Factors associated with meniscal body extrusion on knee MRI in overweight and obese women

Fan Zhang, MD[1], Sita M. Bierma-Zeinstra, PhD[2,5,], Edwin H.G. Oei, MD, PhD[3], Aleksandra Turkiewicz, PhD[1], Martin Englund, MD, PhD[1,4*], Jos Runhaar, PhD[5*]

[*] equal contribution as senior authors

[1] Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Orthopaedics, Clinical Epidemiology Unit, Lund, Sweden

[2] Erasmus MC, University Medical Center Rotterdam, the Netherlands, Department of Orthopaedics

[3] Erasmus MC, University Medical Center Rotterdam, the Netherlands, Department of Radiology & Nuclear Medicine

[4] Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, USA

[5] Erasmus MC, University Medical Center Rotterdam, the Netherlands, Department of General Practice

Email addresses: Fan Zhang: fan.zhang@med.lu.se

Sita M. Bierma-Zeinstra: s.bierma-zeinstra@erasmusmc.nl

Edwin H.G. Oei: e.oei@erasmusmc.nl

Aleksandra Turkiewicz: aleksandra.turkiewicz@med.lu.se

Martin Englund: martin.englund@med.lu.se

Jos Runhaar: j.runhaar@erasmusmc.nl

Corresponding author: Fan Zhang, MD, PhD student

Clinical Epidemiology Unit, Orthopaedics

Klinikgatan 22, Wigerthuset

SE-221 85 Lund, Sweden

Tel: +46-46-171394

Fax: +46 46 177167

ABSTRACT

Objective: To determine factors associated with higher degree of meniscal body extrusion in overweight and obese women at high risk of knee osteoarthritis (OA).

Design: We used baseline data of the PROOF study, Netherlands, comprising overweight or obese women aged 50 to 60 years, free of clinical knee OA. All subjects completed a questionnaire on knee complaints and physical activity, underwent physical examination, radiography, and 1.5 Tesla MRI of both knees. Using the mid-coronal MRI slice, one blinded observer measured tibial plateau width and meniscal body extrusion of both menisci in both knees. The association between baseline factors and meniscal extrusion, were analyzed with a random effects regression model. In addition, we used a fixed effect regression model for evaluation of knee-specific factors.

Results: Mean age of the included women (n=395) was 55.7 years and mean body mass index 32.4 kg/m^2. Of all knees, 23% had an absolute medial meniscus body extrusion ≥3.0 mm and 4% had lateral meniscus body extrusion ≥3.0 mm. In the multivariable model, the medial meniscus extrusion was increased by 0.44 mm (95% confidence interval [CI] 0.11, 0.77) when a medial meniscus tear was present, by 0.20 mm per 5 kg/m^2 (95% CI 0.05, 0.35) increase in body mass index and by 0.25 in the presence of mild knee symptoms (95% CI 0.05 to 0.44). Kellgren-Lawrence grade ≥1 and tibia width were associated with increased both medial and lateral extrusion.

Conclusion: In women, ipsilateral meniscus tear and high body mass index are factors associated with medial meniscus body extrusion.

Key words: Knee, meniscus, magnetic resonance imaging, osteoarthritis, women

INTRODUCTION

The menisci are two crescent-shaped fibrocartilaginous discs located medially and laterally between the surfaces of femur and tibia in the knee joint cavity. The menisci act to disperse the weight of the body, reduce shock and friction during movement and stabilize the knee joint[1, 2]. If the integrity or normal position of meniscus is compromised, these functions may be negatively affected. Findings of meniscus tears or destruction on magnetic resonance imaging (MRI) of the knee are common in the general population and increase with increasing age[3, 4]. Several reports show damage to the menisci is a strong risk factor for the occurrence and progression of knee osteoarthritis (OA) [5-7]. Further, if the outer margin of meniscal body (mid portion of meniscus) is markedly located outside the tibial joint margin, typically by 3 mm or more, this phenomenon is considered as meniscus extrusion[8, 9].

