Combined Pressure and Doppler Flow Velocity Assessment In Pulmonary Hypertension

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In this explorative study, we aim to investigate whether MVR obtained with Doppler flow velocity, is a better predictor of adverse outcome than PVR obtained with Swan-Ganz measurements.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Pulmonary vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON41718

Source
ToetsingOnline

Brief title
COMBO-PH

Condition

- Pulmonary vascular disorders

Synonym
Elevated lung blood pressure, Pulmonary Hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Combowire, Pulmonary Hypertension, Right heart catheterization

Outcome measures

Primary outcome

Study parameters:

- Microvascular resistance obtained using the Combowire

- Pulmonary vascular resistance obtained using Swan-Ganz measurements

Endpoint:

For the prediction of the composite endpoint of all-cause mortality, atrial septostomy, lung transplantation, worsening of WHO functional class, 15% reduction of 6 minute walk test at 1 year.

Secondary outcome

- Pulmonary vascular resistance and microvascular resistance under vasodilated conditions induced by nitric oxide ventilation

- Cardiac output measurements using Swan-Ganz obtained under both resting and vasodilated conditions

CTEPH substudy

- Same Swan-Ganz measurements as in the main study.

- Combowire measurements will be performed proximal and distal to the occlusion site (if deemed technically feasible by the operator), and repeated after

revascularization.

- Combowire measurement in an unobstructed reference artery.

- Optical Coherence Tomography measurements to determine vessel diameter if the patient is revascularized using percutaneous balloon angioplasty. Acquiring the vessel diameter in combination with flow velocity and distal pressure, allows calculation of true microvascular resistance (MVRtrue) in the subtended vascular bed.

1) Paired change in resistance calculated over the obstructed segment before and after angioplasty

2) Paired change in MVRtrue before and after angioplasty

3) Development of the resistance over the obstructed segment and the MVR true at follow-up in both previously obstructed as well as reference vessels in relation to the development of PAP (i.e. needed reductions in resistance over the obstructed segment and MVRtrue for a reduction in 1 mmHg of PAP at a follow-up visit),

Study description

Background summary

Pulmonary hypertension (PH) is an increase of blood pressure in the pulmonary artery, pulmonary vein, or pulmonary capillaries, which can lead to dyspnea, dizziness, fainting, leg swelling and other symptoms. PH can be a severe disease with a markedly decreased exercise tolerance and heart failure. The

underlying cause of PH can be subdivided into five different classes according to the World Health Organization (WHO) classification; pulmonary arterial hypertension, PH due to left sided heart disease, PH secondary to lung disease and/or hypoxemia, chronic thromboembolic pulmonary hypertension (CTEPH) and PH with unclear mechanism. For the diagnosis PH a right heart catheterization is required. Measurements of pulmonary artery pressure (PAP) and cardiac output (CO) of the right ventricle using thermodilution are performed with the use of a Swan-Ganz catheter. If mean PAP exceeds 25 mmHg, the diagnosis of PH is confirmed. Measurements of PAP and CO using the thermodilution method provide no specific information pertaining to the distal pulmonary arterial vasculature. Furthermore, pulmonary arterial flow cannot be assessed in relation to the phase of the cardiac or respiratory cycle and the instantaneous relation between perfusion pressure and flow can also not be assessed. Finally, in the setting of right ventricular overload, tricuspid regurgitation frequently occurs and may cause backflow of the infusate when assessing cardiac output and may hamper the reliability of the measurement.

In the coronary circulation, assessment of blood flow and pressure in the distal coronary artery are readily available using the ComboWire XT® (Volcano Corporation, San Diego, USA) . The ComboWire is a 0.014 inch guidewire equipped with both a distal pressure and Doppler flow velocity sensor, allowing the simultaneous measurement of flow velocity and pressure. In the coronary vasculature, a wealth of data has been documented on the flow, pressure and microvascular resistance (MVR) relationship using this combined assessment of intracoronary Doppler flow velocity and pressure in both physiological and pathological conditions. These measurements are used to estimate prognosis, indicate the need for interventional therapy and to evaluate the result of therapeutic interventions.

In the pulmonary circulation, data on the proximal pulmonary pressure, flow and resistance relationship is abundantly available. The distal vasculature however, remains uncharted territory. Theoretically, MVR derived using Doppler flow velocity, is independent of certain confounding factors such as tricuspid regurgitation or local anatomic variations and thus could provide a more accurate estimate of the localized pulmonary MVR. As such, it is envisioned that it can serve both a diagnostic purpose as well as guide interventional or pharmaceutical therapy.

Study objective

In this explorative study, we aim to investigate whether MVR obtained with Doppler flow velocity, is a better predictor of adverse outcome than PVR obtained with Swan-Ganz measurements.

Study design

This design of this study is a prospective cohort study.
At baseline, additional measurements will be performed during the elective and clinically indicated right heart catheterization. Clinical follow-up will be obtained at 1 year with a visit to the outpatient clinic and at 6 months, 2 years and 5 years via a telephone call. If patients have to undergo a repeat right heart catheterization for clinical indications, measurements will be repeated.

A substudy will take place in patients with a specific type of pulmonary hypertension, namely chronic thromboembolic pulmonary hypertension. For these patients, in addition to the main study Optical Coherence Tomography (OCT) measurement of the distal vessel will also take place. Furthermore, in patients where balloon angioplasty is used to open the vesel, measurements will be repeated after the vessel is openend.

Study burden and risks

For the patients recruited in the study, no specific benefits with regards to the study procedures are anticipated. However, a theoretical benefit is that they will be monitored more strictly than regular care requires because of the study related follow-up visits. Whether this is actually advantageous remains unknown.

With regards to risks, as with any invasive procedure, there are always procedural risks involved both related to the clinically indicated right heart catheterization, but also to the additional study intervention. Arterial dissection, perforation or thrombosis related to the study intervention can all theoretically occur. Given that in the coronary circulation, these complications very rarely occur (own VUmc data between 2012 and 2014: 1 event in 519 coronary arteries measured from 205 patients), and the two previously conducted studies using similar wires in the pulmonary circulation, did not find any safety concerns, we anticipate the risk to be minimal and well below 1%. The study intervention will require the administration of additional radiation (estimated 400 dGy×cm2) and contrast burden (estimated 50-100 cc).

This study does serve clear beneficial scientific purpose, given that it could potentially improve the prognostic power of the index right heart catheterization, which could in turn be clinically relevant in case of treatment selection. The enrolled CTEPH patients will also contribute to this end. Furthermore the substudy will aid in the understanding of the pathophysiology, disease progression and effectiveness of balloon angioplasty in CTEPH.

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

Suspected or proven PH, for which right heart catherization is scheduled
Ability to provide written informed consent
Age between 18 and 90 years old

Exclusion criteria

Pregnancy
Renal failure (defined as eGFR < 30 mls/min/1.73m2, having undergone kidney transplantation or requiring dialysis)
Contrast allergy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2015
Enrollment:	119
Type:	Actual

Medical products/devices used

Generic name:	ComboWire XT
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	22-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL52317.029.15