Perfusion monitoring in lower limbs of patients with peripheral arterial occlusive disease with continuous ICG video angiography - A pilot study

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To investigate the feasibility of skin perfusion measurements of lower limb tissue in 20 PAOD patients with continuous ICG-VA. Feasibility is defined as the ability to detect hypo perfusion in the diseased leg in comparison with the patient's...

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

Summary

ID

NL-OMON51744

Source
ToetsingOnline

Brief title
PERFUSE

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Peripheral arterial occlusive disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: angiography, ICG, peripheral arterial occlusive disease

Outcome measures

Primary outcome

Success of skin perfusion measurements of lower limb tissue with continuous ICG-VA in PAOD patients (Rutherford class 4-6). Success is defined as the ability to detect hypo perfusion in the diseased leg in comparison with the patient's contralateral control leg with continuous ICG-VA in at least half the patients with good signal quality and sufficient sound to noise ratio. Good signal quality defined as: anatomy of interest identifiable and centred in the camera's field of view; no interference from natural lights (e.g. daylight); no rapid movements of camera relative to anatomy of interest; no change in distance from camera to anatomy of interest. Good SNR defined as: change in fluorescent (ICG) intensity following each ICG bolus is larger than 5x the noise level at baseline (before any ICG is injected).

Secondary outcome

- To develop a standardized measurement protocol for continuous ICG-VA measurements, the dose and injection rate will be determined based on: good signal quality, sufficient sound to noise ratio, and no presence of saturation in the QUEST camera (Quest Medical Imaging BV, Middenmeer, The Netherlands). Good signal quality defined as: anatomy of interest identifiable and centred in the camera's field of view; no interference from natural lights (e.g., daylight); no rapid movements of camera relative to anatomy of interest; no

change in distance from camera to anatomy of interest. Good SNR defined as:

change in fluorescent (ICG) intensity following each ICG bolus is larger than

5x the noise level at baseline (before any ICG is injected).

- To investigate the ability of continuous ICG-VA to detect reperfusion after

endovascular revascularisation, the Bland-Altman method will be used to analyze

the agreement between the continuous ICG-VA measurements and TcPO2 and ABI

tests before and after the procedure.

- To test the agreement between continuous ICG-VA and toe pressure measurements

before the procedure using the Bland-Altman method

Study description

Background summary

Peripheral arterial occlusive disease (PAOD) is a common and disabling disease. In the Netherlands, the prevalence of chronic PAOD in patients older than 55 years is estimated to be 7% and for patients older than 85 years, 56%. PAOD is a progressive disease, where the first stage is manifested by intermittent claudication. The intermittent claudication will result in chronic limb threatening ischemia (CLTI) in 15% of patients. Within 10 years after diagnosing PAOD, 2% of patients must undergo major limb amputation. From all patients diagnosed with critical limb threatening ischemia, 25% will undergo a primary amputation. Of these patients with below the knee amputation, only about 60% heals by primary intention and 15% requires a renewed amputation at a higher level (through-knee or transfemoral). Therefore, patients with PAOD suffer from decreased mobility, severe pain and lower quality of life compared to the general population. Patients with PAOD have more comorbidity, and often suffer from diabetes, cardiac and pulmonary diseases.
Symptoms and complications of PAOD, such as (rest) pain and non-healing ulcers result from impaired peripheral tissue perfusion. This is mostly caused by large-vessel atherosclerosis, however microvascular impairment due to peripheral arterial occlusive disease or diabetes can also attribute to hypoperfusion. Most current methods for assessing potential vascular compromise include ankle brachial index, colour doppler ultrasound, toe systolic blood pressure, treadmill test, CT angiography, and sometimes MRA. These methods assess the arterial inflow into a limb and can be used to detect an arterial

stenosis, however cannot measure the actual peripheral tissue perfusion. An accurate method for determining actual tissue perfusion is TcPO2 measurement, which is considered to be the golden standard. Unfortunately, this method is time consuming, operator dependent, and not applicable in everyday practice. Moreover, the quality of evidence is low, and it is often not sensitive enough to detect changes in perfusion during the operation. Assessment of tissue perfusion is not only necessary to determine the presence or severity of PAOD but can also be used to evaluate the efficacy of treatment.

