Ambulatory Monitoring of Knee Loading during ADL, towards Personalized Treatment and Rehabilitation Strategies for Knee Osteoarthritis Patients

Published: 21-04-2011
Last updated: 04-05-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Joint disorders
Study type	Observational non invasive

Summary

ID

NL-OMON36803

Source
ToetsingOnline

Brief title
Ambulatory monitoring of knee loading in knee osteoarthritis during ADL

Condition

- Joint disorders

Synonym
knee osteoarthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

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

Intervention

Keyword: Ambulatory, Daily activity, Knee Osteoarthritis, Rehabilitation

Outcome measures

Primary outcome

The pathomechanics and initiation of OA will be conducted in this cross-sectional study. Also the association between obesity and OA will be examined, which will further unravel the pathomechanics of knee osteoarthritis.

Our study parameters are:

- Lower extremity biomechanics (e.g. knee adduction moment) and knee joint loading will be measured under controlled laboratory conditions using 3D motion analysis (VICON) and surface EMG [15, 16].

- Knee extensor and flexor strength will be assessed with Biodex dynamometer.

- Biomarkers for cartilage metabolism (i.e. C2C, CTX-II) will be analyzed using enzyme-linked immunosorbent assay (ELISA) on urine samples obtained on the same day we perform the 3D-motion analysis (VICON) and MRI. [7, 14, 17].

- Structural adaptations of cartilage will be analyzed by using quantitative magnetic resonance imaging [18-20]. Cartilage thickness shall be graded in the anterior, central, and posterior regions of the medial and lateral knee compartments.

- Activities of daily life (ADL) and knee flexion and extension in the sagittal plane of the knee will be monitored for a single day follow-up study in which subjects are asked to wear an intelligent knee brace for at least 8 hours per day [21] and a CAM activity monitor for 7 days [22].

The endpoints of the study are described above. Our main endpoint is the knee

adduction moment. Our endpoints are:

- 3D-motion analysis: Knee adduction moment. This will be our main endpoint!

- Biomarkers: Urine samples; ELISA (C2C, CTX-II): inter-group differences

- MRI: cartilage thickness graded by region, mentioned above.

- Ambulatory knee brace: ADL and flexion/extension in the sagittal plane.

- CAM: Activity monitor, Activity pattern for 7 consecutive days.

Secondary outcome

nvt

Study description

Background summary

Knee osteoarthritis (OA) is a common musculoskeletal condition, considered as the 4th most degenerative disease in the world. Knee OA is the single most common cause of pain and disability in middle-aged and older adults [1]: 25% of people over 55 years have a persistent episode of knee pain, of whom about 1/6 consult their general practitioner in the Netherlands [2]. The exact etiology of OA is yet to be established, but the main risk factors are well known and commonly include mechanical, biochemical and genetic risk factors. Of these risk factors, obesity is considered a prominent one. Obesity is associated with altered knee kinematics and increased knee loading and systemic and hormonal factors may accelerate the progression of OA [3-8].
Andriacchi and Mundermann (2008) proposed a common framework for the initiation and progression of knee osteoarthritis in which the interplay between abnormal biomechanics and changes in cartilage metabolism lead to degeneration. Studies on ambulatory loads suggests that risk factors such as being obese, may initiate the development of knee osteoarthritis, similar to that in ACL injury.
The cartilage thickness at the knee joint in overweight and obese subjects responds to loading during gait in a manner similar to patients with osteoarthritis. It is argued that increased weight initiates cartilage degeneration prior to the emergence of osteoarthritis symptoms. Unraveling the interactions between obesity, in vivo function, joint anatomy, and cartilage mechanobiology requires combined evaluation of biological changes (biomarkers), structural adaptation (quantitative MRI), and in vivo patient function (gait

analysis).

The pathomechanics of OA should be studied in the context of interacting abnormal, excessive and repetitive loading patterns of the knee joint, which are highly dependent on the daily activity patterns. In addition, OA patients show adaptive locomotion that can be used to identify progression of OA [9]. A smart knee brace was recently developed within the Biosensing project to quantify peak loads and repetitive loading patterns of the knee joint during ADL. This novel technology will enable to tailor treatment and rehabilitation strategies to the needs of the individual patient.

Study objective

Previous studies [10] have proposed that cartilage degeneration due to obesity could be caused by changes in the joint kinematics during ADL that shifts the loading applied to cartilage. Such a shift may cause regions of cartilage to become newly (excessively) loaded, be subjected to altered levels of compression and tension, or become unloaded. The metabolic sensitivity of chondrocytes to such changes in their mechanical environment, combined with the low adaptation potential of mature cartilage, could lead to cartilage degeneration and premature osteoarthritis in obesity [11-14]. Hence, obesity may be used as a model to understand the relationship between mechanics and biology, as well as helping to explain the importance of restoring normal ambulatory kinematics in obese subjects to avoid premature osteoarthritis.

The main questions for this study are;
* Does obesity lead to detrimental kinematics and subsequent load shifts across the articular surface of the knee during daily activity?
* Does obesity affect the biological response to loading measured from biomarkers for cartilage degeneration?
* What kind of compensatory strategies do obese OA patients employ during daily activity/exercise to unload the knee?

Study design

The study will be a cross-sectional study in which three groups will be included. The three groups will consist of an obese (BMI>30) OA group, a non-obese (BMI<25) OA group, and a healthy control group. Groups will be matched for age and gender. All tests are performed only once , in order to compare the three groups to each other on lower limb mechanics (i.e. mechanics regarding the knee joint), cartilage adaptation (i.e. cartilage degeneration) and biological adaptation (i.e. biomarker levels in urine samples).

