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STUDY DESIGN

Design and rationale of haemodynamic guidance with CardioMEMS in patients with a left ventricular assist device: the HEMO-VAD pilot study

Jesse F. Veenis¹ , Olivier C. Manintveld¹, Alina A. Constantinescu¹, Kadir Caliskan¹, Ozcan Birim², Jos A. Bekkers², Nicolas M. van Mieghem¹, Corstiaan A. den Uil^{1,3}, Eric Boersma¹, Mattie J. Lenzen¹, Felix Zijlstra¹, William T. Abraham⁴, Philip B. Adamson⁵ and Jasper J. Brugts^{1*}

¹Department of Cardiology, Erasmus MC Thoraxcenter, Rotterdam, The Netherlands; ²Department of Cardiothoracic Surgery, Erasmus MC Thoraxcenter, Rotterdam, The Netherlands; ³Department of Intensive Care Medicine, Erasmus MC Thoraxcenter, Rotterdam, The Netherlands; ⁴Division of Cardiovascular Medicine, The Ohio State University, Columbus, OH, USA; ⁵Division of Cardiology, Oklahoma Foundation for Cardiovascular Research, Oklahoma City, OK, USA

Abstract

Aims We aim to study the feasibility and clinical value of pulmonary artery pressure monitoring with the CardioMEMS™ device in order to optimize and guide treatment in patients with a HeartMate 3 left ventricular assist device (LVAD).

Methods and results In this single-centre, prospective pilot study, we will include 10 consecutive patients with New York Heart Association Class IIIb or IV with Interagency Registry for Mechanically Assisted Circulatory Support Classes 2–5 scheduled for implantation of a HeartMate 3 LVAD. Prior to LVAD implantation, patients will receive a CardioMEMS sensor, for daily pulmonary pressure readings. The haemodynamic information provided by the CardioMEMS will be used to improve haemodynamic status prior to LVAD surgery and optimize the timing of LVAD implantation. Post-LVAD implantation, the haemodynamic changes will be assessed for additive value in detecting potential complications in an earlier stage (bleeding and tamponade). During the outpatient clinic phase, we will assess whether the haemodynamic feedback can optimize pump settings, detect potential complications, and further tailor the clinical management of these patients.

Conclusions The HEMO-VAD study is the first prospective pilot study to explore the safety and feasibility of using CardioMEMS for optimization of LVAD therapy with additional (remote) haemodynamic information.

Keywords LVAD; HeartMate 3; CardioMEMS; Heart failure; Telemonitoring; Implantable haemodynamic monitoring

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*Correspondence to: Jasper J. Brugts, Department of Cardiology, Erasmus University Medical Centre, 's Gravenhijkwal 230, 3015CE Rotterdam, The Netherlands.
Email: j.brugts@erasmusmc.nl

Introduction

As the prevalence and incidence of heart failure (HF) keeps increasing, more and more patients develop end-stage HF despite improved medical management.^{1–3} About 10–15% of the HF patients develop advanced HF every 3 years and become refractory to drug therapy, leaving heart transplantation or haemodynamic support by left ventricular assist device (LVAD) implantation as the only therapy option.¹

Experience with LVADs is rapidly growing worldwide; however, mortality and morbidity of this advanced therapy remains high. LVAD therapy is life-saving but remains an intensive complex treatment with high rehospitalization rates

and outpatient clinic contacts.⁴ Recently, novel LVAD designs have improved post-operative outcomes with a marked reduction in pump thrombosis and cerebrovascular accidents,⁵ but bleeding, driveline infections, and long-term right ventricle (RV) failure continue to impair the long-term efficacy of this intervention.^{6–8} Patients with long-term LVAD therapy remain particularly vulnerable for RV failure, with up to 20–40% of the patients developing early RV failure^{5,9,10} and 15% late RV failure.¹¹ Severe RV dysfunction remains the leading cause of death in the first month after LVAD implantation.^{12,13} There is a growing clinical demand for physicians to have better ways to predict response to treatment as well as tailor clinical management in these patients. Currently, the pump controller only

reflects a fixed number of rotations per minute (rpm) and notifications of a calculated pump flow and pulse index of the device itself but no actual haemodynamic feedback.