Continuous ICG-VA

ICG-VA is an emerging technique for perfusion assessment and has been used in esophagectomies, breast reconstruction, resection of colorectal liver metastases, sentinel lymph node mapping, and real-time intraoperative assessment of anastomotic perfusion after bowel resection. Furthermore, ICG-VA has been used for the evaluation and quantification of skin perfusion in patients with peripheral arterial occlusive disease (PAOD) with promising results. Drawbacks include limited knowledge on its ability to quantify perfusion and the limited temporal resolution that does not allow for continuous, dynamic measurements.
Continuous ICG-VA is a promising technique to measure local skin tissue perfusion with the potential for high sensitivity and real time measurements, potentially enabling intraprocedural detection of improvement or failure of therapy. This technique has not been used to quantify skin perfusion before. First a study should be undertaken to determine feasibility of skin perfusion measurements with continuous ICG-VA in lower limb tissue in patients with PAOD (Rutherford class 4-6) and to develop a standardized measurement protocol. Furthermore, it is not yet known how the accuracy of these measurements compares to the gold standard TcPO2, ABI, and toe pressure measurements. The technique utilizes microscopic doses of ICG, injected at a frequent and regular time interval, to create regular time-intensity curves with an increasing arterial phase and decreasing venous phase. When occurring in a regular and frequent manner, these curves together form an oscillating fluorescent signal, detectable in all vital tissue.

Conclusion

Continuous ICG-VA of the skin may potentially provide real-time and intraprocedural measurement of tissue perfusion and enable early and even intraoperative detection of success or failure of endovascular therapy in patients with PAOD.

Study objective

To investigate the feasibility of skin perfusion measurements of lower limb tissue in 20 PAOD patients with continuous ICG-VA. Feasibility is defined as the ability to detect hypo perfusion in the diseased leg in comparison with the

patient's contralateral control leg in at least half the patients with continuous ICG-VA with good signal quality and sufficient sound to noise ratio. Good signal quality defined as: anatomy of interest identifiable and centred in the camera's field of view; no interference from natural lights (e.g. daylight); no rapid movements of camera relative to anatomy of interest; no change in distance from camera to anatomy of interest. Good SNR defined as: change in fluorescent (ICG) intensity following each ICG bolus is larger than 5x the noise level at baseline (before any ICG is injected).

The secondary objective(s) are:
- to develop a standardized measurement protocol for continuous ICG-VA measurements
- to investigate the ability of continuous ICG-VA to detect reperfusion after endovascular revascularisation by using the Bland-Altman method to analyze the agreement between the continuous ICG-VA measurements and TcPO2 and ABI tests before and after the procedure
- to analyze the agreement between continuous ICG-VA measurements and toe pressure measurements before the procedure using the Bland-Altman method

Study design

This study is a single centre pilot study to investigate the feasibility of skin perfusion measurements of lower limb tissue with continuous ICG-VA in 20 patients with PAOD (Rutherford class 4-6).

Study burden and risks

The risks and burden associated with participating in this study are low. The patients will be at the hospital as part of standard management and their stay and treatment will not be affected by our study. All subjects will undergo TcPO2, ABI, toe pressure and continuous ICG-VA measurements. The burden regarding this study protocol will be that subjects will receive multiple microscopic doses (0.001-0.02 mg ICG/kg) of ICG with a total ICG dose well below the recommended maximum daily dose (5mg/kg/day). Administration of ICG requires a venous catheter. As part of standard clinical care there patients however have a venous catheter and there will be no need for an extra catheter. ICG is a well-known compound that poses negligible risk to subjects. There are no direct benefits for the patients by participating with this study.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients:

- Written informed consent
- Rutherford class 4-6
- Occlusion at the level of the iliac or femoral arteries
- Unilateral disease. Control leg must have an ABI >= 0.8, no rest pain, and no ulcers

Exclusion criteria

- Insufficient knowledge of the Dutch language, illiteracy, or language barrier.
- Lower leg fracture within the past 12 months.
- (Partial) amputation of one of the feet and/or legs.
- Known hypersensitivity to indocyanine green or to sodium iodide.
- Hyper-thyroidism and autonomic thyroid adenomas.
- Renal insufficiency.
- Concomitant use of the following: anticonvulsants, bisulphite compounds,

haloperidol, heroin, meperidine, metamizole, methadone, morphium, nitrofurantoin, opium alkaloids, phenobarbital, phenylbutazone, cyclopropane, probenecid, and rifamycin.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	12-05-2023
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	Quest Spectrum Platform (Fluorescent imaging system)
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	21-06-2022
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

No registrations found.

In other registers

Register	ID
CCMO	NL80562.042.22