MRI vessel wall characteristics of peripheral arteries and arterial stiffness in hemophilia patients

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The primary objective is to analyze and compare morphological (media- thickness) and functional (stiffness) vessel wall parameters of peripheral arteries between hemophilia patients with an ankle- brachial index >= 1.3 and hemophilia patients...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON41839

Source
ToetsingOnline

Brief title
Hemophilia and medial calcifications in peripheral arteries

Condition

- Other condition
- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Medial arterial calcification, mediasclerosis

Health condition

Bloedvat- aandoeningen: atherosclerose, vasculaire calcificaties, vaatstijfheid

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Pfizer

Intervention

Keyword: Arterial stiffness, Hemophilia, Hypertension, Vascular calcification

Outcome measures

Primary outcome

1. Comparison of both arterial (medial) wall thickness and arterial stiffness

between the two groups with 3T MRI

2. Comparison of the arterial stiffness between the two groups with pulse wave

velocity

Secondary outcome

- Relation between vessel wall characteristics, arterial stiffness and

traditional cardiovascular risk factors.

- Relation between vessel wall characteristics, arterial stiffness and severity

of haemophilia.

Study description

Background summary

We previously showed that patients with hemophilia have the same degree of atherosclerosis compared to control subjects, which predisposes them to vascular complications at older age. In clinical practice, we indeed see an increasing amount of patients with myocardial infarction and ischemic stroke. In our previous studies, formation of atherosclerosis was detected in the coronary and carotid arteries. We therefore recently analyzed the prevalence of atherosclerosis in the peripheral arteries in patients with hemophilia, by measuring the ankle-brachial index (ABI), which assesses perfusion of the large leg arteries. 69 adult patients with hemophilia were investigated. The mean age

was 52 years, and 39% had a severe type of hemophilia. 7% had a previous cardiovascular disease and 26% was treated with antihypertensive medication. 48% of the hemophilia patients had an ABI >=1.3, while the other patients had an ABI of 0.9-1.2. A low ABI (<0.9), which is associated with stenosed vessels, was not found. In summary, nearly half of the hemophiliacs had a high ABI. In general, an ABI >= 1.3 is found in about 0.5% of the general population. The most common conditions that predispose to a high ABI are type II diabetes mellitus and chronic kidney disease, with a prevalence of 20-40%. A high ABI points to vascular calcification of the media of the artery (VCm), caused by deposits of hydroxyapatite with a high degree of crystallization. As a consequence, elasticity of the peripheral arteries decreases which leads to arterial stiffness. It is unclear why hemophilia patients have such a high prevalence of VCm, but it is tempting to speculate that due to recurrent bleeding in either joints or muscles, vascular calcification occurs, as has been shown in hemophilic mice.
Furthermore, the most common cardiovascular risk factor in hemophilia patients is arterial hypertension, which is also more common in this group than in the general population. Since arterial stiffness is an important contributor to arterial hypertension, VCm and consequently arterial stiffness may be more prevalent in hemophiliacs, and this may explain the high rate of systolic hypertension.
Magnetic resonance imaging (MRI) enables transverse 3-dimensional imaging of the vessel wall at high resolution with excellent interscan reproducibility. 3-Tesla MRI directly visualizes the artery wall and the constitution of the artery wall, including the media. The great advantage of MRI compared to CT-scan is the fact that MRI gives no radiation exposure. In addition, it has been shown that 3T-MRI can also visualise endothelial shear stress, an important marker for arterial stiffness and remodelling.
Furthermore, pulse wave velocity (PWV) is the gold standard of measuring arterial stiffness.

Study objective

The primary objective is to analyze and compare morphological (media-thickness) and functional (stiffness) vessel wall parameters of peripheral arteries between hemophilia patients with an ankle- brachial index >= 1.3 and hemophilia patients with a normal ankle- brachial index (0.9-1.3)

The secondary objectives are to explore the relation between media- thickness and arterial stiffness and 1) traditional cardiovascular risk factors, 2) severity of hemophilia.

Study design

Cross-sectional, exploratory, sinlge center study

Study burden and risks

Apart from the drawing of blood, none of the procedures the subjects will undergo are invasive and participation will consist of a single visit to our study centre. Subjects will be asked to come to our study centre in the morning after an overnight fast. Subjects will remain in our study centre for no longer than three hours. MRI scanning will be performed, followed by PWV analysis. Next blood will be drawn and measurement of height, weight and waist/ hip ratio will be performed. We consider the risk of bleeding complications to be very small and MRI scanning has no radiation exposure.

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. Hemophilia A and B patients
2. Males, 18 years and older, mentally competent
3. Documented ABI > 0.9 (previous measurements)
4. Written informed consent for study participation

Exclusion criteria

1. Patients with symptomatic atherosclerotic disease or history of arterial thrombotic events.
2. Patients with chronic kidney disease , defined as eGFR < 60 ml/ min, calculated according to the Modi*cation of Diet in Renal Disease formula.
3. Patients with diabetes mellitus, defined as any history of diabetes or current diabetes (diagnosed by HbA1c >= 6.5% according to the American Diabetes Association diagnostic criteria)
4. Patients with any contraindication to MRI (pacemaker or claustrophobia)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO Date:	23-09-2015
Application type:	First submission
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

ID: 23588
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL52159.042.15
Other	NTR
OMON	NL-OMON23588