The CardioMEMS™ pulmonary artery (PA) sensor allows frequent remote monitoring of haemodynamic information, with proven effectiveness in reducing HF hospitalizations by maintaining normal pulmonary artery pressure (PAP) as surrogate markers of filling pressures (which rise in eminent decompensation) in chronic HF patients.^{14,15} An innovation would be to combine two state-of-the-art strategies such as LVAD therapy and guidance by PA monitoring in order to improve the outcome in this complex patient category and reduce the high burden of complications by early detection of pressure shifts. New insights will be provided by such haemodynamic feedback in order to tailor therapy in this patient group as well as to learn more on RV dynamics and pulmonary hypertension during long-term treatment with daily haemodynamic data. In order to study the feasibility and clinical value of the hybrid construction of CardioMEMS and HeartMate 3 (HM-3), we present the pilot study design to address this hypothesis in LVAD patients.

Study design

This is an investigator-initiated, single-centre, prospective pilot study enrolling 10 consecutive patients who undergo a scheduled semi-elective or elective implantation of an HM-3 LVAD. The decision for LVAD therapy will be established by heart team consensus. Before LVAD implantation, all patients will receive a Swan–Ganz right heart catheterization, and a CardioMEMS PA sensor will be implanted to measure PAP. This study has been approved by the ethics committee (MEC no. 2017-342), and the study will be conducted according to the Helsinki declaration, with all patients providing informed consent prior to participation. The study is registered at clinicaltrials.gov under NTR 2017-6804.

Study population

The HEMO-VAD pilot study involves 10 patients with New York Heart Association functional Class IIIb or IV with Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) Classes 2–5, who undergo a scheduled implantation of an HM-3 LVAD at the Erasmus MC Thoraxcentre, Rotterdam, The Netherlands. Inclusion criteria are presented in *Table 1*, and exclusion criteria are presented in *Table 2*.

Table 1 Inclusion criteria

- Age \geq 18 years
- LVEF $<$ 25%
- NYHA Class IIIb or NYHA Class IV with INTERMACS Classes 2–5
- Scheduled for LVAD implantation within 1 month after heart team consensus
- Life expectancy $>$ 1 year
- Body surface area \geq 1.2 m² and chest circumference, at the axillary level, of less than 65 in. if BMI $>$ 35 kg/m²
- Signed informed consent form

BMI, body mass index; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; NYHA, New York Heart Association.

Table 2 Exclusion criteria

- No signed informed consent form
- INTERMACS 1 emergency LVAD implantations
- Patients with a known coagulation disorder or hypersensitivity to aspirin
- Intolerance to anticoagulant or antiplatelet therapies
- Patients with contraindications for the PAP sensor device, which will include active infection, a history of deep vein thrombosis or recurrent pulmonary embolism, mechanic right heart valve, or unable to tolerate Swan–Ganz
- History of pulmonary embolism within 30 days prior to enrolment or history of recurrent ($>$ 1 episode) pulmonary embolism and/or deep vein thrombosis
- History of stroke within 90 days prior to enrolment or a history of cerebrovascular disease with significant ($>$ 80%) uncorrected carotid stenosis
- Serum creatinine \geq 221 μ mol/L or CKD-EPI eGFR $<$ 25 mL/min not related to cardiac condition or the need for chronic renal replacement therapy
- Psychiatric disease/disorder, irreversible cognitive dysfunction, or psychosocial issues that are likely to impair compliance with the study protocol and LVAD management

CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; PAP, pulmonary artery pressure.

Objectives and endpoints

The objectives of this study are as follows:

- to investigate the feasibility and safety of using haemodynamic guidance by the CardioMEMS PA sensor in LVAD HM-3 patients,
- to investigate the information provided by haemodynamic data of CardioMEMS PA sensor in relation to incident LVAD complications prospectively, and
- to study haemodynamics (PAP) preoperatively and post-operatively of LVAD surgery.

The proposed impact and goals of haemodynamic guidance in LVAD patients are further shown in *Table 3*. All study endpoints are shown in *Table 4*.

