Assessment of the pathophysioLogical bAsis of local tissue compliaNce using augmenteD iMAging techniques to identify Regional flow dynamiCs (LANDMARC): a study with focus on aorta ascendens

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Aneurysms and artery dissections
Study type	Observational invasive

Summary

ID

NL-OMON53960

Source
ToetsingOnline

Brief title
LANDMARC

Condition

- Aneurysms and artery dissections

Synonym
aortic aneurysm, aortic dissection

Research involving

Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Health Foundation Limburg

Intervention

Keyword: - 4D-flow MR, - Aorta pathology, - Aortic Strain, - Wall Shear Stress

Outcome measures

Primary outcome

- Association between the advanced multimodality imaging parameter WSS (peak

WSS and WSS gradient) and (ascending) aortic strain.

Secondary outcome

- Association between aortic elongation/aortic strain and degree of

cardiovascular tissue fibrosis.

Study description

Background summary

Aorta pathology, under which we consider aortic aneurysm and aortic dissection, is a group of potentially fatal conditions that result from weakening of the aortic vessel wall. Thoracic Aortic Aneurysm (TAA) has an incidence of 5.3 per 100,000 people per year and an expected death rate of 11.8 percent in the presence of an aneurysm exceeding 6 cm. Aortic dissection has an incidence of 5-30 per 1 million people per year and a mortality risk of approximately 70 percent.
Aortic dissection can be classified according to the Stanford Classification System: Type A involves the ascending aorta and may progress to involve the arch and thoracoabdominal aorta, Type B involves the descending thoracic or thoracoabdominal aorta distal to the left subclavian artery without involvement of ascending aorta. Type A dissection is much more common than Type B dissection (2/3rd of cases) and requires urgent surgery because of higher mortality rates, while Type B dissections are typically managed conservatively unless they are associated with complications such as unremitting pain,

aneurysmal expansion, and end-organ ischemia.

Aortic diameter is currently used as a gold standard in international guidelines for prediction of aorta pathology (aortic aneurysm and aortic dissection). Preventive surgical intervention leads to positive outcomes, however, the most immediate moment for prophylactic aortic replacement is difficult to determine. Preventive surgical intervention is therefore only available for patients with severe aortic dilation. There is an indication for preventive surgery of the aortic root and/or aorta ascendens in case an internal diameter of >55 mm is established. Earlier intervention for diameters that have not yet reached these cut-off values (45-50 mm) is required when there has been a rapid increase in diameter (>5 mm each year), an affected family history, a significant aortic valve insufficiency and/or pregnancy wish. However, aortic diameter has proven to be insufficiently accurate for making decisions about well-timed preventive interventions (to prevent, among other things, aortic aneurysm/dissection). This is substantiated by the fact that over 90% of the population fails to meet the guidelines for elective (ascending) replacement and a majority presents themselves with aortic dissection and ruptures with diameters below surgical thresholds. When focusing on acute Type A aortic dissections (ATAC) for example, approximately 60% of the ATAC took place in patients with mean aortic diameters <55 mm and mean aortic diameters of <50 mm were observed in 40% of the patients. While the physics of aortic wall tension support the use of aortic diameter as a reliable metric to base decisions for prophylactic surgery, the concept of *one size fits all* has fallen out of favor in the cardiothoracic community. Thus, additional data is required, and new parameters need to be developed to detect aorta pathology more adequately in an early phase.

Physiological increase in aortic length is part of the physiological aging process, based on powerful pulsating forces within this aorta. This subsequently leads to degradation of elastin fibers and thus structural remodeling. Earlier research within the MUMC+ has confirmed that this physiological increase in (ascending) aortic length is an adequate predictor for aortic pathology, which leads to prevention of acute situation in 28% of the cases. Total increasement of aortic length, based upon CT measures, from age 20 to 80 years turned out to be approximately 66 mm in female and 59 mm in male patients. Moreover, different percentages of increasement could be related to various specific aortic segments: 142% ascending aorta, and 169% aortic arch. Furthermore, additional research projects within the MUMC+ have shown that the increase in aortic length is location dependent. By applying additional markers on the ascending aorta, longitudinal strain (the elongation produced by external stress) could be measured between these attached landmarks. By doing this, a significant difference was observed between the outer and inner curvature of the ascending aorta. For further understanding of the aspects of (location dependent) physiological increase in (ascending) aortic length, data on hemodynamics has proven to be particularly important, because of its association with, among other things, hypertension.

4D-flow MR (four-dimensional flow magnetic resonance imaging) provides comprehensive insight into aortic hemodynamics (wall shear stress, flow eccentricity, flow vorticity). 4D-flow sequences have already been implemented within the MUMC+, causing the project group to have demonstrable expertise with these measurements already. This way, more asymmetrically distributed peak WSS (Wall Shear Stress) values at the outer curvature and decreased WSS values at the inner curvature were discovered, as well as a positive WSS gradient from the sinotubular junction to the proximal ascending aorta. However, the exact relationship between the WSS values (and other important hemodynamic parameters (for example, flow eccentricity and flow vorticity)) and dynamic aortic information (specifically longitudinal strain) remains undiscovered.