Meniscus extrusion has been reported to be more prominent in women than men[10, 11]. Knee OA is also more frequent in women after menopause than in men of corresponding age[12-14]. The gender propensity may be attributed to certain female physiological factors which may lead to increased laxity of certain knee structures such as collateral ligaments which serve as important attachment of the medial meniscus in particular[15, 16]. Body mass index (BMI) has also been reported as a risk factor for the development of medial meniscal extrusion [17]. Obesity increases the load that needs to be transmitted by the menisci, which may also lead to meniscus extrusion. Among population without any signs of radiographic OA a previous study has suggested that female sex, incident meniscal tear, and higher baseline value of extrusion are risk factors for increased meniscal body extrusion[18].

In order to get a better understanding of factors associated with meniscus extrusion in women, and potentially better insight into the mechanisms involved in knee OA development, we studied a specific cohort of obese women OA. We paid attention to a number of pre-specified demographic and knee-specific characteristics such as age, BMI, presence of meniscus tear, menopause, knee alignment, the presence of Herberden's nodes, prior knee injury etc. which might be associated with meniscal body extrusion.

METHODS

Study sample

Data of our study were obtained from baseline data of the PRevention of knee Osteoarthritis in Overweight Females (PROOF) study, Netherlands, which comprises 407 women with a BMI ≥27 kg/m^2, aged 50 to 60 years, free of clinical knee OA according to the clinical ACR criteria for knee OA [19]. . However, some of the participants already had evidence of radiographic knee OA. The BMI cut-point of 27 kg/ m^2 was chosen since there is a clear increase in OA incidence beyond this point[20]. All subjects completed a questionnaire on knee complaints and physical activity, underwent physical examination, radiography, and 1.5 Tesla MRI of both knees. PROOF was originally designed to evaluate the effects of a diet, exercise program and glucosamine sulphate on the development of clinical knee OA. During the progress of reading images, we found that 12 subjects' MR images were incomplete (with only one sided knee images) or unreadable. Therefore, the final number of subjects analyzed was 395.

PROOF was approved by the ethics committee at the Erasmus University Medical Center Rotterdam, the Netherlands in 2005.

MRI protocol

MRIs of both knees were acquired at baseline on 1.5 T scanners The MRI protocol included coronal and sagittal non-fat suppressed proton density weighted sequences (slice thickness 3.0 mm/slice gap 0.3 mm), a coronal T2 weighted Spectral Presaturation by Inversion Recovery sequence (slice thickness 5.0 mm/slice gap 0.5 mm, , TE 79ms, TR 2550ms, No of slices 17, Matrix 448x358, No. of signals acquired 2, FOV 480x144, echo train length 7), an axial dual spin-echo sequence (slice thickness 4.5 mm/slice gap 0.5 mm, TE 14 / 100 msms, TR 3000ms, No of slices 19, Matrix 512x512, No. of signals acquired 1, FOV 160x160 mm, echo train length 5,) and a sagittal 3D water selective sequence with fat saturation (slice thickness 1.5 mm, TE 6ms, TR 19.5ms, No of slices 17, Matrix 384x384, No. of signals acquired 1, FOV 160x160 mm, echo train length 1).

MRI measurements

We used a two-dimensional quantitative measurement method of meniscal extrusion previously reported by several other investigators[6, 8]. One observer (FZ), who was blinded to subject characteristics and clinical data, performed measures on both left and right knees on the baseline mid-coronal MR images. We refer 'mid-coronal' to the single slice visually presenting the greatest area of the medial tibial spine. Sometimes this was difficult to differentiate because two slices may depict a similar area of the tibial spine, in which case we used the slice which showed the greatest width of the tibial plateau. The observer measured tibial plateau width from the margin of the tibial plateau excluding any possible osteophytes, medial and lateral meniscus coronal width, and meniscal body extrusion to the closest 0.1 mm using Sante DICOM Editor (64-bit) software (Figure 1). Thirty randomly selected knees were reassessed. Intra-observer reliability (intra-class correlation coefficient) and inter-observer reliability for the tibial plateau width, medial and lateral meniscus width, medial and lateral meniscal extrusion ranged from 0.69 to 0.98 and 0.62 to 0.96, respectively.

