Waveform Analysis for Vascular Evaluation and Cardiovascular Advancements in Research and Enhancement

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Primary Objective:Our overall aim is to develop an easy-to-use, and interpretive method for the early detection of valvular heart disease and thoracic aortic aneurysm based on arterial blood pressure waveforms, collected non-invasively. Therefore,...

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

Summary

ID

NL-OMON56849

Source
ToetsingOnline

Brief title
WAVECARE study

Condition

- Cardiac valve disorders
- Cardiac therapeutic procedures
- Aneurysms and artery dissections

Synonym
valvular heart diseases and aneurysms (or dilation of a blood vessel)

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Edwards Lifesciences

Intervention

Keyword: Machine learning, Thoracic aortic aneurysms, Valvular heart disease

Outcome measures

Primary outcome

The primary endpoint of the study is to assess whether the non-invasive arterial pressure waveform measured at the finger level exhibits any distinctive morphological characteristics. In particular, analysis will be focused on the following characteristics:

· Prolongation of the total duration of ejection: systolic phase of the reconstructed aortic pressure waveform

· Prolongation of the systolic upstroke time

· The slope of the pressure rise during systole: dP/dt

· The presence and position of the anacrotic and dicrotic notches

· Alterations of the shape of the pulse contour

· Increase of time-constant of the diastolic phase of the waveform

· The presence of the high-frequency components in the reconstructed aortic

pressure waveform

· Reduction in pulse pressure

Secondary outcome

- Differences in accuracy of the model between males and females

- Differences in the accuracy of the model related to the cause of thoracic

aortic aneurysm such as genetic or age related

Study description

Background summary

Valvular heart disease (VHD) is frequent in industrialized countries. Aortic stenosis (AS) and mitral regurgitation (MR) are the two most common types of VHD affecting millions of people worldwide. Its prevalence is estimated to be between 5-20%, increasing with age and other risk factors such as cardiovascular disease and hypertension. The consequences of VHD can include heart failure, stroke, arrhythmias, and infective endocarditis, which can lead to significant morbidity and mortality. Early diagnosis and treatment are important to prevent or minimize these outcomes..

The treatment of VHD depends on the type and severity of the condition. In cases of mild VHD, lifestyle changes and medications may be sufficient to manage the symptoms, while in others, surgery may be required. The most common surgical treatments for valvular heart disease include valve repair and valve replacement. Minimally invasive procedures, such as transcatheter aortic valve replacement (TAVR) or percutaneous interventions to treat MR such as transcatheter edge to edge repair (TEER) with MitraClip* are also available for certain types of VHD. The choice of treatment will depend on the individual patient's age, overall health, and the specifics of their condition.

When left untreated, VHD is associated with several serious and potentially life-threatening complications, including heart failure, stroke and arrhythmias . It is possible that the treatment of VHD after the manifestation of symptoms

is suboptimal in some patients, as pathophysiological changes could be irreversible. Early diagnosis could prove helpful in expediting treatment, potentially preventing irreversible changes such as decline in left ventricular function. Currently, trans-thoracic echocardiography (TTE) is the gold standard to confirm diagnosis and assess the severity of VHD. However, TTE is not feasible for screening asymptomatic patients and furthermore known to be highly dependent on the skills of the operator. A more simple, non-invasive and feasible way to detect (early) VHD would therefore be very valuable and could potentially be used in the first line and outpatient clinics to screen patients for major valve abnormalities.

VHD is associated with changes in the distal arterial pressure waveforms. For example, AS causes a delayed pressure rise in the aorta, and an increase systolic ejection period, reflected by a prolongation of left ventricular upstroke time, and a decline in steepness of the pressure slope. This affects the general shape of the pressure waveform as measured in the central aorta, but this change in morphology is transmitted and can be measured more distally in the vascular tree as well. Recently, we performed a feasibility study (CoArt study) in which we created a diagnostic machine learning model to detect patients with AS, based

on non-invasive blood pressure features. The model was able to distinguish none to mild AS from moderate to severe AS with a sensitivity of 0.81, specificity of 0.75, and AUROC of 0.82 in a highly predefined population. Further validation in a more general population is important as well as continued improvement of the model towards the diagnosis of other VHD.

Aortic aneurysms (AA) also lead to changes in the pressure wave form by affecting its propagation through the vascular tree. AA of the ascending aorta or abdominal aortic aneurysms (AAA) are usually asymptomatic until rupture or aortic dissection occur, both of which are associated with extremely high mortality. Consequently, the early detection and monitoring of AA is of major importance in reducing mortality and morbidity. Currently, AA are most often detected as coincidental findings by ultrasound, computed tomography, or magnetic resonance imaging, requiring expert knowledge. Developing a machine learning based algorithm for early detection of AA has been shown feasible in silico. To develop a clinical model based on non-invasive blood pressure waveforms may serve as a non-invasive, easily applicable, early screening tool and thus, save lives.

