# MRI Investigation in Transcatheter Aortic Valve replacement with Claret: a randomized study to assess by MRI the reduction in cerebral embolic lesions during Transcatheter Aortic Valve Replacement with the Claret embolic protection device

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Cardiac valve disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON39581

**Source**
ToetsingOnline

**Brief title**
MISTRAL-C

### Condition

- Cardiac valve disorders

**Synonym**
cerebral embolism, stroke

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** collectebusfondsen worden geprobeerd

## Intervention

**Keyword:** Aortic Stenosis, cerebral embolism, Claret, TAVI

## Outcome measures

### Primary outcome

Primary endpoint

- Incidence, number and volume of new cerebral ischemic lesions as detected by

DW -MRI post TAVI.

### Secondary outcome

Secondary endpoints

• 30-day Neurology endpoint: any new transient or persisting focal neurological

deficit as determined by an experienced neurologist excluding the time the

patient is under influence of anesthetics.

• Changes in Neurocognitive function at 3 months follow up

• 30 day mortality

• Device related bleeding and vascular complications.

• Histlogic examination of debris captured by the Claret Device

# Study description

**Background summary**

Symptomatic severe Aortic Valve Stenosis (AS) has a dismal prognosis. Surgical Aortic Valve Replacement (SAVR) is the standard treatment of care[1-2]. The first Transcatheter Aortic Valve Implantation (TAVI) to treat severe AS was performed in 2002[3]. Since its introduction the technology has progressed through several device and procedure iterations with a current worldwide TAVI experience exceeding 50000 cases. The TAVI technology is reserved for patients with severe AS and a (very) high operative risk. Both surgical and catheter based therapies can be complicated by cerebrovascular events [4]. These cerebrovascular events often have an embolic origin. The embolic nature can be variable (cholesterol particles, air, atherosclerotique plaque material, thrombus, calcified valve material). The incidence of clinical stroke after SAVR and TAVI varies between 2 and 10%[5-8].

Cerebral infarctions can be identified by Computed Tomography (CT), although the smaller (and often clinically silent) ischemic lesions remain undiagnosed. Conventional Magnetic Resonance Imaging (MRI) outperforms CT in its ability to identifiy new cerebral lesions.. Even subclinical subtle ischemic changes can be demonstrated by MRI. MRI studies following cardiac surgery have demonstrated the occurrence of new ischemic cerebral lesions in 0-58% [9-11]. The impact of these new ischemic cerebral lesions after surgery on neurocognitive function is controversial
[12-13]. The variability in frequency and at first glance conflicting results can be explained by 1) timing of MRI following surgery, 2) the fact that these (subclinical) new lesions may be transient and 3) the limitations of MRI in detecting small ischemic lesions.
Diffusion Weighted Magnetic Resonance Imaging (DW-MRI) is a relatively new MRI technique capable of detecting small ischemic lesions in the brain within small time intervals following the ischemic insult. DW-MRI measures microscopic motion of water molecules in the brain. Ischemic areas are characterized by impaired diffusion, which is visible as regions with high density by DW-MRI. Diffusion images of the brain can identify (sub)acute ischemic lesions with very high sensitivity and specificity. This MRI sequence has already proven its performance in the evaluation of ischemic brain lesion during carotid endarterectomy and carotid stenting [14-17].

New cerebral lesions by DW MRI are reported in 48% of patients after valve surgery and in up to 70 - 80% after TAVI [18-19]. Most of these lesions have no immediate clinical consequences but neurocognitive decline in the long term remains to be investigated. Several studies have linked (initially subclinical) micro-emboli after heart surgery to neurocognitive outcome [20-21]. Vascular cognitive impairment (VCI) could also result from multiple initially

subclinical cerebral embolisations.

Embolic Protection Devices (EPD) are endovascular devices aiming to prevent cerebral embolisations. These devices have proven efficacy in carotid and saphenous vein graft stenting with clinically significant reductions in major adverse events (mortality, stroke, myocardial infarction)[22-24].