(Figure 1)

Meniscal tears were read by two trained readers(JR, PvdP) and one experienced musculoskeletal radiologist(EO) as part of MOAKS scoring system [21 22]. After extensive training, high to nearly perfect inter-observer reliability was reached[21].

Other covariates

BMI was defined as the body weight in kg divided by the square of the body height in meters. Both hands were examined for Heberden's nodes. Standardized semi-flexed posterior-anterior knee radiographs were taken, according to the MTP-protocol[23]. Knee radiographs were read by a trained reader, blinded to clinical measures, according to the Kellgren-Lawrence (KL) scale[24]. Medial anatomical knee alignment angle was assessed by digitally determining the angle between the line from the center of the tibial spine through the center of the femoral shaft at approximately 10 cm from the joint margin and the matching line through the tibia[25]. Isometric quadriceps muscle strength was measured as maximal isometric contraction in a supine position, using a hand-held dynamometer. This method has proven to be valid and reliable [26]. Date of birth and information on physical activity level[27], menopausal status, mild knee symptoms (defined as any knee complaints in the last year), and previous knee injury were ascertained by questionnaires.

Statistics

Our pre-specified hypothesized risk factors that we evaluated were: age (continuous), BMI (continuous), physical activity (continuous), menopause status (yes/no), presence of mild knee symptoms (yes/no), Heberden's nodes (yes/no), knee alignment (categorical), Kellgren-Lawrence (KL) grade (0 vs ≥1), ipsilateral meniscus tear (yes/no), history of knee injury (yes/no), and quadriceps muscle strength (continuous). We used a random effects linear regression model with robust standard errors to analyze the association of these risk factors with medial and lateral extrusion, respectively. We adjusted all analyses for the tibial plateau width to take the knee size into account. In a second step, we used a fixed effects linear regression model to analyze the association of the knee-specific risk factors with medial and lateral extrusion, respectively. This method allows to control for all the person-level confounding (both measured and unmeasured) by using a person as her own control [28] .

RESULTS

The mean (SD) age of the study participants (n=395) was 55.7 (3.2) years and the mean (SD) BMI was 32.4 (4.3) kg/m^2. Among all 395 women, 267 (68%) were postmenopausal and 104 (26%) had Heberden's nodes. Of the 790 knees, 313 (40%) had varus malalignment while 98 (12%) had valgus malalignment, 246 (31%) reported an affirmative answer (yes) to the question: "Have you experienced pain in or around the knee during the last 12 months?", 100 (13%) had a history of injury, and 393 knees (50%) had KL grade ≥1 (49 knees with KL grade 2 and 5 knees with KL grade 3) (Table 1).

Medial Compartment

Among all knees, 181 (23%) had medial meniscus extrusion ≥3.0 mm. In the univariable analysis, we found the following baseline factors to be statistically significantly associated with high degree of medial meniscal body extrusion: high BMI, Heberden's nodes, meniscal tear, varus malalignment, knee injury history, mild knee symptoms, KL grade ≥1. In the multivariable random effects analysis, the medial meniscus extrusion was higher in persons with higher BMI by 0.20 mm (95% confidence interval [CI] 0.05, 0.35), with presence of mild knee symptoms 0.25mm (95% CI 0.05, 0.44), meniscal tear 0.44mm (95% CI 0.11, 0.77) and K&L grade ≥1 0.43mm (95% CI 0.26, 0.60) (Table 3).

In the analysis of the knee-specific risk factors while adjusting for all the person level confounding, the estimates of associations remained similar (Table 5).

