Assessment of disease activity of ankylosing spondylitis with [18F]Fluoride PET-CT.

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1.To investigate if [18F]Fluoride PET-CT is a potential imaging technique for assessment of (changes in) disease activity of ankylosing spondylitis on baseline and after anti-TNF therapy (with MRI and clinical outcome as reference).Sub-study in 2...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON38794

Source
ToetsingOnline

Brief title
[18F]Fluoride PET-CT in AS

Condition

- Other condition
- Autoimmune disorders
- Bone disorders (excl congenital and fractures)

Synonym
ankylosing spondylitis, Bechterew's disease

Health condition

Gewrichten

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Reumafonds

Intervention

Keyword: Ankylosing spondylitis, Bone targeting, MRI, PET-CT

Outcome measures

Primary outcome

1. [18F]fluorid uptake in vertebral column and/or SI joints on PET-CT in AS patients with clinically active disease.

Sub-study in 2 patients:

2. Quality of the bone biopsy material of PET positive lesions in the vertebral column.

Secondary outcome

1. The relation between changes in [18F]-Fluoride PET-CT and clinical monitoring as well as CRP levels during anti-TNF treatment.

2. The relation between [18F]-Fluoride PET-CT outcome as tool for AS monitoring and MRI.

Study description

Background summary

Ankylosing Spondylitis (AS) is a chronic, inflammatory, rheumatic disease which usually starts at an early age (< 40 years of age) and can result in irreversible bone deformation and disability on the long term. The introduction of anti-tumor necrosis factor (anti-TNF) therapy made a more effective treatment of AS possible. TNF-blockers have an established comparable and impressive beneficial effect on axial, joint and tendon inflammation, on inflammatory serum parameters and on disease activity and function. In about 70% of the treated AS patients anti-TNF is successful. There is evidence that response to therapy is greater in patients with earlier disease and less damage. Therefore there is a need for sensitive imaging techniques to be able to select patients with active disease in particular in earlier stages and to predict therapeutic efficacy of expensive treatment with anti-TNF in a early phase. Conventional X-rays and CT-scans still play an important role for determination and monitoring of structural damage, but these irreversible changes occur only after 5 years of complaints. MRI has been explored as advanced imaging technique for detection of disease activity of AS, also in relation to treatment. However, conflicting data on the sensitivity and specificity of MRI in (suspected) spondylarthropathies have been published. Therefore, the precise role of MRI in visualizing disease activity of AS, remains unclear.
Positron emission tomography (PET), is another interesting imaging technique for assessment of disease activity of AS. PET allows sensitive imaging of functional tissue changes (pathophysiology) in the whole body by targeting binding sites. The visualisation of pathophysiology makes PET potentially suitable for early detection of inflammatory processes, even before anatomic changes appear. In addition, it allows quantification of disease activity in order to accurately monitor therapeutic effects. Recently, PET-CT scanning was introduced as hybrid imaging technique which combines the unique properties of sensitive imaging of pathophysiology and anatomical CT imaging as reference. In this way, PET-CT offers the opportunity to visualize (early) inflammatory changes as well as (early) structural changes such as new bone formation. Moreover, the specificity of PET by use of receptor targeting tracers may be another advantage for assessment of disease activity of AS. Since the definite pathogenesis of AS is still not clear and different joint structures (synovial tissue, bone marrow, entheses, ligaments) may be involved in inflammatory sites in AS, it is still not known which foci primarily represent disease activity.
In a recent pilot study setting, a subpopulation of 2 patients showed that the bone tracer [18F]fluoride was superior to the inflammation tracers [18F]FDG and [11C](R)PK11195 for depicting disease activity of AS. The present project will further evaluate the potential of the [18F]fluoride tracer in AS patients before and after anti-TNF therapy. Furthermore, in a small sub study of 2 patients, the possibility for obtaining representative bone biopsies of active bone lesions as depicted with PET-CT will be investigated for future pathogenic research.

Study objective

1.To investigate if [18F]Fluoride PET-CT is a potential imaging technique for

assessment of (changes in) disease activity of ankylosing spondylitis on baseline and after anti-TNF therapy (with MRI and clinical outcome as reference).