Table 3 Proposed impact and goals of CardioMEMS in LVAD

Phase A: Pre-LVAD optimization phase	<ul style="list-style-type: none"> • Improve patient selection pre-LVAD implantation • Evaluate timing of LVAD implantation • Optimizing clinical patient status towards surgery <ul style="list-style-type: none"> - INTERMACS class pre-LVAD implantation
Phase B: Clinical phase	Guide post-cardiac surgery treatment Early discovery of major complication, such as: <ul style="list-style-type: none"> • RV failure • Tamponade • Infection
Phase C: Outpatient monitoring phase	Guide LVAD therapy remotely Evaluate further improvement of PA-guided LVAD pump settings Decrease the high rate of HF-related hospitalizations (70% first year) Early discovery of late complications of LVAD Evaluate pulmonary hypertension on LVAD therapy

HF, heart failure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory; LVAD, left ventricular assist device; PA, pulmonary artery; RV; right ventricle.

Study overview: CardioMEMS allocation and patient flow

The study can be divided into three phases (A–C), as is shown in *Figure 1*. The different phases are described below.

Phase A: Pre-left ventricular assist device optimization phase (1 week)

Every consecutive patient, who is accepted by the heart team for scheduled LVAD implantation (both destination therapy and bridge to transplant), is screened for eligibility to participate in the HEMO-VAD study. After the heart team decision has been taken to plan an LVAD implantation, the CardioMEMS sensor is implanted as soon as possible, that is, at 0–1 day. LVAD implantation is to be scheduled with the aim within 1 week in semi-elective to elective patients, with minimum 1 day and maximum within 4 weeks after heart team consensus.

After enrolment and informed consent, but prior to HM-3 implantation, subjects will be implanted with the CardioMEMS HF system. The baseline visit ($t = 0$) includes the day of the right heart catheterization (Swan–Ganz) occurring in all patients and the implantation of the CardioMEMS PA sensor in the left lower lobe PA. PAP data will be utilized to guide adjustments of medical therapy (e.g. diuretics, vasodilators, and inotropes or phosphodiesterase inhibitors) for optimization of the haemodynamic status prior to HM-3 implantation, with the aim to improve the pre-LVAD INTERMACS class, which is one of the best parameters of outcome. The main objective is to ensure optimal status to decompress venous congestion (unloading) of the RV and

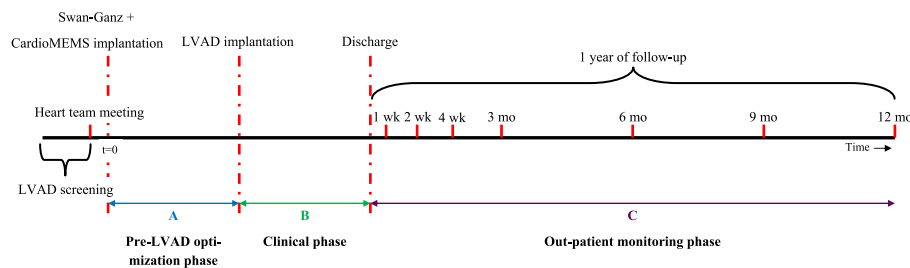
Table 4 Study endpoints

Primary end points	<ul style="list-style-type: none"> - Safety of the hybrid construction of CardioMEMS and LVAD - Feasibility of the hybrid construction of CardioMEMS and LVAD - Clinical endpoints defined as <ul style="list-style-type: none"> • Number of HF-related hospitalizations • Number of LVAD related complications (such as tamponade, RV failure, GI bleeding, infection, pump thrombosis, and haemolysis)
Secondary endpoints	<ul style="list-style-type: none"> - The number of improvements in INTERMACS classes during pre-operative optimization phase - Time to reach optimal condition for surgery in the pre-operative phase (days) - Predictive value of PAP during follow-up in outpatient clinic LVAD patients of risk of RV failure, GI bleeding, suboptimal fluid balance, and development of long-term aortic valve insufficiency - Monitoring of PAP and pulmonary hypertension and reversibility of pulmonary hypertension in LVAD patients - Detection of arrhythmia and heart rate monitoring with CardioMEMS in LVAD - Feasibility of pump optimization using CardioMEMS during rpm test and number of pump changes - Changes in quality of life (KCCQ, EQ-5D-5L, and PHQ-9) - 6MHWd post-HM-3 implantation and changes during outpatient clinic phase - HF medication changes (counts and TDD) during pre-LVAD implantation phase, post-LVAD implantation phase, and outpatient clinical phase - Iron deficiency before and after LVAD treatment, incidence of GI bleeding, and the relationship with PAP and early discovery of occult blood loss - Change in renal function in relation to PAP and diuretic medication dosage - LDH, PAP, and the incidence of pump thrombosis and haemolysis in LVAD patients - Number of days hospitalized, number of days requiring inotropic support, and number of physical contact in the outpatient clinic - Percentage of days PAP in goal range, changes in PAP from baseline, and analysis of PAP waveforms in LVAD