Lateral Compartment

We found that only 4% of all the 790 available knees had lateral meniscal extrusion ≥3.0 mm. We found no statistically significant associations with the included risk factors in the multivariable regression model. When accounting for the person-level confounding, we found the KL≥1 to be associated with an increase in the lateral extrusion by 0.35 mm (95% CI 0.10, 0.60). The lateral extrusion was decreased by 0.17 mm (95% CI 0.08, 0.26) for each mm increase in tibia width.

DISCUSSION

By using a cross-sectional study design we evaluated factors associated with meniscal body extrusion in overweight and obese women using a two-dimensional quantitative measurement technique on coronal MR images. We found meniscus tear and high BMI to be factors associated with medial meniscus body extrusion in women.

A previous longitudinal study has suggested high BMI to be a risk factor for the development of medial meniscus extrusion[17]. Although Crema *et al* suggested that BMI itself has no effect on meniscus position[29] but BMI change affects other concomitant risk factors such as meniscus tears, cartilage damage, and knee malalignment, we hypothesized that obesity would potentially also have a more direct effect on meniscus position in some subjects. Previously, it has been reported that a diet and exercise program aimed to reduce weight did affect the progression of meniscus extrusion over 30 months of follow-up within the population studied here [30]. Whether this would reduce the development of future knee OA remains to be determined.

Heberden's nodes are hard soft tissue or bony swellings that can develop around the distal interphalangeal joints. They have been considered to be connected with generalized OA and have strong genetic determinants[31]. Heberden's nodes have been reported to be associated with the incidence and progression of knee OA[32] as well as meniscus pathology[17]. In our current cross-sectional study, it was however not statistically significantly associated with either medial or lateral meniscus extrusion, although the point estimate of association was elevated.

Knee trauma is strongly linked to meniscus tears[17, 18] and our study confirmed that it is also associated with meniscus extrusion. Though it is not a prerequisite for the development of meniscus extrusion, a knee trauma often compromises the integrity of knee joint structures such as menisci which may then lead to loss of hoop tension and increased risk of meniscus extrusion[33]. Further, meniscus tears are highly prevalent in the general population and are more frequent with increasing age[3]. Such meniscus lesions are strongly associated with the occurrence and progression of knee OA[5, 6]. Little is known of their origin but some cases, e.g. occupational kneeling have been reported to be associated with such tears[34] Conversely, OA could exacerbate the pathological meniscus conditions and form a vicious cycle and biomechanical joint failure[17]. Subjects with KL grade ≥1 have structural changes of OA, although these changes may not necessarily be clinically relevant yet. Joint space narrowing is an integral part of the KL grading system, so it is not unexpected that this turned out statistically significant in the model as meniscus extrusion have been reported to contribute to joint space narrowing on radiographs [6, 35]. In our study, both random-effects and fixed-effects linear regression analysis showed that KL score is a risk factor for medial extrusion and the fixed-effects linear regression analysis showed it is a risk factor for lateral meniscal extrusion as well.

Recently, Øiestad *et al*. [36] published a systematic review and meta-analysis in which they reported that knee extensor muscle weakness is associated with a higher risk of developing knee OA in both men and women. However, we did not find quadriceps muscle strength to be associated with meniscal body extrusion.

In the PROOF study several explanatory variables are measured for each knee separately, such as KL grade, pain or muscle strength. Thus, we used the fixed-effects linear regression analysis to allow estimation of the specific associations of these knee-specific factors after accounting for person-specific confounding factors, e.g., age, BMI, and even other person-level factors that we have not measured such as genetic background. Although, the overall picture remained essentially similar, the associations for ipsilateral meniscus tear and malalignment with meniscus extrusion were somewhat weakened, suggesting that association of these factors with meniscal extrusion may be in part due to unmeasured confounding.

There are limitations to our study. Importantly, our study was cross-sectional, thus we can't make any causal inferences. Second, the MR images were acquired in the supine position without weight-bearing. Load bearing menisci have been reported to have a different position, and extrusion may become more evident in weight-bearing MRI[37, 38]. For instance, Boxheimer *et al.* have reported meniscal positions vary slightly under loading conditions in asymptomatic volunteers[39]. Third, we only measured meniscus extrusion on coronal MR images which are ideal in assessing the meniscal body. No attempts were made to assess potential extrusion of the anterior and (or) posterior horns[6].

