Paraplegia Prevention in Aortic Aneurysm Repair by Thoracoabdominal Staging with *Minimally-Invasive Staged Segmental Artery Coil-Embolization*: A Randomized Controlled Multicentre Trial

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

Summary

ID

NL-OMON56465

Source
ToetsingOnline

Brief title
PAPAartis

Condition

- Aneurysms and artery dissections

Synonym
Aneurysm

Research involving

Human

Sponsors and support

Primary sponsor: University of Leipzig
Source(s) of monetary or material Support: European Committee

Intervention

Keyword: - Aortic Aneurysm, - Coil- Embolization, - Paraplegia, - Thoracoabdominal Staging

Outcome measures

Primary outcome

Primary endpoint:

Successful treatment of the aneurysm. That means:

• The patient is alive and without substantial SCI 30 days after treatment, and

• the aneurysm did not rupture and has been excluded within six months of

randomization.

Secondary outcome

The secondary objective of the trial will focus on further potential treatment

advantages and/or risks of the MIS2ACE-procedure.

Secondary endpoints:

• substantial SCI at 30 days after TAAA repair and at one year

• SCI according to the modified Tarlov scale from TAAA repair to one year

• all-cause mortality at 30 days and one year after TAAA repair

• length of stay in intensive care unit (ICU) and intermediate care unit (IMCU)

after TAAA repair

• sub-group analyses for open repair and endovascular repair separately

• re-operation for bleeding (only for open repair)

• cross-clamping times during open surgery

• residual aneurysm sac perfusion, i.e. type II endoleaks (only for

endovascular repair)

• costs and Quality Adjusted Life Years (QALYs) will be estimated over one year

Safety endpoints:

• kidney failure

• respiratory failure

• embolic events

Study description

Background summary

Based on statistics from the USA, one can estimate that 7,500 people per 100 Mio are diagnosed annually with an aortic aneurysm. Left untreated, the prognosis is very poor, since internal bleeding due to a rupture of the aneurysm brings about sudden death. If diameters have reached 60 mm, mortality is estimated to be 11%/year.
The repair of aortic aneurysms is based on conventional stenting techniques. There are three surgical approaches:
• Open TAAA repair involves surgical removal of a section of the aorta and replacing it with a vascular prosthesis.
• Endovascular approach is a much less invasive approach. Small incisions are made to access blood vessels in the groin. A catheter is inserted and used to deploy a stent graft within the aneurysm.
• Hybrid approaches use a combination of these two techniques.

These methods have achieved a remarkable decrease in the incidence of paraplegia and paraparesis, but they still constitute an incidence of up to 20%. At present there is a tremendous need for state of the art and safe strategies for aortic repair which prevent paraplegia - an individual disaster with profound impact on long-term outcomeand health care cost

Study objective

The primary objective is to greatly reduce incidence of ischaemic spinal cord injury (SCI, potentially resulting in permanent paraplegia) and mortality - the most devastating complications resulting from open surgical and thoracoabdominal endovascular aneurysm repair.

Study design

PAPAartis is a multi-national, prospective, open-label, two-arm randomized controlled phase II b trial to demonstrate that a minimally-invasive taged treatment approach can dramatically reduce paraplegia and mortality in patients undergoing thoracoabdominal aortic aneurysm repair.

Intervention

Experimental group: Minimally-Invasive Staged Segmental Artery Coil-Embolization (MIS2ACE, one up to three stages) prior to open surgical repair and/or endovascular repair

Duration of intervention per patient: one up to three sessions of ca. 45 minutes

Control group: receives treatment of aneurysm as usual - open surgical repair and/or endovascular repair without MIS2ACE

Follow-up per patient: one year after TAAA repair Individual treatment period: 12-18 months including follow-up (depends on group)

Study burden and risks

With the exception of trial-specific visits 0, 1 and 4, the treatment will be performed according to standard treatment of an aortic aneurysm as part of the study. For these visits (0/1/4) trial-specific blood samples are required as listed above. It is extremely rare for blood withdrawal to result in haematomas, vascular injuries or nerve injuries, which in some cases can also lead to long-lasting damage. However, care is taken to avoid these complications.
Further examinations of these visits, such as blood pressure measurements, electrocardiogram and neurological examinations are usually without risk.

Trial-specific risks that only affect the MIS2ACE group:

As a result of treatment with the coils/plugs adverse events may occur. There is a possibility that the aneurysm may rupture in between the time prior to the aneurysm repair, which may be several weeks longer in the MIS2ACE group.

The placement of a catheter will occur multiple times as part of the standard care for aneurysm repair. As part of the MIS2ACE treatment, up to three further catheterizations are performed. As a result of the catheter placement, small hematomas and mild pain can occur at the point of entry. Very rarely, bleeding, vascular injuries and the formation of blood clots and fistulas can occur, especially at the puncture site. The rupture and detachment of plaques or blood clots can lead to vascular occlusion.

Although it has never occurred in previous preclinical and clinical trials, it cannot be excluded that the insertion of the coils/plugs causes paraplegia.

The insertion of the coils/plugs takes place under X-ray control and use of contrast agents. X-ray inspection exposes the patients to a maximum of about 20 mSv of radiation as a result of one MIS2ACE treatment. This corresponds to approximately 10-fold of the natural radiation exposure per year in Germany (2.1 mSv). If the patient receives three MIS2ACE treatments, that would correspond to 30-fold of the natural radiation exposure per year in Germany.

Contrast agents can lead on the one hand to allergies and be problematic on the other hand for patients with impaired kidney function. Renal function is therefore continuously monitored in the trial. Patients with stage 4 chronic renal failure are not included in the study.

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

• TAAA, Crawford type I, II or III or type B dissections of comparable extent
• planned open or endovascular repair of aneurysm within four months
• >= 18 years old

Exclusion criteria

• complicated (sub-) acute type B aortic dissection
• ruptured and urgent aneurysm (emergencies)
• untreated aortic arch aneurysm (patients with a previous successful aortic arch aneurysm repair may be included independent of technique used)
• bilaterally occluded iliac arteries or chronic total occlusion of left subclavian artery
• pre-operative neurological deficits or spinal cord dysfunction
• major untreated cardio-pulmonary disease
• life-expectancy of less than one year
• high risk for segmental artery embolism (*shaggy* aorta, i.e. prominent thromboembolic or atherosclerotic debris)
• severe contrast agent allergy, severe reduction in glomerular filtration rate (CKD stage 4)
• expected lack of compliance (e.g. if the patient may not be willing to have several MIS2ACE sessions and the following repair)
• pregnant or nursing women
• impaired thyroid function, if not under stable treatment
• women of child bearing potential without highly effective contraceptive measures
• current participation in other interventional clinical trial
• patients under legal supervision or guardianship

• patients placed in an institution by official or court order

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-11-2021
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO Date:	11-03-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-09-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-02-2022
Application type:	Amendment

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	NCT03434314
CCMO	NL69212.068.19