Sub-study in 2 patients:

2. To evaluate if it is technically possible to obtain representable bone biopsies under CT guidance from hotspots depicted with [18F]Fluoride CT scans. This procedure could be used in a future study to investigate the relation between lesions on [18F]Fluoride PET-CT and histology.

Study design

Ten AS patients with high disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score* 4) who will start with anti-tumor necrosis factor (anti-TNF) therapy will be included for a [18F]Fluoride PET-CT scan of the total spine as well as of the sacroiliac (SI) joints at baseline. Besides PET-CT, a MRI scan of the spine and SI joints will be performed. The different scans will be made within one week. The imaging procedure will be repeated 12 weeks after treatment. Anti-TNF treatment will be part of clinical care. Clinical disease activity will be monitored up to 24 weeks of anti-TNF treatment, including determination of C* reactive protein (CRP) levels. In a small sub study, two additional patients with the same characteristics as described above will be included for a bone biopsy procedure following the [18F]Fluoride PET-CT scan and MRI of the axial skeleton. These two patients will not be included for clinical and imaging follow-up because of interference of bone biopsy with follow-up of lesions on the scans and to limit the burden on the patients.

Study burden and risks

Radiation exposure
The effective dose equivalent (EDE) of a PET-scan with injection of 100 MBq [18F]fluoride is 1.7 mSv. Including low dose attenuation CTs (8 mSv), the total radiation exposure of the two series of PET-CT scans, baseline and 12 weeks after treatment, result in a total radiation burden of 11.4 mSv. For the two patients that will be scanned once with [18F]Fluoride PET-CT and obtain one diagnostic CT of one segment for bone biopsy, the radiation burden will be 1.7 mSv plus 5.5 mSv is 7.2 mSv per patient. For comparison: the mean effective dose of a diagnostic CT-abdomen is 11 mSv (data RIVM). This radiation burden is about 5 times the yearly natural background radiation dose in the Netherlands. According to the ICRP-62 model, the risk level corresponds to *moderate*, while the social benefit is regarded as *substantial*.

Vena puncture

The PET tracers and the gadolinium-contrast for MRI will be administered intravenously. The necessary vena puncture is similar to that applied for blood withdrawal in clinical practice.

Discomfort during scanning
It may be uncomfortable to lie motionless on the scanning bed of the PET-CT and the MRI scanner. For some patients, the scanning may be anxious. To reduce anxiety and discomfort as much as possible, patients will be made acquainted with the surroundings beforehand. In addition, the staff will be present during scanning and can remove the patient from the scanner if requested.

Risks of bone biopsy of axial skeleton
General risk of complication risk is 0.5% (in experienced hands). A careful preparation is most important to reduce complications. To further limit complications, bone biopsies will not be taken of the anterior vertebral column. The most common risk is post biopsy venous bleeding without other complications.

Benefit and group relatedness
Early diagnosis of AS and hence an early start of therapy as well as prediction of therapeutic outcome will contribute to increase the therapeutic efficacy. For these clinical needs, sensitive imaging techniques are required. Our previous pilot data indicate that [18F]Fluoride PET-CT imaging seems to be a potential image tool for assessment of (changes) of disease activity of AS by the novel approach of targeting
active bone sites. This will be further addressed in the current study protocol.

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. Men and women, * 18 and * 70 years of age
2. Diagnosis of ankylosing spondylitis according to the modified New York criteria.
3. The BASDAI score should be * 4.
4. Patients will start with anti-TNF according to clinical care.
5. Treatment with disease modifying anti-rheumatic drugs (DMARDS) and non-steroidal anti-inflammatory drugs (NSAIDs) is permitted, provided that there is a stable dose for at least 2 weeks prior to inclusion and during the study up to 16 weeks of follow up.
6. Patients must be able to adhere to the study appointments and other protocol requirements.
7. Patients must be capable of giving informed consent and the consent must have been obtained prior to the study related procedures.

Exclusion criteria

1. Treatment with any investigational drug within the previous 3 months.
2. Primary failure of anti-TNF treatment in the past.
3. Pregnancy or breast-feeding.
4. Implanted pacemaker
5. Renal failure with creatinine clearance < 30 ml/min

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-08-2013
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	29-04-2013
Application type:	First submission
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	NL43223.029.13