GI, gastrointestinal; HF, heart failure; HM-3; Heart Mate 3; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; KCCQ, Kansas City Cardiomyopathy Questionnaire; LDH, lactate dehydrogenase; LVAD, left ventricle assist device; PAP, pulmonary artery pressure; PHQ-9, Patient Health Questionnaire 9; rpm, rotations per minute; RV, right ventricle; TDD, total daily dose; 6MHWd, 6 min hall walk distance.

mean PAP (mPAP) below 25 mmHg. Recommendations for these adjustments will be provided with options for the physician as deemed clinically appropriate.

In this PAP-guided phase prior to LVAD implantation, the physician will use the PAP obtained by the sensor to optimize the patient condition and fluid status proceeding towards LVAD surgery. This contains optimal fluid status (euvoemia) and lowered right heart pressures (unloading the RV) to optimal capacity as judged by the treating clinician, laboratory values, and echocardiographic parameters. The clinician normally uses a treatment course of phosphodiesterase inhibitors or inotropes and titrates diuretics, angiotensin-converting enzyme inhibitors, and nitrates dosages. Another aspect of the pre-LVAD optimization phase is to learn more

Figure 1 Study overview. LVAD, left ventricular assist device.

on optimal timing window of LVAD surgery. When optimal timing window to proceed to LVAD surgery is reached, the HM-3 implantation follows. Based on clinical judgement or clinical urgency, this timing can be adjusted.

Phase B: Clinical phase

After LVAD implantation, the patients will be admitted to the intensive care unit (ICU), where patients will receive regular care. At the ICU, potential interference between the implanted PAP sensor, LVAD controller, and potential other equipment will be tested, as an important part of the feasibility and safety of this novel hybrid construction. In addition to the regular care, daily pressure readings provided by the CardioMEMS system will be used to guide HF treatment, according to the predefined goals: diastolic PAP will be targeted and maintained between 8 and 15 mmHg as well as mPAP below 25 mmHg. Furthermore, PAP changes might indicate the presence of complications such as RV failure, infection, or cardiac tamponade, on top of echocardiography in an earlier stage. At the moment, haemodynamic recordings after LVAD implantation are very limited in the current literature to provide insights in these mechanisms. Recently, a retrospective sub-analysis of the CHAMPION trial provided some information of PAP changes after LVAD implantation, suggesting that additional haemodynamic information has the potential to improve LVAD management.¹⁶ However, information during the hospitalization for LVAD implantation and during potential LVAD-related complications is still lacking.

When clinically stable, patients will be transferred to the HF department. Patients will receive the usual care, and at least once a day, pressure readings will be continued. Haemodynamic feedback will be used for optimizing HF medication titration, leading to tailored therapy (maintain normal PAP), and evaluating haemodynamic changes during potential complications. During admission, LVAD care echocardiography will be performed to optimize pump settings (rpm testing), as is standard care, only with additional pressure feedback for the CardioMEMS system, which will be analysed separately. Furthermore, patients will be trained in using the LVAD device, controller, and exchange batteries as well as operating the home monitoring unit and instructed to take daily PAP measurements.

