Validation of four quantitative radiological techniques to image cartilage quality in patients with knee osteoarthritis scheduled to undergo total knee replacement.

Published: 08-10-2012
Last updated: 26-04-2024

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

Summary

ID

NL-OMON37160

Source
ToetsingOnline

Brief title
QUICK study

Condition

- Joint disorders

Synonym
knee osteoarthritis, knee wear

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Articular cartilage quality, Knee osteoarthritis, Quantitative radiological technqiues

Outcome measures

Primary outcome

The main endpoints in this study are the correlation coefficients between the

in vivo outcomes of the quantitative MRI and CT techniques under investigation

and the in vitro reference standards for cartilage sGAG and collagen content.

Secondary outcome

The secondary endpoint of this study is the relation between the outcomes of

the DCE-MRI and the outcomes of the WOMAC and ICOAP questionnaires.

Study description

Background summary

Osteoarthritis (OA) is a very frequent degenerative joint disease causing substantial morbidity. It has been demonstrated that compared to other chronic disorders, OA contributes most to impaired physical quality of life in the general population, and leads to considerably higher costs to society than other musculoskeletal diseases such as rheumatoid arthritis and osteoporosis. These costs are largely attributable to joint replacement surgery in patients aged 65 years or older, which is nowadays the only definitive treatment strategy in end stage OA. Due to the ageing population, this OA associated socio-economic burden will only increase in future. It has been estimated that the number of OA patients in the Netherlands will have increased by almost 50% in 2040.
Because of this growing impact of OA to our society, current research in the field of OA is mainly focused on the pathogenesis, prevention and the development of disease modifying osteoarthritic drugs. Radiological imaging is

of utmost importance to gain more insight into the pathogenesis of OA, as well as to monitor prevention and treatment strategies both in the setting of research and in clinical care. Radiography has been extensively been used to detect and follow OA development over time. There are, however, major limitations of radiography applied for OA. Radiography cannot depict cartilage directly, which is an important tissue affected by OA. Instead, radiography only depicts joint space narrowing due to gross cartilage loss in moderate to advanced stage OA and is incapable of detecting OA progression sensitively within a reasonable time interval. Because of this, radiography should not be used as an outcome measure in OA research anymore. Therefore, magnetic resonance imaging (MRI) has been regarded as the most accurate radiological tool for imaging of OA related cartilage change nowadays. Until now, however, radiological evaluation of OA with MRI has usually been based on rather subjective assessment of morphologic cartilage damage.
For accurate monitoring of treatment strategies or detecting and following OA in an early stage, the current morphology based MRI techniques are insufficient: they lack quantitative (numerical) outcome measures of cartilage quality. Because of the lack of these quantitative outcome measures in OA research, many pharmaceutical companies have abandoned the OA research field, since no good outcome measures for efficacy studies of potential treatments were available which could also show an effect within a reasonable period of time.
To overcome the need of quantitative outcome measures to detect subtle changes and to evaluate early stages of OA before morphologic alterations occur, novel radiological techniques have been introduced in the past decade. These new techniques enable a sensitive and objective quantitative outcome measure of cartilage quality in terms of the glycosaminoglycan (sGAG) and/or collagen content of cartilage, which are known to be lost from the cartilage during the early stages of the disease. Currently, the most widely used quantitative technique in clinical research is delayed gadolinium enhanced magnetic resonance imaging of cartilage (dGEMRIC), which uses the inversed relation between a contrast agent and the sGAG content of cartilage. Recently, It has been shown that Computed Tomography arthrography (CTa) may also be used as a technique to quantitatively measure cartilage quality similar to dGEMRIC.
In addition to dGEMRIC and CTa, other promising techniques which have been introduced are T1rho and T2 mapping. These techniques also measure cartilage quality using MRI, but without the use of a contrast agent. The latter is a potential benefit of these techniques compared to dGEMRIC and CTa.
Although these quantitative MRI and CT based techniques have been reported as sensitive and accurate to detect abnormal cartilage quality in certain patient groups and healthy volunteers, no systematic comparison of the outcomes these different techniques in vivo against established reference standards for cartilage quality in-vitro have been performed.
In the present study, quantitative imaging of cartilage quality using MRI and CT will be evaluated in patients scheduled to undergo total knee replacement surgery, but with a discrepancy in OA stage between both compartments of the tibiofemoral joint (one compartment severe and one

compartment mild to moderate OA). By doing so, we have can validate the different techniques in different stages of OA within the same study. Outcomes of the imaging techniques in-vivo will be compared with in-vitro reference standards for cartilage quality (contrast-enhanced µCT (EPIC-µCT), histology (biochemical staining quantification) and biochemical sGAG and collagen assays on specimens of the knee cartilage obtained during total knee replacement surgery. This multi-parametric approach will enable us to thoroughly validate novel quantitative imaging techniques for cartilage, which has not been performed before.

