Bone - MRI in Renal Insufficiency

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The objective of this study is to assess the diagmostic accuracy of microMRI to detect ROD in children with ESRD and metabolic bone disease by oxalosis in patients suffering from oxalosis.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bone, calcium, magnesium and phosphorus metabolism disorders
Study type	Observational non invasive

Summary

ID

NL-OMON38866

Source
ToetsingOnline

Brief title
Bone-MRI

Condition

- Bone, calcium, magnesium and phosphorus metabolism disorders
- Bone disorders (excl congenital and fractures)
- Nephropathies

Synonym
End Stage Renal Disease, Hyperoxaluria

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: nader te bepalen

Intervention

Keyword: Bone, ESRD, Micro-architecture, MicroMRI

Outcome measures

Primary outcome

Primary objectives:

- To asses the validity of microMRI in imaging trabecular and cortical bone

- To asses the feasibility to diagnose ROD in pediatric ESRD with microMRI in an early stage

- To asses the feasibility to diagnose oxalosis associated bone disease with microMRI

Secondary outcome

Secondary objectives

- To investigate the possibility to distinguish between high and low turnover bone disease in pediatric ESRD with microMRI

- Compare microMRI with conventional radiography and/or DEXA scanning in children with ESRD

- Compare microMRI with conventional radiography and/or DEXA scanning in patients suffering from oxalosis

- Compare microMRI with pathological changes found in bone biopsies from adult ESRD patients who have clinical indication for bone biopsy

Study description

Background summary

Metabolic bone disease in pediatric end stage renal disease
Children with end stage renal disease (ESRD) usually also suffer from extrarenal manifestations of their disease. One of those extrarenal manifestations is metabolic bone disease (MBD), frequently referred to as Renal Osteodystrophy (ROD). In 2004 ROD was defined by the (American) National Kidney Foundation as a constellation of bone disorders, present in or exacerbated by renal failure which leads to bone fragility and fractures, abnormal mineral metabolism and extraskeletal manifestations. Earlier research has shown that adult survivors of pediatric onset ESRD frequently (39%) suffer from bone disease1.The abnormalities of bone turnover consist of either high turnover or low turnover. High turnover bone disease results in thickened, but irregular trabeculae and eventually to a decreased bone volume. Low turnover bone disease, also referred to as adynamic bone disease, is characterized by decreased bone volume and changed architecture of the trabeculae2. Both low and high turnover disease lead to a decreased bone mineral density and osteoporosis. Bone mineral density (BMD) is most frequently measured with Dual Energy X-Ray Absorptiometry (DEXA) which has many of advantages: it is non-invasive, easy and relatively cheap. Furthermore, it has a low dose radiation. For example, a DEXA-scan provides only 30 microSV, whereas qCT provides 5000 to 10000 microSV. This makes DEXA-scanning favorable, especially in the pediatric population. But DEXA also encounters a few problems. First of all, since DEXA provides a two dimensional reproduction of what actually is a three dimensional figure, it can underestimate the bone mineral density. Especially in the growing bone, as in children, this may lead to frequent misdiagnosing3;4;. Moreover, in ROD, where low bone turnover can lead to high bone mineral density, but low bone strength, the sensitivity of DEXA is insufficient for clinical purpose . And since the resolution of DEXA is low, DEXA isn*t capable to distinguish between cortical and trabecular bone. Finally, the association between bone mineral density measured with DEXA and fracture risk in chidlren is yet not clear5. The current Gold Standard to assess bone quality and bone strength is a bone biopsy, but due to its invasiveness this is not applicable in children. Therefore, a less invasive, but accurate way of assessing bone quality and strength is needed. Quantitative Ultrasound (QUS) to assess peripheral skeletal bone mineral status has been studied in children. Although it has many advantages such as low radiation, possibility to use it bedside and low costs, normative data in children are lacking. There are also important differences in accuracy and technical characteristics between several QUS-machines, which limits its usefulness in daily practice6. Conventional radiography is also frequently used to diagnose low bone density or osteoporosis. However, low bone density and bone loss is not detected with radiography until approximately 30% of bone loss has occurred. Besides, the way the film is developed, the extent of soft-tissue thickening and the variability in radiographic exposure all nfluence the quality and the interpretation of the imaging7. Finally, (micro) Magnetic Resonance Imaging (MRI) is an imaging technology that has the ability to acquire high resolution images of both cortical and trabecular bone. MRI uses a strong magnetic field and a sequence of radiofrequency pulses to produce a