In conclusion, we found evidence that ipsilateral meniscus tear and high BMI are factors associated with medial meniscal body extrusion in women. Meniscus extrusion may be a key event on the causal pathway between obesity and knee OA. Future research should evaluate the causal pathway leading to meniscal extrusion and to radiographic and clinical knee OA with the aim to identify potential targets for therapeutic intervention(s) to prevent or slow down OA from developing.

ACKNOWLEDGMENTS

Peter van der Plas, MD is acknowledged for his contribution to the semi-quantitative evaluation of the study MRI's, using MOAKS. .

AUTHOR CONTRIBUTIONS

FZ participated in the design of the study, acquired the data, contributed to statistical analyses, made interpretation of results, and drafted the manuscript.

SB-Z acquired the data, made interpretation of the results, and revised the manuscript

EO acquired the data, made interpretation of the results, and revised the manuscript

AT participated in the design of the study, analysed the data, made interpretation of the results, and revised the manuscript.

ME designed the study, interpreted results, and revised the manuscript.

JR designed the study, acquired the data, interpreted results, and revised the manuscript.

All authors have approved the final version for submission.

ROLE OF THE FUNDING SOURCE

This work was supported by the Swedish Research Council, China Scholarship Council, Kock Foundations, Region Skåne, Governmental Funding of Clinical Research within National Health Service (ALF) and the Faculty of Medicine, Lund University, Sweden. The PROOF study was funded by The Netherlands Organisation for Health Research and Development and by a program grant of the Dutch Arthritis Foundation for their center of excellence “osteoarthritis in primary care”.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

COMPETING INTERESTS

None.

REFERENCES

1. Chivers MD, Howitt SD. Anatomy and physical examination of the knee menisci: a narrative review of the orthopedic literature. J Can Chiropr Assoc 2009; 53: 319-333.
2. Walker PS, Erkman MJ. The role of the menisci in force transmission across the knee. Clin Orthop Relat Res 1975: 184-192.
3. Englund M, Guermazi A, Gale D, Hunter DJ, Aliabadi P, Clancy M, et al. Incidental meniscal findings on knee MRI in middle-aged and elderly persons. N Engl J Med 2008; 359: 1108-1115.
4. Guermazi A, Niu J, Hayashi D, Roemer FW, Englund M, Neogi T, et al. Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: population based observational study (Framingham Osteoarthritis Study). BMJ 2012; 345: e5339.
5. Englund M, Guermazi A, Roemer FW, Aliabadi P, Yang M, Lewis CE, et al. Meniscal tear in knees without surgery and the development of radiographic osteoarthritis among middle-aged and elderly persons: The Multicenter Osteoarthritis Study. Arthritis Rheum 2009; 60: 831-839.
6. Hunter DJ, Zhang YQ, Niu JB, Tu X, Amin S, Clancy M, et al. The association of meniscal pathologic changes with cartilage loss in symptomatic knee osteoarthritis. Arthritis Rheum 2006; 54: 795-801.
7. Guermazi A, Hayashi D, Jarraya M, Roemer FW, Zhang Y, Niu J, et al. Medial posterior meniscal root tears are associated with development or worsening of medial tibiofemoral cartilage damage: the multicenter osteoarthritis study. Radiology 2013; 268: 814-821.
8. Costa CR, Morrison WB, Carrino JA. Medial meniscus extrusion on knee MRI: is extent associated with severity of degeneration or type of tear? AJR Am J Roentgenol 2004; 183: 17-23.
9. Gale DR, Chaisson CE, Totterman SM, Schwartz RK, Gale ME, Felson D. Meniscal subluxation: association with osteoarthritis and joint space narrowing. Osteoarthritis Cartilage 1999; 7: 526-532.
10. Bloecker K, Englund M, Wirth W, Hudelmaier M, Burgkart R, Frobell RB, et al. Revision 1 size and position of the healthy meniscus, and its correlation with sex, height, weight, and bone area- a cross-sectional study. BMC Musculoskelet Disord 2011; 12: 248.
11. Bruns K, Svensson F, Turkiewicz A, Wirth W, Guermazi A, Eckstein F, et al. Meniscus body position and its change over four years in asymptomatic adults: a cohort study using data from the Osteoarthritis Initiative (OAI). BMC Musculoskelet Disord 2014; 15: 32.
12. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, et al. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthritis Rheum 1995; 38: 1500-1505.

13. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. J Rheumatol 2007; 34: 172-180.
14. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 2008; 58: 26-35.
15. Shultz SJ, Kirk SE, Johnson ML, Sander TC, Perrin DH. Relationship between sex hormones and anterior knee laxity across the menstrual cycle. Med Sci Sports Exerc 2004; 36: 1165-1174.
16. Shultz SJ, Sander TC, Kirk SE, Perrin DH. Sex differences in knee joint laxity change across the female menstrual cycle. J Sports Med Phys Fitness 2005; 45: 594-603.
17. Englund M, Felson DT, Guermazi A, Roemer FW, Wang K, Crema MD, et al. Risk factors for medial meniscal pathology on knee MRI in older US adults: a multicentre prospective cohort study. Ann Rheum Dis 2011; 70: 1733-1739.
18. Zhang F, Kumm J, Svensson F, Turkiewicz A, Frobell R, Englund M. Risk factors for meniscal body extrusion on MRI in subjects free of radiographic knee osteoarthritis: longitudinal data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2015.
19. Runhaar J, van Middelkoop M, Reijman M, Willemsen S, Oei EH, Vroegindeweij D, et al. Prevention of knee osteoarthritis in overweight females: the first preventive randomized controlled trial in osteoarthritis. Am J Med 2015; 128: 888-895 e884.
20. Reijman M, Pols H, Bergink A, Hazes J, Belo J, Lievense A, et al. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip: the Rotterdam Study. Annals of the rheumatic diseases 2007; 66: 158-162.
21. Runhaar J, Schiphof D, van Meer B, Reijman M, Bierma-Zeinstra SM, Oei EH. How to define subregional osteoarthritis progression using semi-quantitative MRI osteoarthritis knee score (MOAKS). Osteoarthritis Cartilage 2014; 22: 1533-1536.
22. Hunter DJ, Guermazi A, Lo GH, Grainger AJ, Conaghan PG, Boudreau RM, et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). Osteoarthritis Cartilage 2011; 19: 990-1002.
23. Buckland-Wright JC, Wolfe F, Ward RJ, Flowers N, Hayne C. Substantial superiority of semiflexed (MTP) views in knee osteoarthritis: a comparative radiographic study, without fluoroscopy, of standing extended, semiflexed (MTP), and schuss views. J Rheumatol 1999; 26: 2664-2674.
24. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957; 16: 494-502.
25. Kraus VB, Vail TP, Worrell T, McDaniel G. A comparative assessment of alignment angle of the knee by radiographic and physical examination methods. Arthritis Rheum 2005; 52: 1730-1735.
26. Stark T, Walker B, Phillips JK, Fejer R, Beck R. Hand-held dynamometry correlation with the gold standard isokinetic dynamometry: a systematic review. PM R 2011; 3: 472-479.
27. Wendel-Vos GC, Schuit AJ, Saris WH, Kromhout D. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. J Clin Epidemiol 2003; 56: 1163-1169.
28. Allison PD. Fixed effects regression models. Volume 160, SAGE publications 2009.
29. Crema MD, Roemer FW, Felson DT, Englund M, Wang K, Jarraya M, et al. Factors associated with meniscal extrusion in knees with or at risk for osteoarthritis: the Multicenter Osteoarthritis study. Radiology 2012; 264: 494-503.
30. Landsmeer ML, Runhaar J, van der Plas P, van Middelkoop M, Vroegindeweij D, Koes B, et al. Reducing progression of knee OA features assessed by MRI in overweight and obese women: secondary outcomes of a preventive RCT. Osteoarthritis Cartilage 2015.

