SEAL - Safety & Feasibility Evaluation of the Aortoseal Endostapling System for seal and fixation of abdominal aortic aneurysms (AAA) endovascular grafts to the aortic wall

Published: 23-07-2024
Last updated: 31-01-2025

The objective of the SEAL Early Feasibility Study (STUDY) is to provide proof of concept and initialclinical safety data for the Aortoseal Endostapling System for the fixation and seal of abdominal aorticaneurysms (AAA) endovascular grafts to the...

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

Summary

ID

NL-OMON57055

Source
ToetsingOnline

Brief title
SEAL

Condition

- Aneurysms and artery dissections

Synonym
aneurysms, endoleak

Research involving
Human

Sponsors and support

Primary sponsor: Endoron Medical Ltd.
Source(s) of monetary or material Support: Endoron Medical Ltd

Intervention

Keyword: AAA Abdominal Aortic Aneurysms, Endostaplingsystem, Endovascular Grafts, fixation

Outcome measures

Primary outcome

The STUDY does not have defined primary endpoints nor any powered endpoints.

The SEAL Study

is not hypothesis driven. All endpoints will be analyzed descriptively. The

limitation of the design for

this study is that there are no pass/fail criteria from a statistical

hypothesis testing.

All endpoints will be analyzed descriptively. Event rates will be analyzed by

calculating the distribution

frequencies and the associated 1- sided 95% confidence limits using an exact

method.

In general, qualitative parameters will be described by their distribution

frequencies; quantitative

parameters will be described by their mean, standard deviation, minimum,

maximum, median, and

number of subjects with assessable data.

For events, such as AEs, deaths and secondary interventions, that can occur or

are observed at any time

during the study, no time window will be applied. For such events, an event

that occurs *within 30

days* is an event that takes place between Days 0 to 30, inclusive. Similarly,

an event that occurs

within 365 days is an event occurring between Day 0 to Day 365, inclusive.

Date of event onset will

be used to determine when the event occurred. Day 0 is referring to the day of

index procedure

(Aortoseal procedure).

10.3. Sub-Groups/Data Presentation

Patients enrolled in the study will either have the Aortoseal Endostapling

System implanted at the same

time as the Medtronic Endurant/Endurant II/IIs Endovascular Graft or in a

secondary procedure. Data

will be presented descriptively as one combined cohort.

Secondary outcome

see above

Study description

Background summary

Abdominal aortic aneurysm (AAA) is a focal enlargement of the abdominal aorta such that the diameter
is greater than 3 cm or more than 50% larger than normal (1). Approximately 80% of aortic aneurysms
occur between the renal arteries and the aortic bifurcation. Aneurysms develop as a result of

degeneration of the arterial media and elastic tissues. Risk factors for AAA are similar to those of(2)
other cardiovascular diseases. The key risk factors are male gender, smoking, age older than 65 years,
coronary artery disease, hypertension, previous myocardial infarction, peripheral arterial disease, and a
family history of AAA. The prevalence of AAA increases with age. It is uncommon in persons younger
than 50 years; however, 12.5% of men and 5.2% of women 74 to 84 years of age have AAA (3).
The natural history of AAA is to enlarge slowly over years. AAA of 4.0-5.5 cm grow at a rate of 0.3
cm/year with less than 25% enlarging 0.5 cm or more per year with larger aneurysms expanding more
quickly than smaller ones. The main risk of an untreated AAA is progressive expansion, leading to
aneurysm rupture or aortic dissection and eventually to death. Rupture occurs most commonly into the
retroperitoneal space; aneurysms may also bleed into the pleural space, gastrointestinal tract, inferior
vena cava, or left renal vein. Symptoms of rupture include abdominal or back pain, hypotension, and a
tender abdominal mass. Embolism of thrombus may result in occlusion of lower limbs. Additional
complications include infection, and embolization. Only about 50% of patients with ruptured AAAs
reach the hospital alive, and for those who reach the hospital, 50% do not survive repair treatment (4).
AAAs account for approximately 11,000 deaths each year in the United States, with mortality rates
from ruptured AAAs reaching up to 90% (5).
Aneurysms producing symptoms, especially pain and tenderness on palpation, are at increased risk for
rupture. AAAs can also present with complications due to thrombosis, embolization or, rarely, as
clinically overt disseminated intravascular coagulation causing hemorrhagic and thrombotic
complications.
The majority of AAAs are asymptomatic and are most often detected as an incidental finding on
ultrasonography (USG), abdominal computed tomography (CT) or magnetic resonance imaging
performed for other purposes. Most AAAs are silent until they rupture, although some (30%) are
identified during evaluation for abdominal symptoms.
The U.S. Preventive Services Task Force (USPSTF) updated its 2005 guideline on ultrasonography

screening for AAA. The USPSTF continues to recommend one-time screening with ultrasonography
for men 65 to 75 years of age with a history of smoking and women 65 years or older who have smoked
or have a family history of AAA(6). The natural history of AAA shows that as aneurysms increase in
size, they expand at a greater rate and the risk of rupture increases. Therefore, in persons found to have
aneurysms, regular surveillance is needed every six months to three years, depending on aneurysm size.

