 ms and left bundle branch pattern
4.2. Pacemaker-dependent patients with right ventricular paced rhythm and QRS width of > 180 ms
4.3. Evidence of left ventricular dyssynchrony with Tissue Doppler Imaging (TDI)
5. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Myocardial infarction within the past 3 months
2. A history of gastric or esophageal disease
3. Allergy to sulphur hexafluoride

Date of first enrolment
29/01/2010

Date of final enrolment
01/01/2015

Locations

Countries of recruitment
Netherlands

Study participating centre
Michelangelolaan 2
Eindhoven
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Sponsor information

Organisation
Catharina Hospital Eindhoven (Catharina Ziekenhuis Eindhoven) (Netherlands)

ROR
https://ror.org/01qavk531

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Catharina Hospital Eindhoven (Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2015	29/05/2020	Yes	No