Peripheral Blood Mononuclear Cell Single Photon Emission Computed Tomography in Patients with Atherosclerotic Disease; Shedding light on the migration of immune cells in vascular disease.

Published: 10-09-2012
Last updated: 26-04-2024

Primary: 1. To demonstrate migration of circulating white blood cells into atherosclerotic lesions in subjects with atherosclerotic disease via quantification with SPECT.Secondary: 2. To evaluate the relation between FDG-PET signal (reflection of...

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

Summary

ID

NL-OMON37041

Source
ToetsingOnline

Brief title
Illuminate

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerosis, vascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Atherosclerosis, PBMC, SPECT, Technetium

Outcome measures

Primary outcome

Main study parameters:

The assessment of SPECT images at the site of atherosclerosis, reported as geometric mean counts per minute per 100 pixels divided by the injected dose of radioactivity.

Secondary outcome

Secondary study parameters/endpoints

- Association between the degree of monocyte influx/tracer uptake at the site of atherosclerosis and TBR as measured with FDG-PETCT.

- Association between the degree of monocyte influx/tracer uptake at the site of atherosclerosis and DCE-MRI signal.

- Association between the degree of monocyte influx/tracer uptake at the site of atherosclerosis and laboratory parameters; for example but not limited to inflammatory parameters.

- To evaluate differences between SPECT signal in subjects with cardiovascular disease and healthy controls.

Study description

Background summary

Inflammation has now been widely acknowledged as one of the driving factors behind the development of (advanced) atherosclerotic plaque and/or clinical events. Macrophages and T-cells have been shown to accelerate atherosclerotic plaque development, but data is scarce on actual influx of immune cells into atherosclerotic lesions in humans. In mice, atherosclerosis drives a rapid influx of inflammatory monocytes and other immune cells. Once in the vessel wall, subsets of mononuclear cells differentiate to a phenotype consistent with inflammatory macrophages. Here, we propose to quantify the influx of mononuclear cells with SPECT and 99m-Technetium labelling to enhance our understanding on influx of immune cells into the vascular wall in humans. Increasing our understanding of a *continuous* influx of new white blood cells into the vessel wall will have profound implications for strategies aimed at decreasing this influx of new white blood cells instead of reducing the *resident* inflammatory cells.

Study objective

Primary:
1. To demonstrate migration of circulating white blood cells into atherosclerotic lesions in subjects with atherosclerotic disease via quantification with SPECT.

Secondary:
2. To evaluate the relation between FDG-PET signal (reflection of number and metabolic activity of macrophages in the vessel wall) and the influx of circulating white blood cells (SPECT).

3. To evaluate the relation between DCE-MRI (reflection of vessel wall inflammation) and the influx of circulating white blood cells (SPECT).

4. To evaluate the relation between SPECT signal and plasma levels of inflammatory markers (e.g. CRP, IL1b)

5. To evaluate differences between SPECT signal in subjects with cardiovascular disease and healthy controls.

Study design

This study is designed as a single-center, cross-sectional and observational study.
Patients will undergo a FDG-PETCT scan and DCE-MRI. Within three months after

PET-CT scan and DCE-MRI a scintigraphy of 99mTc-labeled autologous monocytes will be performed. Subjects will undergo monocytes cell separation, isotopic labelling with technetium-99m (99mTc) and re-infusion of labelled cells under the investigator*s supervision. No investigational products will be used in this study.

Study burden and risks

The results of this study contribute to the development of our understanding on the roll of immune cells in atherosclerotic diseases. Also, it contributes to the development of novel anti-inflammatory directed atherosclerotic treatment strategies. Patients receive no direct benefits.

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

Healthy controls
* Adults (either gender) * 18 years
* Willing and able to participate in study protocol
Cardiovascular patients
* Adult patients (either gender) * 18 years
* For patients using statins, angiotensin-converting enzyme (ACE) inhibitors (ACE-I) or angiotensin-receptor blockers (ARBs), non-statin lipid-modifying therapy, thiazolidinediones, inhaled steroids, or leukotriene modifying agents; use of a stable dose for at least 6 weeks prior to the first visit.
* Documented * atherosclerotic vascular disease (e.g., CAD, peripheral arterial disease, aortic atherosclerosis or abdominal aortic aneurysm (< 5 cm), carotid disease or cerebrovascular disease) and clinically stable for at least 3 months prior to screening, or or at elevated risk for CVD:
oBMI > 27.
oHDL < 1.0.
oMetabolic syndrome, as defined by the worldwide definition by the International Diabetes Federation criteria.
oDiabetes mellitus type II . ;* Documentation will include one or more of the following: history of myocardial infarction or stroke or, objective diagnostic testing. (Examples include but are not limited to: Exercise treadmill test, Stress echocardiography, Myocardial perfusion scintigraphy, Right or left common carotid intima-media thickness (CIMT) by ultrasound > 75th percentile by American Society of Echocardiography, Presence of carotid plaque by carotid ultrasound (focal thickening > 50% or CIMT > 1.5 mm), Abdominal aortic aneurysm by CT or ultrasound, Coronary artery calcium score > 100 Agatston units in patients < 60 years of age, CT or conventional coronary or peripheral angiography with at least one moderate or severe luminal stenosis, CT coronary angiography with one or more atherosclerotic plaques demonstrating positive remodeling or hypodense plaque morphology, Moderate or severe aortic atherosclerosis by CT or Transesophageal echocardiography, History of revascularization procedure (e.g., coronary or peripheral arterial bypass grafting, percutaneous coronary or peripheral intervention, carotid endarterectomy).

Exclusion criteria

Healthy controls are not eligible if they meet one of the criteria listed below:
* Any known systemic chronic disorders/medical condition or chronic use of systemic medication that could interfere with the conduct of the study in the opinion of the investigator.
*Standard contra-indications to MRI, PET, and CT.
* Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study.
Cardiovascular patients are not eligible if they meet one of the criteria listed below:
*Auto-immune disease/vasculitis, other active inflammatory diseases, proven or suspected

bacterial infections. Recent (<1 month prior to screening) or ongoing serious infection requiring IV antibiotic therapy that could interfere with the conduct of the study in the opinion of the investigator.
*Known systemic disorders such as hepatic, renal, hematologic, and malignant diseases or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator.
*Recent (< 1 month prior to screening) or current treatment with medications that may have a significant effect on plaque inflammation as measured by plaque TBR, including: oral, rectal, or injectable corticosteroids or immunosuppressive medications (e.g., cyclosporine, methotrexate, tacrolimus, azathioprine, anti-thymocyte globulin, sirolimus, anti-TNF agents such as infliximab, anti-IL6 therapy such as tocilizumab, or anti-IL1 therapy such as anakinra).
*Poorly controlled diabetes defined as hemoglobin A1c (HbA1c) >7.5% due to inability to comply with recommended diabetes treatment.
*History of anaphylaxis, anaphylactoid (resembling anaphylaxis) reactions, or severe allergic responses.
*Planned cardiac surgery, PCI or carotid stenting, or major non-cardiac surgery during the course of the study period that could interfere with the conduct of the study in the opinion of the investigator.
*Standard contra-indications to MRI, PET, and CT.
*Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-10-2012
Enrollment:	30

Type:	Actual

Ethics review

Approved WMO Date:	10-09-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL41040.018.12