**Study objective**

The Claret device (Claret Inc.) is an Embolic Protection Device (EPD) consisting of two nitinol baskets to be introduced through the right radial artery. One basket is positioned in the brachiocephalic trunk, the other in the left common carotid artery. The baskets consist of a mesh graft that will capture particles and debris of at least 90um in diameter.
The device has CE mark approval for use in Transcatheter Aortic Valve Implantation. The first-in-man experience demonstrated procedural safety. Whether the use of the Claret device will reduce the number and extent of new ischemic lesions by DW-MRI has not been established yet.

**Study design**

This is a multi center randomized study including 54 patients with aortic stenosis scheduled for TAVI. Randomisation will be performed by sealed envelopes.

Patients who are excluded from follow up MRI because of pacemaker issues will continue clinical follow up per protocol. Enrollment will continue until a total of 54 patients have an analyzable DW MRI exam within 3 days post TAVI. A senior interventionalist at the outpatient clinic or on the ward will approach eligible patients and ask written information. Patients will be randomized after signing the informed consent form.

All patient data will be entered in a dedicated database. Baseline DW-MRI will be performed within 1 week prior to the procedure. Follow up DW-MRI will be obtained within 3 days after the procedure. During the follow up MRI exam, a ward nurse will accompany the patient. In case of clinically significant and/or unexpected new findings by follow up MRI, this will be communicated to the patient by the treating physician and appropriate follow up will be organised. A second follow up DW-MRI exam of the brain will be organized 3 months after the TAVI procedure.

**Intervention**

A 6F radial artery sheath is introduced using the Seldinger Technique. The Claret device is advanced through a right radial access deploying the distal basket in the left common carotid artery and the proximal basket in the

brachiocephalic trunk. The Claret is introduced in the catheterization lab with the patient under general anesthesia and prior to insertion of the 18F arterial sheath in the common femoral artery.

**Study burden and risks**

With an aging population the incidence of symptomatic aortic stenosis is expected to rise. SAVR is the standard of care. The operative risk increases with age and in up to one third of contemporary AS patients AVR is denied because of age, comorbidities or patient preference. TAVI is an established option in this selected patient cohort at (very) high operative risk.

The TAVI experience is rapidly mounting worldwide. DW-MRI detects subclinical new ischemic cerebral lesions after TAVI in the majority of cases. Although the immediate clinical impact seems negligible, the implications on the longer term are unknown. These subclinical cerebral lesions may play a role in neurocognitive deterioration. If the use of the Claret device in TAVI procedures may reduce the incidence of these cerebral lesions this may have considerable clinical significance in the long run. Patients who are participating in this study may potentially have a significant clinical benefit.

This study may indicate whether use of the Claret device will reduce the occurrence of new cerebral lesions and/or the extent of these lesions detected by DW-MRI. If a clear reduction of new cerebral lesions (e.g. >25% reduction) and/or extent of these lesions are demonstrated, the results should be reproduced in a prospective randomized trial. This may then also assess whether the Claret device will reduce the number of clinical ischemic strokes and whether subclinical cerebral lesions play a role in neurocognitive function in the longer term.

The established contraindications for MRI apply. Prolonged (>72 hours) continuous rhythm monitoring is required in all patients. During the post procedural MRI the monitoring will be interrupted. Therefore a nurse of the cardiology/ ward will accompany the patient during the MRI exam.

During the introduction of the Claret device potential arterial damage and thrombo-embolic phenomena (air, thrombus etc*) are possible. Its identification is a secondary endpoint of this 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

1) Patients with severe AS at high operative risk who will undergo planned TAVI
2) Informed consent to participate in the study (i.e. use of Claret device yes or no) and undergo DW -MRI before and after the procedure.
3) Compatible left common carotid artery (>= 5 mm) and brachiocephalic artery (>= 9 mm) diameters without significant stenosis (> 70%) as determined by Multi-Slice Computed Tomography (MSCT) scan

## Exclusion criteria

1) No written informed consent
2) Standard exclusion criteria for MRI study (see Appendix 4)
3) Anatomical exclusion for filter deployment
4) Permanent Pacemaker/AICD in situ before TAVI
5) Planned implantation of a pacemaker implantation after TAVI.
6) Previous stroke with residual neurological symptoms or dementia
7) Not native Dutch speaking

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |

**Primary purpose:** Prevention

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 09-01-2013 |
| Enrollment: | 54 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 26-10-2012 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 24-05-2013 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-05-2014 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 22229
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL40999.078.12 |
| OMON | NL-OMON22229 |