Phase C: Outpatient monitoring phase (long-term follow-up)

Throughout the long-term follow-up period and subsequent hospitalizations, the pressure data upload will be performed at least daily using the home monitoring system and the Merlin.net website. Pressures will be reviewed remotely at least once a week and more frequently when pressures are outside the target range, on the Merlin.net website, with anticipation of treatment alterations based on maintaining normal PAP. Patients will be followed during regular outpatient clinic visits, approximately at 1, 2, and 4 weeks and 3, 6, 9, and 12 months. During these visits, patients will receive standard care, expanded with specific blood, urinary, and echocardiography parameters, as well as questionnaires on quality of life, and the performance status will be assessed.

Parameters of interest

Primary study parameter(s) of CardioMEMS device

Daily PAP measurements will be performed in the preoperative period towards LVAD implantation, direct post-operative period on ICU, clinical department, and the regular outpatient clinic setting. Measurements record systolic PAP, diastolic PAP, mPAP, mean trend, and heart rate.

Our study protocol will further study PAP in relation to the following:

- serial lactate dehydrogenase levels, international normalized ratio values, and pump thrombosis;
- serial creatinine clearance, urinary samples, and kidney dysfunction;
- serial iron status and gastrointestinal bleeding incidence; and
- serial measurements of quality of life at 3, 6, and 12 months.

Other parameters of interest

Baseline Swan–Ganz measurements (including cardiac index, systolic PAP, diastolic PAP, mPAP, wedge pressures, RV pressures, right atrial pressures, and PA pulsatility index) are

recorded at baseline during CardioMEMS implantation (protocol describing the Swan–Ganz procedure and CardioMEMS implantation is described in detail in *Table 5*). Vasoreactivity is tested during the LVAD screening, using continuous administration of an i.v. vasodilating agent, such as nitroglycerin, in increased dosage. During the entire study, at regular intervals, clinical parameters (such as heart rate, blood pressure, weight, and symptoms of congestion), laboratory results (including standard routine care laboratory results, renal function, haemolysis parameters, iron status, and biomarkers), urine analysis (proteinuria), LVAD parameters log file (rpm, flow, pulse index, power, pulsatility index events, and suction events), echocardiography parameters (such as ventricle dimensions, valve patency, ventricle and vena cava dimensions, tricuspid annular plane systolic excursion, and rpm measurements), electrocardiogram, performance status (New York Heart Association and INTERMACS classification, and 6 min hall walk test), and quality of life questionnaires (EQ-5D-5L, Kansas City Cardiomyopathy Questionnaire, and Patient Health Questionnaire 9) will be assessed.

Device description and implantation procedure

The device description and implantation procedure of the CardioMEMS HF sensor system (Abbott Inc., Atlanta, GA,

Table 5 Swan–Ganz and CardioMEMS implantation protocol

1. Insert, using ultrasound guidance, a 7F balloon-tipped Swan–Ganz pulmonary artery catheter through the femoral vein.
2. Obtain standard Swan–Ganz right heart catheterization pressure reading at RA, RV, PA, and pulmonary capillary wedge pressure. Preferably right pulmonary artery.
3. Obtain the cardiac output using thermodilution (using 10 mL NaCl 0.9% per measurement), calculated as the average of at least three adequate measurements.
4. Introduce the adequate pigtail shaped into the venous sheath and localize the pigtail with fluoroscopy into the left lower pulmonary artery. And perform a standard pulmonary artery angiogram of the left lower pulmonary artery.
5. Perform standard measurements of vessel size and reassure maximum vessel size diameter and anatomical requirements (inner vessel diameter must be >7 mm) suited for CardioMEMS.
6. Insert the CardioMEMS catheter in the left lower pulmonary artery targeted vessel site and confirm adequate positioning by fluoroscopy.
7. Turn the catheter switch button to release the wires of the CardioMEMS sensor, which fixes itself in the pulmonary artery. Confirm adequate positioning of the device by the radiopaque markers with fluoroscopy.
8. Reintroduce the Swan–Ganz catheter and position the catheter in the right pulmonary artery. Start calibrating and equilibrate the CardioMEMS pressure readings with the simultaneous Swan–Ganz pressure readings (nulling of the sensor). Perform baseline measurements and calibration three times and confirm measurements and baseline recordings are identical.
9. Remove Swan–Ganz catheter. Remove the venous sheath from the femoral vein. At preference of the operator, use a closure device for the femoral vein, manual compression, or pressure bandage at the venous puncture site.

