Real-time Pressure volume Loop monitoring as a guide for enhanced Understanding of changes in elemental cardiovascular physiology during Therapeutic strategies aiming for hemodynamic Optimization. Cohort II: Structural heart interventions (PLUTO-II).

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The primary objective of this study is to describe and to quantify the change in cardiac mechanoenergetics, expressed by PVL monitoring (reflected by the parameters stroke work, potential energy and pressure-volume area), in patients undergoing...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac valve disorders
Study type	Observational invasive

Summary

ID

NL-OMON51694

Source
ToetsingOnline

Brief title
PLUTO-II

Condition

- Cardiac valve disorders
- Cardiac therapeutic procedures

Synonym

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Valvular dysfunction, valvular insufficiency

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Mitraclip), mitral TEER (Transcatheter Edge-to-Edge Mitral valve Repair, PV (Pressure-Volume) loops, TAVI (Transcatheter Aortic Valve Implantation), Triclip), tricuspid TEER (Transcatheter Edge-to-Edge Tricuspid valve Repair

Outcome measures

Primary outcome

The main study endpoints comprise the differences in cardiac mechanoenergetics in individual patients, measurements before the intervention will be compared to measurements obtained immediate following the structural heart intervention in all cohorts. Cardiac mechanoenergetics are reflected by the parameters stroke work (SW, mmHg ml-1) and potential energy (PE, mmHg ml-1), together forming the pressure volume area (PVA, mmHg ml-1). SW, PE and PVA are obtained using real-time PVL measurements. Study parameters will be investigated for both ventricles, irrespective of study cohort.

Secondary outcome

Secondary endpoints of the study are differences in the following parameters, all derived from PVL plots and subsequent calculations. According to the primary endpoints, measurements before the intervention will be compared to measurements obtained immediate following the structural heart intervention. All parameters will be investigated for both the left and right ventricle,

irrespective of study cohort. The following parameters will be investigated:

• Stroke volume (SV, mL).

• Preload recruitable stroke work (PRSW in mmHg ml-1, calculated as SW / EDV) (reflecting myocardial contractility, largely independent of heart size).

• Tau (reflecting lusitropy in ms).

• Intraventricular dyssynchrony (in % on a systolic as well as diastolic level).

• dP/dt (reflecting the maximal and minimal intraventricular pressure changes in mmHg s-1 as dP/dt max and dP/dt min).

• End-systolic elastance (Ees) and effective arterial elastance (Ea), both in mmHg -1 with Ees/Ea indicating ventricular-arterial coupling.

• End-diastolic volume (EDV, mL).

• End-diastolic pressure (EDP, mmHg).

• End-diastolic pressure-volume relation (EDPVR, mmHg mL-1).

• EDV / dP/dt max (reflecting the myocardial contractile state).

• End-systolic volume (ESV, mL).

• End-systolic pressure (ESP, mmHg).

• End-systolic pressure-volume relation (ESPVR, mmHg mL-1).

• Starling contractile index (SCI, dP/dt max / EDV) (the preload adjusted contractility index in mmHg s-1 ml-1).

• SW / PVA ratio (an index of ventricular function and efficiency from perspective of cardiomechanics).

• V0 (mL, ventricular volume at 0 mmHg) (for the correct interpretation of ESPVR).

• V15 (mL, ventricular volume at 15 mmHg) (as a guide for RV contractility).

• V30 (mL, ventricular volume at 30 mmHg (reflecting ventricular compliance).

• V100 (mL, ventricular volume at 100 mmHg (reflecting LV contractility).

• Ventricular stiffness constant β (ml-1).

The following parameters will also be obtained at the time of PVL measurement (i.e. before and after the structural heart intervention):

• Cardiac output (L min-1 measured by thermodilution, making use of a Swan-Ganz pulmonary artery catheter). Cardiac output measurements facilitates stroke volume estimation, necessary for the volumetric calibration of PVL estimates). Both forward as well as power cardiac output will also be obtained.

• PAP and PCWP (both in mmHg).

• Level of vasopressor and inotropic drug support (e.g. norepinephrine in x µg kg min-1), defined according to the vasoactive-inotropic score (VIS) (25).

• Details obtained from routine cardiac imaging (transthoracic or transesophageal echocardiography or CT) assessments during procedural work-up, especially focussing on ventricular dimensions and valvular (mal)functioning.

During a 30-day follow-up (irrespective of study cohort), patient records will be screened for all-cause mortality, hospital and ICU stay (in days) and necessity for vasopressor in inotropic drug support. The following laboratory results (available results closest following surgery) will be copied from patient records (no additional blood test required): creatinine level (µmol L-1), NT-pro-BNP (pmol L-1) and high-sensitive troponin T level (ng L-1). Acute

kidney failure in the 30-day follow-up period will be defined according to 2005 KDIGO guidelines (26). Patients records will also be screened 1 month and 1 year following the structural heart intervention to appreciate patient morbidity as well as routine echocardiographic quantifications reflecting ventricular dimensions and valvular (mal)functioning.

