Osteoarthritis and Cartilage 25 (2017) 227–233

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

The interaction between weight and family history of total knee replacement with knee cartilage: a 10-year prospective study

F. Pan †, L. Blizzard †, J. Tian †, F. Cicuttini ‡, T. Winzenberg †, C. Ding †, G. Jones † *

† *Menzies Institute for Medical Research, University of Tasmania, Private Bag 23, Hobart, Tasmania 7000, Australia*
‡ *Department of Epidemiology and Preventive Medicine, Monash University Medical School, Commercial Road, Melbourne 3181, Australia*

ARTICLE INFO

Article history:
Received 7 July 2016
Accepted 17 October 2016

Keywords:
Weight
Osteoarthritis
Family history
Knee cartilage
Longitudinal study

SUMMARY

Objective: Although being overweight or obese is an important risk factor for the development of knee osteoarthritis (OA), the interplay between weight and genetic factors remains unclear. This study aimed to examine the associations between weight and knee cartilage volume/defects over 10 years in offspring having at least one parent with a total knee replacement (TKR) for primary knee OA and in controls without a knee OA family history.

Method: 367 participants (183 offspring and 184 controls) aged from 26 to 61 years were recruited at baseline, and followed at 2 and 10 years later. T1-weighted magnetic resonance imaging (MRI) of the right knee was used to measure cartilage volume/defects at each time-point. Mixed-effects models were used with adjustment for potential confounders.

Results: Study participants were middle-age adults (mean age 45 years, mean weight 77.5 kg at baseline). In multivariable analysis, increasing body weight was deleteriously associated with medial tibiofemoral cartilage volume ($\beta = -0.28$ ml, per 1 SD increase, 95% CI −0.49 to −0.07) and presence of medial tibiofemoral cartilage defects (RR = 1.27, per 1 SD increase, 95% CI 1.07 to 1.51) in offspring over 10 years. Similar associations were observed for lateral tibiofemoral cartilage volume ($\beta = -0.19$ ml, $P = 0.059$), and defects (RR = 1.24, $P = 0.049$). However, there were no statistically significant associations between weight and cartilage volume or defects in controls.

Conclusion: The adverse effects of increasing weight are stronger in the offspring of people with knee replacement for knee OA suggesting genetics–environment interaction with regard to overweight/obesity in the pathogenesis of knee OA particularly in the early stages.

Introduction

Knee osteoarthritis (OA) is the most common form of arthritis worldwide and affects an estimated 30% of individuals aged over 65 years, often leading to pain, disability and reduced quality of life[1,2]. Despite this, its etiology remains poorly understood.

Knee OA is considered to be a multifactorial and heterogeneous disease affected by genetic and multiple environmental factors[3,4]. Previous family-based studies have shown a strong genetic basis for OA, with the estimated heritability of approximately 39–65%[5,6]. There are 11 loci associated with OA now identified in genome-wide association studies (GWAS), although the effect sizes are small[2]. Being overweight or obese is one of the strongest environmental risk factors for the development and progression of radiographic knee OA (ROA)[7,8]. A recent meta-analysis has shown an over two-fold increased risk of ROA in those who are overweight or obese[7]. An earlier study has reported that the effect of variation in the fat mass and obesity-associated (FTO) gene on increased risk of OA is mediated solely through its effect on body mass index (BMI)[9].

Cartilage volume and defects, measured by magnetic resonance imaging (MRI), are examples of the early structural changes of pre-radiographic knee OA. Both predict clinically relevant endpoints such as knee replacement[10–12]. Most studies investigating the effect of weight/BMI on knee cartilage have mainly been cross-sectional or short-term follow-up studies and have reported generally consistent detrimental relationships of increasing weight

* Address correspondence and reprint requests to: G. Jones, Menzies Research Institute Tasmania, University of Tasmania, 17 Liverpool Street, Hobart, Tasmania 7000, Australia. Fax: 61-3-6226-7704.
E-mail addresses: Feng.Pan@utas.edu.au (F. Pan), Leigh.Blizzard@utas.edu.au (L. Blizzard), J.Tian@utas.edu.au (J. Tian), Flavia.Cicuttini@monash.edu (F. Cicuttini), Tania.Winzenberg@utas.edu.au (T. Winzenberg), ChangHai.Ding@utas.edu.au (C. Ding), Graeme.Jones@utas.edu.au (G. Jones).

http://dx.doi.org/10.1016/j.joca.2016.10.013
1063-4584/

with cartilage defects but not cartilage volume[13]. Given that overweight/obesity is a strong risk factor for knee OA, and genetic factors are implicated in the pathogenesis of knee OA, it is important to understand how genetic factors interact with weight to influence the risk of pre-radiographic knee OA. The aim of this longitudinal study was, therefore, to examine the effects of weight on knee cartilage volume and defects over 10 years in offspring having at least one parent with a total knee replacement (TKR) for severe primary knee OA, and in controls with no family history of knee OA.