Subjects will be divided into 3 groups depending on BMI (BMI<25 which is the non-obese group or BMI>30, which is the obese group), and a healthy control group.

This creates three groups:
1. Obese (BMI>30) with knee osteoarthritis (according to the American College of rheumatology classification criteria).
2. Non-obese (BMI<25) with knee osteoarthritis
3. Healthy control group (BMI<25 and no knee osteoarthritis and or other diseases according to the exclusion criteria).
In addition, there will be no blinding. The researchers do know in which group the subjects belong and the subject will know to which group they will be assigned.

The measurements will take place on two different locations (the movement laboratory of the department of Human Movement Sciences of the University of Maastricht and the department of Radiology at the University Hospital of Maastricht). Subjects will be measured in one day according to the time schedule mentioned above. First the subjects will be measured in the Motion laboratory of the department of Human Movement Sciences at the University of Maastricht. Before starting the tests, subjects are asked to turn in their urine samples (i.e. first urine of the day and midstream) that they collected themselves in the morning in a previously send urine jar. These are processed in our laboratory of the department of Orthopedic Surgery and frozen for further analysis. Thereafter, maximal isometric and dynamic knee extensor and knee flexor strength will be measured by use of a Biodex dynamometer in the Motion Laboratory. Furthermore a 3D-motion-analysis is performed in combination with EMG measurements using a wireless 8-channel EMG recording unit. Hereafter, a MRI scan will take place at the radiology department in the University Hospital Maastricht. Subjects are guided by one of the researchers. After all the measurements are performed subjects return home with a smart knee brace for a day (i.e. 8 hours) of ambulatory datarecording. Besides the kneebrace a CAM activity monitor is used in this study. The CAM will measure activity in daily life for 7 days in a row. Subjects will receive all information of both ambulant systems at the end of the measurements in the laboratory of human movement sciences. The knee brace and CAM activity monitor is picked up again by one of the researchers after the measurement period for data-analysis.

Study burden and risks

Subjects will be tested in the Motion Laboratory through the Biodex system requiring them to maximally apply force in an isometric setting. These tests have been widely accepted as applicable when testing MVC. The risks involved are minimal and could be some muscle soreness the next few days. No other risks are involved or otherwise described in other studies. Next 3D-motion analysis is performed, which requires preferred walking speed, getting up from a chair en walking a one step stairs with side-bars. The entire walking surface is flat, the room is fully lighted and a research-assistant will help the subjects in performing the tests at all times. Otherwise there are no risks involved. EMG measurement only requires shaving of the skin if necessary. We ask about

allergies before applying the stickers and using chloorhexidine. There are no risks involved in EMG measurement. Next a MRI scan is performed. This requires lying down very still from a subject for about an hour. The Radiology department will assist in preparing the subject and explaining the protocol. All metal objects are removed from the subject. The potential risks involved could be previously not mentioned claustrophobia. If this ought to be an acute problem to the subject, then subjects as well as the MRI-performing radiology-assistant are allowed to withdraw from testing at all times! Otherwise we conclude there are no other risks involved.
The ambulatory knee brace does not include any risks. It is a closed system, fitted upon a registered NEA *Push*-brace, which can be worn only in one way and is recharged by the common 220V in Dutch homes. The CAM activity monitor does not involve any risk, subjects will be informated about the placement of the CAM.

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

The subjects have to be standardized by age. Only women between the age of 50 and 65 will be included for this study. The cut-off age of 50 is determined by epidemiological data about prevalence of knee osteoarthritis. In which osteoarthritis is more common in women and in women at an age of >50 years. The age of 65 is set as a cut-off point because the risks of co-morbidity increases severely after the age of 65 and so does the risk of altered mechanics of the lower-limb due to other diseases and/or musculoskeletal or neurological problems. Males are not included because we want to standardize for gender. OA patients with a Kellgren-Lawrence(KL)-knee score of 1 and 2 are included in the OA groups. Obese OA patients will be recruited from the *artrose kliniek maastricht*. The American College of Rheumatology clinical classification criteria are used to define knee OA. This requires the presence of knee pain and at least 3 of the following: age > 50 years, morning stiffness < 30 min, crepitus, bony tenderness, bony enlargement, and no palpable warmth. Subjects with a BMI < 25 will be included in the non-obese group; subjects with a BMI > 30 will be included in the obese group. A normalized knee adduction moment has been shown to be the most sensitive marker for progression of OA (15,16). A total of 81 subjects will be included in the study (27 per group) based on the following assumptions; i) a 2% difference in normalized adduction torque differentiates between subjects prone to progression of OA and those that are not(i.e. a 2% difference in knee adduction moment distinguishes between onset of cartilage degeneration or not, which is clinically represented with pain and movement dysfunction, as suggested by Andriacchi and Muendermann 2004) and ii) a dropout rate of 20%.

Exclusion criteria

Clinical exclusion criteria: any inflammatory arthritis, trauma, patellofemoral osteoarthritis, ACL-injury, medial and collateral ligament injury;MRI exclusion criteria: knee replacement surgery; weight > 150 kg; knee circumference > 52 cm; claustrophobia. dGEMRIC exclusion criteria: glomerular filtration rate (eGFR) < 60 mmol/l, pregnancy, or breast feeding. These exclusion criteria go for all subjects including our healthy controls.
We consider subjects healthy controls in this study when they are non-obese (BMI<25), have no knee osteoarthritis (according to the American College of Rheumatology classification criteria) and do not meet any of the other exclusion criteria mentioned above.

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:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2011
Enrollment:	81
Type:	Actual

Ethics review

Approved WMO Date:	21-04-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-11-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	NL34412.068.10