Study description

Background summary

Pressure-Volume Loop (PVL) monitoring is a monitoring tool for the direct visualization of individual cardiac and hemodynamic physiology, including parameters reflecting cardiac mechanoenergetics (a derivative of the myocardial metabolic demand, reflected by the parameters stroke work, potential energy and pressure-volume area) as well as the ventricular-arterial coupling. The concepts surrounding changing (biventricular) cardiac and hemodynamic physiology induced by structural heart interventions, including Transcatheter Aortic Valve Implantation (TAVI), Transcatheter Edge-to-Edge Mitral Repair (mitral TEER) and Transcatheter Edge-to-Edge Tricuspid Repair (tricuspid TEER) are largely based on hypotheses, computer simulations and non-invasive (echocardiographic) estimations. PVL monitoring has the potential to identify unique characteristics of TAVI, mitral and tricuspid TEER from the perspective of changing baseline cardiovascular physiology, including (a change in) interference between both ventricles (i.e. the ventricular crosstalk). Perprocedural (biventricular) PVL monitoring can be of direct clinical relevance given the ability of PVL monitoring to appreciate the ventricular tolerance of increased cardiac afterload induced by the particular intervention in individual patients. In future, real-time PVL analysis can be adjunctive to the individual decision-making process during routine structural heart interventions.
A substudy will be added to the protocol investigating the interaction between PEEP and LV Pressure-Volume Area for patients who will undergo mitral TEER.

Study objective

The primary objective of this study is to describe and to quantify the change in cardiac mechanoenergetics, expressed by PVL monitoring (reflected by the parameters stroke work, potential energy and pressure-volume area), in patients undergoing structural heart interventions. Study objectives will be investigated throughout multiple patient cohorts addressing structural heart

interventions: patient undergoing TAVI (cohort A), mitral TEER (cohort B) and tricuspid TEER (cohort C).

Secondary objectives of this study are:
(1) to assess the change in different parameters reflecting cardiac and hemodynamic physiology induced by structural heart interventions, derived from PVL-monitoring, beyond the change in cardiac mechanoenergetics
(2) to compare changes in cardiac and hemodynamic physiology (derived from PVL-monitoring) induced by structural heart interventions, between patients with improved or stabilized functional capacity versus worsening in functional capacity (reflected by New York Heart Association (NYHA) class)
(3) to assess changing interventricular dependence (i.e. the ventricular crosstalk) induced by endovascular valvular interventions, expressed by biventricular PVL measurements.
(4) for cohort A: to investigate the hemodynamic impact of ventricular tachypacing during TAVI on PVL-derived parameters reflecting cardiac and hemodynamic physiology, including an appraisal of (the physiological effects of) conceivable ventricular stunning

Study design

Single-center prospective observational (non-therapeutic, medical device) study with invasive measurements.

Study burden and risks

Participating in the PLUTO-II trial does not offer any benefit to the included patient, apart from ameliorating (scientific) perspectives regarding cardiac physiology surrounding structural heart interventions as well as regarding hemodynamic research in general. Study questions could not be answered without participation of patients belonging to the study group in question (i.e. patients undergoing elective TAVI, mitral TEER or tricuspid TEER) and the study is thereafter considered group-related. The risks and burden directly attributable to study participation are considered moderate. Potential complications directly attributable to invasive PVL monitoring are comparable to diagnostic heart catheterization, including (groin) hematoma, retroperitoneal bleeding, pseudoaneurysm, arteriovenous fistula, vascular dissection, thrombosis and embolism, death, myocardial infarction, stroke and arrhythmia. Diagnostic heart catheterization includes a risk for developing major complications of less than 1% and a mortality risk of 0.05%. Additional vascular access including sheath insertion might be mandatory for pressure-volume loop monitoring. Of note, the aforementioned risk is already present and inherent to the scheduled intervention. Swan-Ganz pulmonary artery catheter insertion is always necessary, allowing thermodilution-based volumetric calibration of PVL measurements. The insertion of a Swan-Ganz pulmonary artery catheter comprehends a risk of possible complications,

including development of pulmonary infarction, vascular lesions as well as morbidity directly attributable to central venous access, but can be customary in structural heart interventions. The incidence of complicated Swan-Ganz insertion is estimated between 2 and 17%, with an incidence of pulmonary artery lesions between 0.1 and 1.5% and puncture site infection approaching 17% (the latter increasing with prolonged Swan-Ganz insertion). Individual enrolled patients do not benefit from participation in this prospective study.
Potential complications of the alveolar recruitment (e.g. barotrauma and hemodynamic instability) are considered negligible as the safe airway pressure threshold (defined as Peak Pressure < 40 cmH20) will be safeguarded continuously during the study measurement.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Scheduled for TAVI.
- Scheduled for mitral TEER (Mitraclip).
- Scheduled for tricuspid TEER (Triclip).

Patients undergoing elective TAVI, mitral TEER or tricuspid TEER are eligible for study participation irrespective of device specifications or device manufacturer. Such technical details, (including valve size or brand), do not preclude study eligibility.

Exclusion criteria

- Age < 18 years.
- Confirmed or suspected (concomitant) congenital heart disease.
- Mechanical circulatory support (including Impella, PulseCath, Intra-Aortic Balloon Counterpulsation or Extracorporeal Membrane Oxygenation) used during the procedure aiming for improved cardiac output.
- No (written) informed consent was obtained.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-11-2022
Enrollment:	157
Type:	Actual

Medical products/devices used

Generic name:	Conductance catheter
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	13-10-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL79303.078.22
Other	Wordt t.z.t. geregistreerd