31. Kellgren JH, Moore R. Generalized osteoarthritis and Heberden's nodes. Br Med J 1952; 1: 181-187.
32. Cooper C, Snow S, McAlindon TE, Kellingray S, Stuart B, Coggon D, et al. Risk factors for the incidence and progression of radiographic knee osteoarthritis. Arthritis Rheum 2000; 43: 995-1000.
33. Fithian DC, Kelly MA, Mow VC. Material properties and structure-function relationships in the menisci. Clin Orthop Relat Res 1990: 19-31.
34. Rytter S, Jensen LK, Bonde JP, Jurik AG, Egund N. Occupational kneeling and meniscal tears: a magnetic resonance imaging study in floor layers. J Rheumatol 2009; 36: 1512-1519.
35. Hunter DJ, Zhang YQ, Tu X, Lavalley M, Niu JB, Amin S, et al. Change in joint space width: hyaline articular cartilage loss or alteration in meniscus? Arthritis Rheum 2006; 54: 2488-2495.
36. Oiestad BE, Juhl CB, Eitzen I, Thorlund JB. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. Osteoarthritis Cartilage 2015; 23: 171-177.
37. Paparo F, Revelli M, Piccazzo R, Astengo D, Camellino D, Puntoni M, et al. Extrusion of the medial meniscus in knee osteoarthritis assessed with a rotating clino-orthostatic permanent-magnet MRI scanner. Radiol Med 2015; 120: 329-337.
38. Stehling C, Souza RB, Hellio Le Graverand MP, Wyman BT, Li X, Majumdar S, et al. Loading of the knee during 3.0T MRI is associated with significantly increased medial meniscus extrusion in mild and moderate osteoarthritis. Eur J Radiol 2012; 81: 1839-1845.
39. Boxheimer L, Lutz AM, Treiber K, Goepfert K, Crook DW, Marincek B, et al. MR imaging of the knee: position related changes of the menisci in asymptomatic volunteers. Invest Radiol 2004; 39: 254-263.

Figure legends

Figure 1 Example of measurements on mid-coronal 1.5 T intermediate weighted knee magnetic resonance images using Sante DICOM Editor (the two dashed white vertical lines perpendicular to the tibial plateau mark the edge of the tibial plateau and the peripheral border of the meniscus body, respectively).

TABLES

Table 1. Characteristics of the study subjects

Women	N=395
Age, mean (SD) years	55.7 (3.2)
Body mass index, mean (SD) kg/m^2	32.4 (4.3)
Physical activity*, mean (SD)	6837 (3714)
Postmenopausal status	68%
Heberden's nodes	26%
Knees	**N=790**
Varus malalignment	40%
Valgus malalignment	12%
History of knee injury	13%
Kellgren-Lawrence grade ≥1	50%
Quadriceps muscle strength, mean (SD) Newton	253 (47)
Mild knee symptoms	31%
Meniscus tear, medial	9%
Meniscus tear, lateral	5%

*Measured with the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) questionnaire

Table 2. The random-effects linear regression analysis (univariable analyses).

	Medial	Lateral
Age	0.02 (-0.01, 0.05)	0.01 (-0.02, 0.04)
Body mass index, per $5kg/m^2$ increase	0.25 (0.13, 0.36)	0.00 (-0.11, 0.11)
Physical activity, per 1 SD	0.04 (-0.05, 0.14)	0.04 (-0.06, 0.13)
Menopause	-0.10 (-0.32, 0.11)	-0.07 (-0.28, 0.15)
Heberden’s nodes	0.23 (0.01, 0.46)	0.20 (-0.02, 0.42)
Knee alignment: Neutral	reference	reference
Varus	0.27 (0.09, 0.45)	0.00 (-0.17, 0.18)
Valgus	-0.15 (-0.40, 0.10)	0.14 (-0.10, 0.37)
History of knee injury	0.25 (0.02, 0.49)	0.19 (-0.03, 0.42)
Kellgren-Lawrence grade ≥1	0.54 (0.38, 0.71)	0.14 (-0.03, 0.30)
Quadriceps strength, per 1 SD increase	0.02 (-0.07, 0.11)	0.01 (-0.07, 0.10)
Mild knee symptoms	0.38 (0.21, 0.55)	0.10 (-0.06, 0.27)
Ipsilateral meniscus tear	0.53 (0.26, 0.80)	0.28 (-0.06, 0.62)