PA, pulmonary artery; RA, right atrium; RV, right ventricle.

USA)¹⁷ and of the HM-3 LVAD (Abbott Inc., Pleasanton, CA, USA) have been published previously.¹⁸

Statistical analysis

For the purpose of this study, all data will be recorded on a case report form and introduced into the study database environment. All patient data will be collected by a dedicated research fellow or PhD student. Baseline quantitative data will be presented with mean \pm standard deviation or median with interquartile range when appropriate. In general, statistical analyses in this pilot study will be descriptive in nature. The data will be summarized using descriptive statistics (e.g. *N*, mean, standard deviation, median, minimum, and maximum) or frequency (e.g. *N*, %) as appropriate. Changes in PAP will be measured as area under the curve of PAP relative to the baseline. Changes in quality of life (assessed using EQ-5D-5L, Kansas City Cardiomyopathy Questionnaire, and Patient Health Questionnaire 9) will be analysed. The primary time point for safety analyses is 6 months post-enrolment. The time point for analyses of feasibility and haemodynamic performance is at 6 and 12 months post-enrolment.

Discussion

The HEMO-VAD pilot study is the first prospective study investigating haemodynamic guided management of HM-3 LVAD patients with an implantable pressure sensor (CardioMEMS). The primary goal is to assess the safety and feasibility of this hybrid construction and evaluate its additive value in optimizing treatment in LVAD patients. Reaching and maintaining optimal fluid status and maximizing optimal medical treatment and timing of surgery towards LVAD therapy (preoperative and post-operative stages) are the main focus. Additionally, this study will evaluate the use of frequent remote measurement of PAP to discover early and late complications of LVAD therapy during hospitalization. Finally, we evaluate whether direct haemodynamic feedback can influence outpatient clinical management and optimize pump settings on top of current standard care.

Left ventricular assist device therapy is a complex entity with high risk of mortality and morbidity without clear tools to predict outcome or complications during treatment.^{9,19–23} From a haemodynamic point of view, RV failure is the most common serious complication after LVAD implantation. RV failure after LVAD implantation can be divided into early or late RV failure (<4 weeks and >4 weeks after implantation, respectively). Early RV failure occurs in as much as 20–40%^{5,9} and late RV failure in 15% of LVAD patients.¹¹ Preoperative assessment of RV function is essential in LVAD screening but dependent on filling status and right heart pressures. Prolonged elevated PAP is a major cause of RV failure,

but pulmonary hypertension alone is not a contraindication for LVAD implantation, unless there is already severe RV failure pre-LVAD. One of the caveats is that RV failure after LVAD implantation is highly unpredictable.^{5,12} Current risk assessment scores have limited predictive value and clinical usefulness for predicting LVAD-related complications, especially RV failure.^{9,10,24} Recently, the EUROMACS-RHF risk score has been developed and aims to predict early RV failure and associated mortality after LVAD implantation.¹⁰ At the moment, the best predictive variable for RV failure post-LVAD implantation is RV function prior to surgery as assessed by echocardiography, which largely depends on fluid status, vascular resistance, degree to which pulmonary pressures are elevated, and severity of tricuspid valve regurgitation. Echocardiography can be used to evaluate RV function but correlated poorly with the development of RV failure. Right heart catheterization is the gold standard to assess RV workload and function; however, this is an invasive procedure, performed at one moment in time, and greatly depends on loading conditions at that moment. More tools are needed to adequately predict and assess the risk of post-LVAD RV failure.

We hypothesize that PAP is key in the preoperative stage to deliver the patient to the surgeon in optimal decongested state to lower the impact of the surgery on the RV. After implantation, we hypothesize that PAP can be used as a marker of treatment success of left ventricular (LV) unloading by the LVAD with insight into residual fixed vascular resistance, which may be a target for therapies with the goal of protecting RV function by reducing afterload. Additionally, PAP information may predict potential complications of LVADs such as occult bleeding, haemolysis, or pump thrombosis in association with the fixed measurement from the pump. Better prediction of upcoming RV dysfunction, directed by measuring PAP combined with optimization of therapy based on haemodynamic feedback, might lead to a better LV unloading, lowering the PAP and lowering chances of RV failure.