Methods

Participants

This study was carried out in Hobart, Tasmania. Baseline measurements were taken from June 2000 to December 2001, and follow-up evaluations were conducted after approximately 2 and 10 years. Participants were selected from two sources, as described previously[14,15]. Half of the participants were the adult children (offspring) of people who had a TKR performed for primary knee OA (defined as OA lacking known cause) at any Hobart hospital from 1996 to 2000. This diagnosis was confirmed by reference to the medical records of the orthopaedic surgeon and the original radiograph where possible. The other half were controls selected at random from the state Electoral Roll (2000), without a history of knee OA in either parent which was confirmed by history and medical records. Participants from either group were excluded on the basis of contraindication to MRI (including metal sutures, presence of shrapnel, iron filing in eye, and claustrophobia). The study was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee and all participants provided informed written consent.

Anthropometrics

Anthropometrics were measured at baseline, 2 and 10 years. Weight was measured to the nearest 0.1 kg (with shoes, socks and bulky clothing removed) using a single pair of electronic scales (Seca Delta Model 707) calibrated at the beginning of each clinic. Height was measured to the nearest 0.1 cm (with shoes and socks removed) using a stadiometer. BMI (kg/m^2) was calculated.

History of knee injury and smoking

Knee injury was assessed at baseline by asking 'Have you had a previous knee injury requiring non-weight-bearing treatment for more than 24 h or surgery?'. Smoking history was assessed at baseline by asking 'Have you ever smoked at least seven cigarettes, cigar or pipes every week for at least 3 months?'.

Radiographs

A standing anteroposterior semiflexed view of the right knee was performed at baseline and scored using the Altman atlas for osteophytes and joint space narrowing (JSN) on a scale of 0–3 as previously described[16]. The presence of ROA was defined as any score ≥ 1 for JSN or osteophytes.

Knee MRI

An MRI scan of the right knee was performed with a 1.5T whole-body magnetic resonance unit (Picker, Cleveland, OH, USA) using a commercial transmit-receive extremity coil at baseline, 2-year and 10-year follow-up. The following image sequences were used: a T1-weighted fat suppression three-dimension gradient-recalled acquisition in the steady state, flip angle 55°, repetition time 58 ms, echo time 12 ms, field of view 16 cm, 60 partitions, 512 × 512–pixel matrix, slice thickness of 1.5 mm without an interslice gap.

Cartilage volume

Knee cartilage volume was determined by means of image processing on an independent work station using Osiris (University of Geneva) as previously described[17,18]. The volumes of individual cartilage plates (medial tibia and lateral tibia) were isolated from the total volume by manually drawing disarticulation contours around the cartilage boundaries on a section by section basis. These data were then resampled by means of bilinear and cubic interpolation (area of 312 × 312 mm and 1.5 mm thickness, continuous sections) for the final three-dimensional rendering. The coefficient of variation (CV) for cartilage volume measures was 2.1% for medial tibial, and 2.2% for lateral tibial cartilage[17]. Knee femoral cartilage volume was determined by means of image processing on an independent workstation using Cartiscope™ (ArthroVision Inc., Montreal, QC, Canada), as previously described[19–21]. The segmentation of the cartilage–synovial interfaces was carried out with the semi-automatic method under reader supervision and with corrections when needed. Cartilage volume was evaluated directly from a standardized view of three-dimensional cartilage geometry as the sum of elementary volumes. The CV was approximately 2.0%[19]. The cartilage volume assessment was done for the medial and lateral condyles delineated by the Blumensaat's line[20]. The medial and lateral tibiofemoral cartilage volume created for this study were the sum of the cartilage volume of the corresponding sites.

Cartilage defects

Cartilage defects were assessed as previously described[22] on T1-weighted MRI at the medial tibial, medial femoral, lateral tibial, and lateral femoral sites, as follows: grade 0 = normal cartilage; grade 1 = focal blistering and intracartilaginous low-signal intensity area with an intact surface and base; grade 2 = irregularities on the surface or base and loss of thickness <50%; grade 3 = deep ulceration with loss of thickness >50%; and grade 4 = full-thickness chondral wear with exposure of subchondral bone. The intraclass correlation coefficients (ICCs) ranged from 0.89 to 0.90 for intra-observer repeatability. Interobserver reliability was assessed in 50 MR images and yielded an ICC of 0.85–0.90[23]. The presence of any cartilage defect at medial or lateral tibiofemoral compartment was defined as a score of ≥ 2 at either tibial or femoral site.

Bone area

The tibial plateau bone area was determined, as described previously[17]. Medial and lateral tibial plateau area was determined by creating an isotropic volume from the three input images closest to the joint after reformatting in the axial plane. The areas of the medial and lateral tibial plateaus were then directly measured from these images. The CV was 2.3% and 2.4% for the medial and lateral tibial plateau[17].

Data analysis

The continuous and categorical variables were respectively presented as Mean ± SD and percentages. *t*-Test and χ^2 tests were used to compare the differences in means and percentages where