Study objective

Primary Objective:

Our overall aim is to develop an easy-to-use, and interpretive method for the early detection of valvular heart disease and thoracic aortic aneurysm based on arterial blood pressure waveforms, collected non-invasively. Therefore, we will

develop and validate (internally and externally) a machine learning algorithm that can detect major cardiovascular pathologies (moderate to severe - mild to none) in patients scheduled to have surgical correction. We identified the most relevant pathologies, with respect to prevalence and potential detectability.

a) aortic valve stenosis

b) aortic valve insufficiency

c) mitral valve insufficiency

d) thoracic aortic aneurysm

e) healthy controls (matched on age)

Secondary Objective(s):

To determine whether there are differences in accuracy of the model between males and females, and recalibrate the model accordingly

To determine whether there are differences in the accuracy of the model related to the cause of thoracic aortic aneurysm such as genetic (tissue elasticity deficits) or age related (calcification/stiffening of the vasculature)

To compare the waveform characteristics in supine and upright position.

Study design

We will conduct a prospective cohort (data collection study) in two phases. The different phases of the study are depicted in figure 1. Based on our experience in previous algorithm development we expect to analyse up to 10 variables per model, per predicted deviation. Following the widely employed *10 events per variable* rule of thumb, we will include 100 patients per studied deviation.

- Phase 1: Procedure specific, internal validation. In this phase the algorithm is developed including a highly selective population of patients already diagnosed with the disease and scheduled for surgery. Patients with aortic valve stenosis or insufficiency, mitral valve insufficiency, thoracic AA and a healthy control group of 100 patients each.

- Phase 2A: external validation of the algorithm; 150 patients suspected of VHD or AA and scheduled for diagnostic evaluation are included.

- Phase 2B: external validation in another center; 150 patients suspected of VHD or AA and scheduled for diagnostic evaluation are included.

Arterial pressure waveforms will be measured in patients at hospital admission

to obtain waveform data whilst being awake. Electronic data collection of continuous non-invasive arterial pressure waveform signals takes place with the CS/EV1000 system. In addition, we will require de-identified patient medical records, including data from TTE and/or computed Tomography/ Magnetic Resonance Imaging. No interventions will be done in phase 1 and 2.

The patient medical records charts will include demographic information and intermittently

recorded pre, intra, and postoperative data.

Demographic information will include but not be limited to the following:

- Age, Height, Weight, Sex, BMI

- Procedures

- Comorbidities

- Admission Status, etc.

- Patient history

- Premedication

- Medication

- Pre-admittance blood pressure

Intermittently recorded pre, intra, and postoperative clinical data will include but not be limited to the following (based on the monitoring devices used as a standard of care for a specific patient):

- All hemodynamic parameters including, heart rate, blood pressure, SpO2, etc.

- All induction and post-induction medication used, dosing and speed of injection, including vasopressors

- All ventilator variables including respiratory rate and ventilator settings

- Laboratory and microbiology tests

- Patient outcomes

- Hemodynamic and respiratory adverse events

The data collection will take place in the Amsterdam UMC, location AMC in the

Netherlands. The external validation dataset will be collected in a hospital to be determined later.

We estimate that inclusion will take up to 36 months from initiation of study (aim January 2023)

Study burden and risks

Participation in the study will involve non-invasive measurements of blood pressure waveforms. The procedures have no additional risks or benefits. There are no investigational devices used in this study. There are no additional risks associated with the use of the CS/EV1000/HemoSphere monitor other than described in the Instructions for Use. There are also no risks associated with the study procedures.

The study's findings hold potential benefits for both individuals and healthcare systems. The development of a non-invasive, easily applicable screening tool for VHD and AA could expedite early diagnosis and intervention, leading to improved patient outcomes and reduced morbidity and mortality

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

- >18 years of age - informed consent - diagnosed with valvular heart disease or thoracic aortic aneurysm for surgerical procedure - scheduled for coronary artery bypass grafting with good left ventrical function

Exclusion criteria

Subjects of which the non-invasive blood pressure cannot be measured with the finger cuff according to the Instruction for Use of the CS/EV1000 system

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-06-2024
Enrollment:	800
Type:	Actual

Medical products/devices used

Generic name:	ClearSight fingercuff and EV1000 monitor

Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	08-05-2024
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	NL84635.018.23