three-dimensional image.
By imaging trabecular bone, trabecular bone itself is not actually visualized, but the network of trabeculae is shown indirectly trough visualization of the marrow. It appears as a signal void surrounded by high-signal-intensity fatty bone marrow. The appearance is influenced by technical variability, such as gradient echo sequences, longer echo times and higher field strengths. Most frequently bone MRI is performed on the calcaneus, knee and wrist with high resolution 3 Tesla MRI. One disadvantage of MRI is the amount of time it takes to perform MRI and possible artefacts that could overestimate the trabecular bone6. However, it is non-invasive, provides no radiation and showed great improvement in fracture discrimination in adults with high reproducibility in comparison with other imaging techniques8-10. Furthermore, MRI can discriminate differences in trabecular structure depending on the age of the patient, BMD and osteoporotic status. Since MRI for this cause is not common, there are no guidelines yet for the use for daily practice in assessing bone mineral status6.
Oxalosis associated bone disease
Primary hyperoxaluria is a rare autosomal recessive disorder of glyoxylate metabolism which results in overproduction of oxalate11;12. Oxalate is mainly eliminated by the kidneys and is both filtered in the glomerulus and secreted by the tubules 12. High concentration of oxalate causes formation of crystals within the tubules and eventually leads to a decline in renal function and even End-Stage Renal Disease (ESRD) in over 50% of all patients. With decreasing renal function, plasma oxalate levels are increasing, which causes extrarenal tissue deposition. Sites of deposition include myocardium, bone, retina, vessels and nerves 13. The only curative treatment is liver transplantation. Therefore treatment is mainly focused on preventing and delaying the onset of ESRD12. Due to improvement of the non-curative treatment of oxaluria, survival is prolonged, which has lead to new problems, such as oxalosis associated bone disease. Oxalosis associated bone disease is a combination of both renal osteodystrophy and oxalate deposition, leading to bone pain, growth retardation, deformities and even pathological fractures 13. Gold standard in diagnosing oxalosis associated bone disease is bone biopsy. However, this is an invasive procedure. X-ray shows a wide variety of findings (osteosclerosis, bone resorption, rickets, bone-in-bone appearance), but none of them reflects the actual clinical severity of the bone disease 13-15. Also, there are indications that X-ray is not a sensitive method for detecting bone disease in oxalosis. Studies with pQCT have shown more reliable results in order to detect and monitor skeletal disorders in primary hyperoxaluria13. In other bone diseases, microMRI has shown to be able to discriminate differences in e.g. trabecular structure16. MRI is potentially more sensitive than pQCT and has not the disadvantage of radiation burden. Early detection of metabolic bone disease by oxalosis might prevent the development of irreversible disabilities by earlier treatment.

Study objective

The objective of this study is to assess the diagmostic accuracy of microMRI to detect ROD in children with ESRD and metabolic bone disease by oxalosis in patients suffering from oxalosis.

Study design

This is a multi-center, observational study in five groups; healthy young and adult volunteers, pdiatric patients with ESRD (either on dialysis or after renal transplantation), adult patients with ESRD (either on dialysis or after renal transplantation) and adult oxalosis patients.
Pediatric patients from the Academic Medical Center (AMC) with ESRD will be asked to participate in this study. Each pediatric patient will have one MRI scan of approximately 45 minutes within 3 months after conventional radiography and/or DEXA scan. Each oxalosis patient will also have one MRI scan of approximately 45 minutes, within 3 months after conventional radiography. Finally, adult patients with ESRD who will need a bone biopsy for the clinical indication of therapy-resistant ROD be asked to participate in this study as well. MRI will be performed within 6 weeks after bone biopsy. Patients will be included after giving informed consent.

Study burden and risks

Participation in this study will not lead to immediate advantage for the patient. However, with this study we might be able to diagnose ROD and oxalosis associated bone disease in an earlier stage of the disease. As a consequence, we might be able to improve the health outcome in children with ESRD and oxalosis patients in the future. MRI examination is non-invasive and is a non-ionizing examination. Participants will have to lie still in the MRI for approximately 45 minutes. Participation in this study will require one extra visit to the hospital. There will be no delay in the treatment for the disease of the patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

ESRD on dialysis or after renal transplantation OR
hyperoxaluria, AND
age >8 years

Exclusion criteria

* Any co-morbidity causing bone disease, such as osteogenesis imperfecta, Marfan syndrome, Ehler Danlos, panhypopituitarism, malignancy and musculoskeletal disorders
* Inability to perform adequate MR imaging, for example not being able to lie still
* absolute contra-indications for MR imaging, such as metal in eyes, cardiac pacemakers, implanted cardioverter defibrillators, neurostimulation systems and cochlear implants

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:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	14-10-2013
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	NL44966.018.13