Patterns of systemic arterial calcification in patients with chronic critical limb ischemia and its relationship to the ankle-brachial index and survival

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The purpose of this study is to determine the patterns of vascular calcification in 5 different vascular beds in patients with CLI and a high ABI or incompressible vessels and compare these to the pattern found in CLI patients with a low ABI. As a…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational non invasive

Summary

ID

NL-OMON54634

Source
ToetsingOnline

Brief title
Systemic vascular calcification patterns in critical limb ischemia

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis

Source(s) of monetary or material Support: geen.

Intervention

Keyword: ankle-brachial index, Computed tomography angiography, Criticical limb ischemia, vascular calcifications

Outcome measures

Primary outcome

Our hypothesis is that there are two groups of patients. One, with low ankle brachial index and one with high ankle brachial index or incompressible vessels. In the group with the low ABI we expect atheroclesoriss (intimal disease) to be the main cause. We expect in this group intimal calcifications to be found in all vascular territories.

In the group with the high ABI we expect arteriosclerosis and atherosclerosis in all territories. We hypothesized by identifying those two groups, we can stratify high risk patients. Furthermore, we expect that the ABI is related to the degree of calcification.

Secondary outcome

nvt

Study description

Background summary

Chronic critical limb ischemia (CLI), the endstage of peripheral artery disease (PAD) is associated with high rates of amputation and a high mortality (Abu Dabrh et al., 2015; Bertele, Roncaglioni, Pangrazzi, Terzian, & Tognoni, 1999; Dormandy & Rutherford, 2000; Norgren et al., 2007; Rutherford et al., 1997; Teraa, Conte, Moll, & Verhaar, 2016). However, the cause for this poor amputation free survival is unknown.
Recently it was shown that within the patients group with CLI a subgroup can

be identified that is at a very high risk for amputation and death. This group is characterized by a high ABI or incompressible crural vessels (Aboyans et al., 2011; Arain et al., 2012) (Spreen et al. 2017, JAMA in revision). This subgroup with high ABI has also a higher risk for diabetes, chronic kidney disease, heart failure (Criqui et al., 2014; Spreen et al., 2016). Lack of vessel compressability is probably caused by calcification of the vessel wall and fibrosis. It is now believed that there are two types of calcification. The calcifications causing vessel wall imcompressability are probably medial arterial calcifications (Ix, Miller, Criqui, & Orchard, 2012; Potier, Abi Khalil, Mohammedi, & Roussel, 2011). Atherosclerosis in the intima that can have more dotlike calcified lipid lakes. On the other hand, arteriosclerosis, which is stiffening of the vessel wall, is caused by medial arterial calcification and is frequently circular (Janzen & Vuong, 2001; Monckeberg, 1903; Mustapha & Diaz-Sandoval, 2014). The calcifications are found in CLI patients are probably medial calcifications.
Research about relationship between cardiovascular disease events and vascular calcification are mainly limited to the coronary and carotid arteries. In coronary artery disease, the patterns of these vessel wall calcifications are associated with increased cardiovascular morbidity (Criqui et al., 2014; Ehara et al., 2004). Some of these patterns are of more clinical importance than other (e.g. dotted patterns). There are only a few studies on CT angiography plaque identification and the results of these studies do not all show correlation with clinical outcome. For example, the extent of the calcification in carotid plaques is not associated with cardiovascular outcome (Hellings et al., 2010). Recently, also the meaning of crural calcifications was investigated. Guzman et al showed that severe tibial artery calcification was an excellent predictor for amputation (Feiring, 2008; Guzman et al., 2008), and Lew showed that a high ABI or poorly compressible arteries are due to calcification of these vessels and also related to a low amputation free survival (Lew, Nicolosi, & Botek, 2015).
Thus far, to the best of our knowledge, there are no studies known about the patterns of calcified vessels in other flow territories than peripheral vessels. Also, the correlation with calcified vessel with on of its clinical measurements, the ankle-brachial index (ABI), is not known. So, the aim of our study is to visualize the pattern of vascular calcifiction in all vascular beds and investigate whether they can explain the low amputation free survival in CLI patients with a high ABI or incompressible vessels.
Second we want to correlate the calcification pattern in the crural vessels to the ABI to explain the stiff vessel wall. We hope that this insight can lead to effective risk-stratification of individual patients and possibly better treatment.

Study objective

The purpose of this study is to determine the patterns of vascular calcification in 5 different vascular beds in patients with CLI and a high ABI or incompressible vessels and compare these to the pattern found in CLI

patients with a low ABI.
As a secondary goal, we wanted to evaluate the relationship of these vascular calcification patterns with the ABI.

Study design

This study has a prospective, descriptive design.

Study burden and risks

nvt

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

patients with critical limb ischemia of lower extremities (Rutherford score of 4, 5 and 6)

Exclusion criteria

if the patient is unable to give consent.
Patients with allergy for intravenous contrast.
patients with an eGFR under 20 will be excluded from this study.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-01-2019
Enrollment:	64
Type:	Actual

Ethics review

Approved WMO

Date:	27-07-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-07-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	26-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	23-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	NCT00471289
CCMO	NL64059.098.17