3.2. Standard of Care (Patients with an Asymptomatic AAA)
For AAA, diameter is the most important factor predisposing to rupture. The risk increases significantly
for aneurysm diameters greater than 5 cm for women and 5.5 cm for men (7). An aortic diameter of 5.5
cm is currently considered the threshold for repair in an *average* healthy patient (8). The primary
goal in the management of AAAs is to slow the expansion rate and reduce the risk of dissection or
rupture. Management options for patients with an asymptomatic AAA include observation with followup/medical therapy, open surgical repair and endovascular repair. Each of these options is described in
more detail below:
Medical Therapy/Observation: There is general agreement that small aneurysms, <4.0 cm in
maximum diameter, are at low risk of rupture and should be monitored. Several approaches have been
proposed by the US society of vascular surgery to prevent further enlargement. Smoking cessation is
the most important intervention for a patient with an aneurysm. Patients should be encouraged to seek
appropriate medical management for hypertension, hyperlipidemia, diabetes, and other atherosclerotic
risk factors. A statin and ACE inhibitor should be considered, given the broad potential benefits to
cardiovascular disease and acceptable safety profile. Insufficient data currently exist to recommend use
of doxycycline or roxithromycin. Patients should be counseled that moderate physical activity does not
precipitate rupture or influence AAA growth rate. (9)
The US SVS guidelines recommend that aneurysms >4.9 cm in diameter in women and >5.4 cm in
diameter in men should be repaired in an otherwise healthy patients. Elective repair is also
recommended for patients who present with a saccular aneurysm, and although size guidelines are

currently lacking because of their infrequent presentation, repair is generally recommended at a smaller
diameter. (9)

Open Surgical Repair OSR:
The traditional treatment for AAA is elective open surgery that involves a large abdominal incision and placement of a synthetic graft sutured from the proximal end of the
aneurysm to the distal aorta or iliac segments. Flow is then restored to the lower extremities and the
aneurysm sac is closed over the graft. The graft materials used in stent grafts are typically polyester or
expanded polytetrafluoroethylene (ePTFE). It can be expected that surgical repair will be very durable
and protect from AAA rupture for the lifetime of the patient.(10-14)
Endovascular Repair: The EVAR procedure is a minimally invasive repair technique performed under
aortography, in which a stent graft (endovascular graft) is inserted through the femoral and iliac arteries
to the location of the aneurysm using a delivery system. It was first performed by Parodi et al. in 1991
using a Dacron graft sutured onto balloon expandable Palmaz-Schatz stent. Endovascular stent grafts
rely on radial forces from self-expanding stents for fixation (passive fixation) or self-expansion with
the addition of hooks or barbs (active fixation) to position and secure the device to the aorta. These
devices are designed to prevent aortic pulsatile flow and sheer stresses from being transmitted to the
aneurysmal sac.

To be a suitable candidate for EVAR, certain general anatomic criteria must be fulfilled including an
aortic aneurysm proximal neck diameter that measures 18-32 mm in diameter and is generally
greater than 10 mm in length, a neck angulation that is typically less than 45-60 degrees (depending
on the endovascular graft used), a common iliac artery diameter between 8-22 mm and an external iliac
diameter greater than 7 mm. Anatomy generally unfavorable for EVAR include various anatomic
features such as excessive aortic tortuosity and angulation, a hostile proximal neck with
circumferential calcification, excessive mural thrombus, an extremely conical configuration, and
extremely small-caliber access vessels. There are also other considerations such as the patient*s

inability or unwillingness to comply with post-procedural surveillance imaging. Compared with open surgical repair, EVAR is associated with lower operative mortality risk, lower
perioperative morbidity faster recovery time, and shorter hospital stays (15) (16). Conversely, OSR is
known to be more durable and the repair is likely to last for the rest of the patient*s lifetime

Study objective

The objective of the SEAL Early Feasibility Study (STUDY) is to provide proof of concept and initial
clinical safety data for the Aortoseal Endostapling System for the fixation and seal of abdominal aortic
aneurysms (AAA) endovascular grafts to the aortic wall.
Data from this study will inform a future pivotal clinical study.

Study design

The clinical study is a prospective, non-randomized, single arm, multi-center, open-label Early
Feasibility Study that is designed to provide initial clinical safety data regarding the Aortoseal
Endostapling System.