Table 3. The random-effects linear regression analysis (multivariable analysis); model adjusted for tibia width.

	Medial	Lateral
Age	0.01 (-0.02, 0.05)	0.01 (-0.02, 0.05)
BMI, per 5kg/m² increase	0.20 (0.05, 0.35)	-0.01 (-0.14, 0.12)
Physical activity, per 1 SD	0.05 (-0.05, 0.15)	0.00 (-0.12, 0.11)
Menopause	-0.13 (-0.36, 0.10)	-0.12 (-0.35, 0.11)
Heberden's nodes	0.17 (-0.05, 0.38)	0.20 (-0.03, 0.44)
Knee alignment: Neutral	reference	reference
Varus	0.17 (-0.02, 0.35)	-0.05 (-0.22, 0.13)
Valgus	-0.19 (-0.42, 0.05)	0.15 (-0.18, 0.48)
History of knee injury	0.06 (-0.19, 0.32)	0.13 (-0.14, 0.40)
Kellgren-Lawrence grade ≥1	0.43 (0.26, 0.60)	0.13 (-0.05, 0.30)
Quadriceps strength, per 1 SD increase	0.03 (-0.07, 0.13)	0.07 (-0.03, 0.17)
Mild knee symptoms	0.25 (0.05, 0.44)	0.11 (-0.08. 0.29)
Ipsilateral meniscus tear	0.44 (0.11, 0.77)	0.26 (-0.18, 0.70)

Table 4. The fixed-effects linear regression analysis (univariable analyses) of knee-specific risk factors.

	Medial	Lateral
History of knee injury	0.28 (-0.03, 0.60)	0.20 (-0.08, 0.49)
Kellgren-Lawrence grade ≥1	0.40 (0.14, 0.66)	0.29 (0.05, 0.53)
Quadriceps strength, per 1 SD increase	-0.03 (-0.21, 0.14)	-0.01 (-0.17, 0.15)
Knee alignment: Neutral	reference	reference
Varus	0.27 (0.09, 0.45)	0.00 (-0.17, 0.18)
Valgus	-0.15 (-0.40, 0.10)	0.14 (-0.10, 0.37)
Mild knee symptoms	0.38 (0.15, 0.62)	0.14 (-0.08, 0.35)
Ipsilateral meniscus tear	0.38 (0.02, 0.73)	-0.10 (-0.53, 0.32)

Table 5. The fixed-effects linear regression analysis (multivariable analysis) of knee-specific risk factors; model adjusted for tibia width.

	Medial	Lateral
History of knee injury	0.11 (-0.20, 0.43)	0.09 (-0.20, 0.39)
Kellgren-Lawrence grade ≥1	0.43 (0.17, 0.69)	0.35 (0.10, 0.60)
Quadriceps strength, per 1 SD increase	-0.04 (-0.22, 0.13)	0.03 (-0.14, 0.19)
Knee alignment: Neutral	reference	reference
Varus	0.13 (-0.14, 0.40)	0.04 (-0.22, 0.29)
Valgus	-0.27 (-0.60, 0.06)	0.19 (-0.12, 0.50)
Mild knee symptoms	0.24 (-0.01, 0.49)	0.10 (-0.13, 0.34)
Ipsilateral meniscus tear	0.29 (-0.07, 0.65)	-0.19 (-0.62, 0.23)