As described previously, pulmonary hypertension alone is not a contraindication for LVAD implantation. Often PAP and pulmonary vascular resistance normalize several months after LVAD implantation, which cannot be matched by any medical therapy. Furthermore, LVAD implantation appears to be the best tool for reversal of 'fixed' pulmonary hypertension.¹² However, continuous data of PAP after LVAD implantation are not available at this moment. This study will provide novel insights of changes in PAP data during LVAD therapy.

Despite existing risk scores,^{21,25–27} an adequate measuring tool for determining the ideal LVAD implantation timing is still missing. Multiple studies^{13,21,26,27} demonstrated that sicker and more instable patients, indicated by a lower INTERMACS profile, had worse survival outcome than less sick patients, indicated by a higher INTERMACS profile.

It has been shown that an improvement in risk score shortly before LVAD implantation lead to a better outcome after LVAD implantation.²⁵ We hypothesize that the

haemodynamic feedback, provided by the implantable haemodynamic monitoring, will lead to a tailor made, optimized medical therapy pre-LVAD. By doing so, we think that the patient will get in an optimal clinical condition, potentially rising the INTERMACS class from 2 to 3, or 3 to 4. Furthermore, we hypothesize that haemodynamic feedback provides additional information in order to determine the optimal timing of LVAD implantation. We hypothesize that optimizing the patients' clinical condition and the timing of LVAD implantation will lead to a better clinical outcome.

Other research areas of interest

Pulmonary artery pressure data provided by the CardioMEMS during LVAD therapy provide a unique opportunity of a wealth of novel haemodynamic data.

In the post-operative period, one of the major complications of LVAD is bleeding (40%) or tamponade requiring surgical intervention (20%).^{20,22} The clinical diagnosis of tamponade is often missed in this complex patient group, as the pump keeps on providing flow even in the late stages of tamponade.²⁰ In case of tamponade, we expect to detect a decrease in PAP if the pericardial fluid impairs the filling of the right side of the heart; at the left side, located pockets could also impair pump function and increase PAP. CardioMEMS might be a valuable tool to detect the changes in a much earlier stage. In contrary, a major post-operative bleeding might lead to a drop in PAP due to loss of circulating volume. Additionally, in the outpatient clinical phase, the haemodynamic data could provide important feedback on development of frequent complications such as gastrointestinal bleeding (20–40%),^{19,28} pump thrombosis (8–10%),²³ or renal dysfunction (12%)²¹ at an earlier stage.

As described previously,²⁹ filling pressures will rise as a result of congestion. Congestion can be a sign of development of aortic valve regurgitation and pump dysfunction (kinking outflow graft or bent relief), resulting in higher PAP. For example pump thrombosis leads to LVAD dysfunction and impaired LV unloading. This will lead to signs and symptoms of HF and pulmonary congestion.^{23,30}

Additionally, considering renal function,⁸ lowering PAP by better unloading LV and providing better cardiac output will improve renal function. However, when kidney failure occurs and patients' urine production declines, PAP might rise. We will study these issues with separate research subthemes within the HEMO-VAD pilot study.

Limitations

The design of our study has some limitations. Due to the pilot study design we include only a small number of patients, with the aim to test the feasibility of this hybrid construction. Also,

we have not included a control group in the study design, because of the observational nature. Still, the current study is the first prospective study investigating this new hybrid combination of CardioMEMS with an LVAD providing a wealth of novel haemodynamic data. After feasibility is demonstrated, we need to test the clinical value of this concept in a large-scale randomized clinical trial in patients scheduled for LVAD therapy as is currently anticipated.

Conclusions

The HEMO-VAD study will test the safety and feasibility of the hybrid construction of PAP measurements by the CardioMEMS device and LVAD therapy during 6 and 12 months of follow-up.

Conflict of interest

Dr P.B.A. is a salaried employee of Abbott and an adjunct associate professor of physiology at the University of

Oklahoma Health Sciences Center in Oklahoma City, OK, USA. Dr W.T.A. is a consultant to Abbott. All other authors have no conflicts of interest.

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Author Contributions

All authors contributed to the analysis of the data and writing of the report. All authors approved the final version of the manuscript.

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