Intervention

Open Surgical Repair OSR:
The traditional treatment for AAA is elective open surgery that involves
a large abdominal incision and placement of a synthetic graft sutured from the proximal end of the
aneurysm to the distal aorta or iliac segments. Flow is then restored to the lower extremities and the
aneurysm sac is closed over the graft. The graft materials used in stent grafts are typically polyester or
expanded polytetrafluoroethylene (ePTFE). It can be expected that surgical repair will be very durable
and protect from AAA rupture for the lifetime of the patient.(10-14

Study burden and risks

The investigational device is used as an adjunct to endovascular exclusion of an abdominal aortic
aneurysm. There are risks associated with the interaction of the investigational device and the
endovascular graft, as well as the risks associated with a failure to provide

adequate fixation and seal
between the endovascular graft and the aortic neck.

The following device-specific potential risks may possibly be caused by, or associated with, the use of
the investigational device:
• Endovascular graft migration
• Type Ia or III endoleak
• Aneurysm expansion
• Aneurysm rupture.
These observations may require secondary interventions. If left untreated, aneurysm rupture is likely to
result in death.
The following risks may possibly be caused by, or associated with, the investigational device implant
procedure:
• Endovascular graft migration
• Type Ia or III endoleak
• Vascular trauma
• Thromboembolic events

Contacts

Public
Endoron Medical Ltd.

Atir Yeda 21
Kfar Saba 4464316
IL
Scientific
Endoron Medical Ltd.

Atir Yeda 21
Kfar Saba 4464316
IL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age >18
2. Subject has a previously implanted Medtronic Endurant Stent
Graft that
a. has a Type Ia endoleak with >= 8 mm apposition of endovascular graft to the
aorta
b. Or has migrated, but has a length of apposition >= 8 mm
c. Or has a conical neck
Or
3. Subjects diagnosed with a AAA and planned treatment with the Medtronic
Endurant II/IIs Stent Graft due to:
a. AAA >= 5.0 cm in diameter for women and >= 5.5 cm in diameter for men, or
b. Aneurysm is >= 4 cm, and has increased in size >= 0.5 cm within the past 6
months, or
c. Saccular abdominal aortic aneurysm >= 4cm as measured from opposite wall to
the external aspect of the saccular outpouching
And:
Has a AAA proximal neck internal diameter between 19mm and 25mm And has a AAA
neck length of at least 10 mm
4. Internal diameter at the aortic bifurcation >= 18 mm
5. A patent iliac or femoral artery that allows endovascular access to the
aneurysmal site with 18Fr (6.0mm) delivery system
6. Adequate iliac or femoral access that is compatible with vascular access
techniques, devices, or accessories
7. Infrarenal neck angulation of <= 60°
8. Iliac diameters with a range of 8 to 25mm
9. Morphology suitable for endovascular aneurysm repair

Exclusion criteria

1. An inability to provide informed consent.
2. Enrolled in any other interventional clinical study that could interfere
with the outcomes associated with the endpoints for this study.
3. Unable or unwilling to comply with study requirements.
4. More than minimal thrombus, calcification, and/or plaque in the implantation
level of the Aortoseal in the aorta.

5. Planned use of an aortic cuff to provide complete exclusion of the AAA prior to introduction of the Aortoseal Endostapling System into the vasculature.
6. Insufficient circumferential apposition of the endovascular graft to the aorta
7. Insufficient length of apposition (< 8 mm) of the endovascular graft to the aorta
8. Planned use of HeliFX EndoAnchor System.
9. Concomitant TAA or thoracoabdominal aortic aneurysms which upon physician discretion prevents the patient from participating in the study.
10. Requires emergent AAA surgery.
11. Ruptured AAA.
12. Mycotic or inflammatory AAA.
13. Known Genetic connective tissue disorder (e.g., Marfan*s or Ehlers-Danlos Syndromes).
14. Previous open surgical AAA repair.
15. Myocardial infarction and/or major hear surgery within the past 12 weeks.
16. Serum creatinine > 2.0 mg/dL.
17. Active systemic infection.
18. History of bleeding diathesis or hypercoagulable condition and thrombocytopenia.
19. Cerebrovascular incident within 12 weeks prior to the procedure.
20. History of allergy to or intolerance of radiopaque contrast agents that cannot be managed medically.
21. Known sensitivity or allergy to implant materials.
22. Body habitus that would prevent imaging required by the study.
23. Significant comorbid conditions that pose undue risk of general anesthesia or endovascular surgery.
24. Requires additional planned major procedure at the time of AAA repair or within 30 days before or after AAA repair.
25. Cannot discontinue oral anticoagulation or antiplatelet therapy at the time of the study procedure.
26. Pregnant or a lactating female. For females of child-bearing potential, based on a positive pregnancy test within 7 days prior to the procedure or refusal to use a medically accepted method of birth control for the duration of the study.
27. Life expectancy < 2 years.
28. Post-endograft deployment:
Any observation which upon physician discretion could pose potential risk for unsuccessful Aortoseal implantation, (e.g., MAE prior to introduction of the Aortoseal into the vasculature, use of a cuff or HeliFX, graft material covering a renal artery)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-11-2024
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Aortoseal Endostapling System
Registration:	No

Ethics review

Approved WMO Date:	23-07-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-11-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL85488.000.23