Study objective

The LANDMARC study aims to reveal the undiscovered relationship between the WSS values and aortic strain. By doing this, it strives to achieve a better understanding of the origin, pathogenesis, and clinical presentation of cardiovascular disease (with focus on aorta pathology).

The LANDMARC study will take place in line with the FIBAA-bank (*Correlatie tussen cardiovasculaire FIBroseringsgraad en Aorta elongatie, dilatatie en Atria dilatatie (FIBAA-bank): een biobank & databank onderzoek met focus op aorta en atria* (METC-number 2022-3164)). FIBAA-bank is performed under supervision of Dr. E Bidar (Cardiothoracic Surgery Department MUMC+) as well, and is also based on the concept of (hemo)dynamic processes being responsible for the development of cardiovascular pathology. FIBAA-bank demonstrates that adjustments of cardiovascular cells are based on changes in (hemo)dynamic values/processes, and that biomechanical interactions are incredibly important for the functional adaptations of these cells. It also demonstrates that the balance between mechanical stress and tissue properties is said to be disrupted when cardiovascular pathology occurs, which manifests itself through impairment of tissue specific features within concepts such as elasticity and compliance. The FIBAA-bank focusses mainly on correlation of the degree of tissue fibrosis to the degree of aortic elongation. The LANDMARC study, however, aims to link these outcomes to parameters (WSS values) derived from advanced multimodality imaging techniques used specifically for this purpose. This way, our hypothesis, which states that increased aortic WSS values indeed lead to increased (ascending) aortic strain, can be examined.

In combination with data from the FIBAA-bank, the LANDMARC study will hopefully provide more accurate information for future risk stratification models for cardiovascular pathology (with focus on aortic disease).

Primary Objective:
- Indication of the association between WSS (peak WSS and WSS gradient) (through 4D-flow MR and CT) and aortic strain.

Secondary Objective:
- Indication of the association between (hemo)dynamic processes within the body (aortic elongation/aortic strain) and (patho-)physiological changes (degree of cardiovascular tissue fibrosis).

Additional objectives:
- Association between WSS (peak WSS and WSS gradient) (through 4D-flow MR and CT) and aortic diameter.
- Association between flow curves (through 4D-flow MR and CT) and exact location of aortic elongation.

Study design

In this prospective cohort, single-center study, 4D-flow MR and CT will be used to obtain more precise data on (hemo)dynamic processes within the cardiovascular system. Multiple imaging techniques are utilized, so that individual advantages of techniques (e.g. temporal and spatial resolution) can be merged, and advantages will accumulate. Obtained data can then be combined with data extraction from the established biobank in order to achieve a better understanding of the origin, pathogenesis and clinical presentation of cardiovascular disease.

This observational study will take place at MUMC+ within the departments of Cardiothoracic Surgery, Radiology and Cardiology.

Study burden and risks

The LANDMARC study takes place in line with the FIBAA-bank, which received METC approval already (METC-number 2022-3164).

Through the LANDMARC study, patients can undergo additional postoperative imaging. Therefore, participants will undergo more existing advanced imaging techniques than would be necessary in general follow-up. This will be an additional MR-scan with 4D-flow protocol and an additional postoperative CT-scan (CT thoracic aorta).
A (4D-flow) MR does not entail any risks in terms of radiation but takes extra time (approximately 45-60 minutes, where patients have to lay still on their back and occasionally hold their breath a few seconds). The physical burden is therefore very low, which means that the examination can be performed without any problems both immediately after the operation or a few months afterwards. We aim to combine this scan with regular follow-up appointments, so that

patients do not have to visit the hospital more often than necessary according to regular care. The moment at which the scan is performed (directly postoperatively/several months after the operation) has no influence on the final results of the examination. It is therefore wise to wait for a suitable moment with regard to general postoperative follow-up planning in order to combine appointments.
A CT scan will take about 5-10 minutes and will lead to radiation exposure. The estimated effective dose will be less than 10 mSv per scan. This effective dose will be the same as the effective dose used in regular patient care. Therefore, an increased risk or complication rate due to this scan is not expected.

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

Patients who underwent open heart surgery and have participated in FIBAA-bank.

Exclusion criteria

- Patients with abnormal congenital cardiothoracic anatomy, with exception of presence of a bicuspid aortic valve
- Patients with history of chemotherapy, or radiotherapy within thoracic region
- Patients with an age >80 years
- Patients with a weight >120 kg
- Patients with a contra-indication for MRI according to the MUMC+ ODIN protocol nr. 004952
- Patients with impaired renal function (GFR <30)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-04-2023
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO

Date:	05-01-2023
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT05655767
CCMO	NL82141.068.22