A Randomized multicenter clinical trial of Unruptured Brain AVMs

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Primary: To determine whether medical management improves long-term outcomes of patients with unruptured BAVMs compared to invasive therapy (with endovascular procedures, neurosurgery, or radiotherapy, alone or in ombination). The trial has been...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON30249

Source
ToetsingOnline

Brief title
ARUBA

Condition

- Central nervous system vascular disorders
- Vascular therapeutic procedures

Synonym
intracerebral vascular malformation, intracranial vascular malformation

Research involving
Human

Sponsors and support

Primary sponsor: Doris & Stanley Tananbaum Stroke Center, Columbia University Medical Center, Department of Neurology
Source(s) of monetary or material Support: National Institute of Neurological Disorders and Stroke;USA

Intervention

Keyword: arteriovenous malformation, brain, stroke

Outcome measures

Primary outcome

Composite event of death from any cause or stroke (hemorrhage or infarction revealed by imaging). Clinical outcome status will be measured by the Rankin Scale, a widely-used outcome measure for stroke.

Secondary outcome

The secondary measures of outcome include adverse events, quality of life and cost.

Study description

Background summary

Current invasive therapy for brain arteriovenous malformations (BAVMs) is varied and includes endovascular procedures, neurosurgery, and radiotherapy alone and in combination, largely dependent on the decisions of the local clinical team. All of these invasive therapies are administered on the assumption that they will decrease the risk of initial or subsequent hemorrhage and lead to better long-term outcomes. Despite these laudable goals, the literature contains almost no reference to the outcome for medical management before or after hemorrhage, or for intervention outcome for unruptured BAVMs. The most contentious issue at present is whether invasive therapy should be considered for those increasingly being discovered incidentally by brain imaging, with lesions that have not bled.

Study objective

Primary: To determine whether medical management improves long-term outcomes of patients with unruptured BAVMs compared to invasive therapy (with endovascular procedures, neurosurgery, or radiotherapy, alone or in ombination). The trial has been designed to test whether medical management or invasive therapy will reduce the risk of death or stroke (due to hemorrhage or infarction) by at least 40% (an absolute magnitude of about 7.5% over 5 years). It will require

800 patients to detect the hypothesized 40% reduction in event rate, analyzed using the intention-to-treat principal. This sample size will support a test of non-inferiority if the medical management is not superior to invasive therapy.

Secondary: To compare the impact of medical management to invasive therapy with respect to adverse events, quality of life and cost

Study design

The study design is a prospective, multi-center, parallel design, randomized, controlled trial. Treatment assignment will not be masked; however, clinical coordinating center personnel and outcome events committees will be blinded to treatment assignment.

Intervention

The invasive therapy arm of the trial involves prophylactic efforts with a plan for
eradication of the observed BAVM utilizing endovascular procedures, microsurgery, or radiosurgery, alone or in combination with pharmacological therapy for existing risk factors and coexisting medical conditions. The medical management arm will involve pharmacological therapy as deemed appropriate for medical symptoms.

Study burden and risks

Participants are expected to visit the outpatient clinic for follow-up visits every 6 months in the first two years and on a yearly basis thereafter for a maximum period of 7.5 years. After the first two years, ther will be a yearly follow-up by telephone as well.

Medical management or interventional treatment with medical management are both well recognized clinical options. Both are accepted ways to treat AVMs. Neither approach is considered experimental. It is not known whether medical management alone or interventional treatment with medical management is better.

The principal risk from an AVM is the occurrence of a stroke. This can occur if the AVM ruptures and significant bleeding occurs. This risk is present whether one is treated medically or has an interventional procedure(s). The risk of stroke is between 1% and 8% per year for individuals with an AVM who have medical management. For patients with an AVM who have one or more interventional procedures, the risk of stroke may be between 4 and 9% per year in the first years.

The interventions themselves carry a small risk as well. The principal risk to

all of the procedures is the risk of hemorrhage in the brain that may result in new neurological deficits, or death.

For endovascular treatment, bleeding may occur in the groin, the standard site for all angiograms. Emboli may occlude cerebral vessels and lead to brain infarction.

Neurosurgery for brain AVMs carries a small risk that healthy brain tissues may be displaced and damaged during the approach to the site of the brain AVM.

Radiotherapy for brain AVMs carries the same risks as radiotherapy to the head and brain for treatment of other conditions, such as brain tumors. For AVM, the doses are usually lower than those used for brain tumors but it is possible the radiation can cause injury to the arteries and veins around the AVM that results in bleeding to occur before the effects of the radiation reduce the blood supply to the malformation. In addition, hair loss in the path of the beam can occur. Finally, the radiation may cause damage to healthy brain tissue adjacent to the AVM.

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. Patient must have an unruptured BAVM diagnosed by MRI/MRA and/or angiogram
2. Patient must be 18 years of age or older
3. Patient must have signed Informed Consent Form

Exclusion criteria

1. Patient has BAVM presenting with evidence of recent or prior hemorrhage
2. Patient has received prior BAVM therapy (endovascular, surgical, radiotherapy)
3. Patient has BAVM deemed untreatable by local team, or has concomitant vascular or brain disease that interferes with/or contraindicts any invasive therapy type (stenosis/occlusion of neck artery, prior brain surgery/radiation for other reasons)
4. Patient has baseline Rankin *2
5. Patient has concomitant disease reducing life expectancy to less than 10 years
6. Patient has thrombocytopenia (< 100,000/nl),
7. Patient has coagulopathy (spontaneous or iatrogenic INR>1.5, PT>30)
8. Patient is pregnant, lactating, or plans to become pregnant
9. Patient has known allergy against iodine contrast agents
10. Patient has multiple-foci BAVMs

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-04-2007
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	23-01-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
ISRCTN	ISRCTN44013133
CCMO	NL14909.041.06