Study objective

We hypothesize that all different novel quantitative radiological imaging techniques under investigation in this project are a measure for cartilage quality in terms of the sGAG content, collagen content, or a combination of both.

The primary objectives of the present study are:
1. To assess to which extent in vivo dGEMRIC does measure cartilage quality in terms of the sGAG and/or collagen content of cartilage as determined by the reference standards for sGAG and collagen content.
2. To assess to which extent in vivo T1rho does measure cartilage quality in terms of the sGAG and/or collagen content of cartilage as determined by the reference standards for sGAG and collagen content.
3. To assess to which extent in vivo T2 mapping does measure cartilage quality in terms of the sGAG and/or collagen content of cartilage as determined by the reference standards for sGAG and collagen content.
4. To assess to which extent in vivo CTa does measure cartilage quality in terms of the sGAG and/or collagen content of cartilage as determined by the reference standards for sGAG and collagen content.

Although the pathogenesis of OA and associated pain has not been fully clarified, it has been suggested and we hypothesize that altered blood perfusion in the subchondral bone may play an important role by affecting the structure of articular cartilage and by inducing specific patterns of OA pain possibly through blood vessel and nerve proliferation.
Quantification of subchondral bone perfusion is possible with dynamic contrast enhanced (DCE)-MRI. Although DCE-MRI has not been widely applied in OA research, patients included in this study get an intravenous injection with contrast agent for acquisition of dGEMRIC anyway. This contrast agent also can be used to acquire a DCE-MRI and therefore, without extra burden for the participants, we will also acquire a DCE-MRI prior to dGEMRIC in this research project.

The secondary objective of the present study is:
To assess if different symptom phenotypes of OA are associated with findings on the novel quantitative radiological imaging studies mentioned above by

comparing their outcomes with the outcomes of clinical examination and the outcomes of two questionnaires validated for OA (the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) and the Intermittent and Constant OsteoArthritis Pain (ICOAP).

Study design

The present study has a cross-sectional observational design. Participating patients will undergo a MRI scan and a CTa scan, both in a separate session. The investigations will take place before surgery during which a total knee replacement is performed.

Study burden and risks

The measurements needed for the data collection of the present study consist of a blood test to determine the kidney function, two questionnaires (the Western Ontario and McMasters Universities Osteoarthritis Index and the Intermittent and Constant OsteoArthritis Pain, a MRI scan (combination of dGEMRIC, T1rho and T2 mapping in one session) of the knee and a CTa of the knee (separate session). The burden for the patients consists of an extra visit to the hospital to undergo CTa (approximately one hour total time) and an intravenous (MRI) and intra articular (CT) injection with contrast agent before undergoing the MRI and CT examination.

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

Patient is older than 18 years, knee pain for more than one month, a discrepancy in radiological OA stage between both compartments of the tibiofemoral joint (one compartment severe and one compartment mild to moderate OA according to Kellgren & Lawrence, and one of the following: patient is older than 38 years, there is less than 30 minutes of morning stiffness in the knee or crepitures and bony enlargement are present during physical examination.

Exclusion criteria

Severe knee OA without asymmetric distribution in severity between both compartments of the tibiofemoral joint, varus or valgus deformity in the knee > 10 degrees, chondrocalcinosis, absolute and relative contra-indications to undergo MRI: brain aneurysm clip, implanted neural stimulator, cardiac pacemaker or defibrillator, cochlear implant, ocular foreign body, other implanted medical devices: (e.g. catheters, insulin pump, metal shrapnel or bullet or metallic implant in the region of the target knee joint), pregnancy, lactating women, renal insufficiency (defined by a glomerular filtration rate of <60 milliliter/minute), allergy to contrast agents for dGEMRIC or CTa (Magnevist ®, Bayer Schering AG, Berlin, Germany or Hexabrix 320, Mallinckrodt, Hazelwood, MO, USA), alcoholism or insufficient command of the Dutch language: spoken and/or written.

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):	04-12-2012
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO

Date:	08-10-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL40603.078.12