Study Protocol

Study Title: Portal Vein Flow Variability to Quantify Right-Sided Hemodynamic Congestion: A Proof-Of-Concept study
Study Acronym: PORTAL
Phase of Development: N/A
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Sponsor: UZ Brussel
Coordinating/Principal Investigator: Prof. Dr. Frederik Verbrugge

PROTOCOL SIGNATURE PAGE

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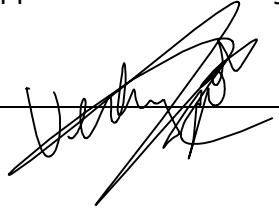
Sponsor: UZ Brussel

Principal Investigator: Prof. Dr. Frederik Verbrugge

I agree:

- to assume responsibility for the proper conduct of this study
- to conduct the study in compliance with this protocol and any future amendments
- not to implement any deviations from or changes to the protocol without prior review and written approval from the Ethics Committee, except where necessary to eliminate an immediate hazard to the subjects, or for administrative aspects of the study (where permitted by all applicable regulatory requirements)
- that I am thoroughly familiar with the appropriate use of the investigational drug, as described in this protocol
- to ensure that all persons assisting me with the study are adequately informed about the investigational drug and their study-related duties and functions as described in the protocol
- that I am aware of and will comply with the current good clinical practice (GCP) guidelines and ethical principles outlined in the Declaration of Helsinki
- to conduct the study in accordance with all applicable laws and regulations

Printed name: Frederik Verbrugge Signature  Date: 30/05/2022

Study Protocol

Portal Vein Flow Variability to Quantify Right-Sided Hemodynamic Congestion (PORTAL):

A Proof-Of-Concept study

Simon Vanhentenrijk M.D. Pharm.D. & Frederik H. Verbrugge M.D. Ph.D.

1. Study design

- Prospective
- Interventional
- Single centre (UZ Brussel)
- Proof-of-concept

2. Purpose & rationale

Right ventricular hemodynamic congestion or elevated central venous pressure (CVP) is an independent predictor of morbidity and mortality in heart failure (1). Persistent elevations of right atrial pressure (RAP) cause upstream venous congestion in the abdominal compartment, which leads to organ dysfunction in liver and kidney function, with effects on the lungs as well (2), (3). According to contemporary echocardiography guidelines, non-invasive assessment of RAP is performed by measuring inferior vena cava (IVC) size and respiratory variation (i.e., collapsibility) (4). However, assumptions that are not always valid (especially in critically ill patients) hamper the use of this technique and misinterpretation due to 'pseudo-collapse' could lead to erroneous interpretation.

Portal vein Doppler flow patterns may be a simple and attractive tool to aid in the evaluation of RAP/CVP and predicts acute kidney injury after cardiac surgery (5). The aim of this proof-of-concept study is to assess the feasibility of portal vein Doppler flow to quantify RAP/CVP in a population of consecutive patients with advanced heart failure undergoing invasive right heart catheterization.

3. Objective

To evaluate the accuracy of the portal vein pulsatility index (PVPI=Vmax-Vmin)/Vmax) to quantify invasively measured right-sided venous pressures.

4. Study population

a. Inclusion criteria

- At least 18 y/o and able to provide informed consent
- Consecutive patients scheduled for right heart catheterisation by a dedicated heart failure specialist at the Centre of Cardiovascular Diseases (University Hospital Brussels, Jette, Belgium)

b. Exclusion criteria

- Major anatomical variations of the portal veins (agenesis of left and right portal vein) and/or arterio-portal vein fistula
- Patients with Child-Pugh B or C liver cirrhosis or liver transplant
- Body Mass Index < 20 kg/m²

5. Intervention

All patients will undergo right heart catheterisation for clinical reasons. As part of the hemodynamic assessment, RAP and CVP assessed at the level of the intrathoracic and intra-abdominal IVC as well as the vena Hepatica is measured. In addition, the hepatic venous wedge pressure (HVWP) is measured.
PVPI is simultaneously obtained using point-of-care ultrasound by placing the transducer at the right hypochondrium/right lateral region of the corpus. Portal vein flow velocity is obtained by using pulsed

wave Doppler measurements of the left portal vein. In addition, a non-invasive measuring device to assess the mechanical energy of the heart by registering its vibrations (i.e., Kinocardiography, HeartKinetics, Waterloo, Belgium) is put on the participant with sticky-gel electrodes. A 90-second measurement is done once the patient is in the supine position. The same measurement is performed simultaneously by a smartphone application with the smartphone placed centrally on the participant's chest.

To minimize interobserver variability, the same sonographic equipment will be used by the same, independent researcher. Measurements are obtained in supine position at the end of the respiratory cycle (end-expiratory). In order to correlate the study outcome with clinical situations, demographic characteristics of the participants are collected.

6. Safety precautions

There are no known risks except for those of the clinically indicated right heart catheterisation. Echocardiography can cause local discomfort and in rare occasions contusion from local pressure. The Kinocardiography device is completely non-invasive as well, although theoretically, there might be some skin irritation due to its attachment with sticky-gel electrodes.

7. Statistical analysis

a. Main statistical analysis

The correlation between PVPI and RAP, CVP and HVWP will be assessed by classic regression and Bland-Altman plots. A regression formula for RAP will be constructed based on PVPI and age, gender, height and weight if the latter are contributory.

8. References

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