Patellofemoral and tibiofemoral articular cartilage and subchondral bone health following arthroscopic partial medial meniscectomy

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Abstract

Purpose: To examine articular cartilage and subchondral bone changes in tibiofemoral and patellofemoral joints following partial medial meniscectomy.

Methods: For this cross-sectional study, 158 patients aged 30-55 years, without evidence of knee osteoarthritis at arthroscopic partial medial meniscectomy (APMM), and 38 controls were recruited. MRI was performed once on the operated knee for each subcohort of 3 months, 2 years, or 4 years post-surgery, and the randomly assigned knee of the controls. Cartilage volume, cartilage defects, and bone size were assessed using validated methods.

Results: Compared with controls, APMM patients had more prevalent cartilage defects in medial tibiofemoral (OR=3.17, 95%CI 1.24-8.11) and patellofemoral (OR=13.76, 95%CI 1.52-124.80) compartments, and increased medial tibial plateau bone area (B=143.8, 95%CI 57.4-230.2). Time from APMM was positively associated with cartilage defect prevalence in medial tibiofemoral (OR=1.02, 95%CI 1.00-1.03) and patellofemoral (OR=1.04, 95%CI 1.01-1.07) compartments, and medial tibial plateau area (B=2.5, 95%CI 0.8-4.3), but negatively associated with lateral tibial cartilage volume (B=-4.9, 95%CI -8.4 to -1.5). The association of APMM and time from APMM with patellar cartilage defects was independent of tibial cartilage volume.

Conclusions: Partial medial meniscectomy is associated with adverse effects on articular cartilage and subchondral bone, which are associated with subsequent osteoarthritis, in both tibiofemoral and patellofemoral compartments.

Level of Evidence: Level III

Keywords Meniscectomy; Cartilage; Subchondral bone; Magnetic Resonance Imaging; Osteoarthritis

Introduction

Partial meniscectomy is a common surgical procedure used to treat a symptomatic meniscal tear [4,1]. Although its role in the management of degenerative meniscal tears is unclear [21], it effectively relieves pain and improves function of symptomatic, traumatic meniscal tears [4,1]. Meniscectomy has been recognized as an important risk factor for tibiofemoral osteoarthritis (OA) [8,18,5,27,35,36,34]. However, whether partial meniscectomy is associated with adverse effects on the patellofemoral compartment is not clear [17]. Biomechanical, histological, and immunohistochemical changes in patellar articular cartilage observed in an ovine model following bilateral lateral meniscectomy, suggest an association between meniscectomy and the development of patellofemoral OA [3]. To date, the only study in humans reported increased frequency of patellofemoral OA coexisted with tibiofemoral OA 15 to 22 years post-surgery in a partial meniscectomy population free of radiographic knee OA at the index surgery compared with controls [17]. However it remains unclear whether this was simply due to the coexistence of patellofemoral OA in a knee with tibiofemoral OA or whether patellofemoral OA developed as a consequence of the meniscectomy.

Magnetic resonance imaging (MRI) allows visualization of all knee tissues, with superior assessment of early structural change associated with the development of knee OA compared to x-ray [15,10,28]. In previous MRI studies we showed an increased rate of knee cartilage loss over 2 years, and a greater prevalence and severity of cartilage defects over 3-5 years in tibiofemoral joint following partial meniscectomy when compared with healthy controls [9,29]. Another MRI study found abnormal cartilage surfaces, subchondral sclerosis, and condylar squaring in tibiofemoral compartment 7-8 years following partial meniscectomy in participants with arthroscopically normal articular cartilage at the time of initial meniscectomy [42]. Moreover,

changes in gait patterns are present as early as 3 months following a partial meniscectomy [37,38]. Given the role of biomechanical factors in the pathogenesis of OA [32,33], it may be that tibiofemoral and patellofemoral joint changes related to knee OA may both develop early after the initial surgery. It remains unknown whether time from surgery is associated with the development of morphological alterations in the tibiofemoral and patellofemoral compartments.

Since there is currently very limited literature on the relationship between development patellofemoral osteoarthritis and partial knee meniscectomy, we used this cross-sectional study to identify if patients who had previously undergone arthroscopic partial medial meniscectomy (APMM) 3 months, 2 years or 4 years prior, exhibited morphological differences in tibiofemoral and patellofemoral joints assessed by MRI compared with healthy controls. A second aim was to determine whether time from APMM was related to morphological differences in tibiofemoral and patellofemoral joints. It was hypothesised that patients undergoing APMM would have morphologic differences in their tibiofemoral and patellofemoral joint in comparison to un-operated controls, and these differences would increase with time from surgery.

Materials and Methods

Participants

For this study participants recruited from three separate studies, two based in Perth and one based in Melbourne, Australia were included. All studies used the same inclusion and exclusion criteria. The protocol was approved by University of Western Australia and University of Melbourne Human Research Ethics Committees. All participants provided their informed written consent prior to starting the study. Individuals who had undergone arthroscopic partial meniscectomy (APM) at orthopaedic clinics in Perth or Melbourne were identified by their surgical billing codes. Initially, surgical records of these individuals were reviewed and potential participants excluded if they were younger than 30 or older than 55 years, or if their surgical

records indicated that they had lateral meniscal resection; > 33% of their medial meniscus resected; > 2 tibiofemoral cartilage lesions; a single tibiofemoral cartilage lesion greater than 10 mm in diameter or exceeding 50% of cartilage thickness (i.e., > 2a cartilage lesion); concomitant knee ligament damage or signs of knee OA. Individuals that met the initial inclusion criteria were sent an information sheet by mail. They were contacted by telephone approximately 1 week later and invited to undergo further screening. During the telephone screening the following secondary exclusion criteria were applied: previous lower limb bone or joint injury (other than that leading to the meniscectomy); history of knee pain; clinical or structural signs of OA; post-operative complications; cardiac, circulatory or neuromuscular conditions; diabetes; stroke; multiple sclerosis and contraindication to MRI. Further entry into this study was limited to those who had undergone isolated APMM. One hundred and fifty-eight participants met the eligibility requirement and agreed to participate (Figure 1).

Three independent groups were created (Table 1). The *four year* post-surgical *group* had MRIs taken 41-75 months post-surgery. The *two year* post-surgical *group* underwent MRI 25-32 months post-surgery. The *three month* post-surgical *group* underwent MRI 1-7 months post-surgery. The *control group* consisted of 38 individuals aged 30-55 years who responded to advertisements in newspapers and university emails. Control group exclusion criteria were the same as the APMM group, except for the baseline surgical criteria. They presented with apparently healthy knees.

MRI assessment of knee structure

MRI of the patients' operated knee and a randomly assigned knee of the controls was performed on a 1.5-T whole body magnetic resonance unit (Four Year, Three Month and Control Groups: Magnetom Symphony, Siemens, Erlangen, Germany; Two Year Group: Phillips, Philips Medical Systems, Eindhoven, the Netherlands), using the sequence and parameters as previously

described[29]. Body mass and height were measured in light clothing and no footwear, and body mass index (BMI) calculated.

Cartilage defects (see Figure 2) were graded in tibiofemoral and patellofemoral compartments using a classification system previously described where grade 0 represents normal cartilage and grade 4 full-thickness cartilage wear with exposure of subchondral bone [14]. A prevalent cartilage defect was defined as a cartilage defect score of ≥ 2 at any site. Intra- and inter-observer reliability (expressed as intra-class correlation coefficient) were 0.89 to 0.94, and 0.85 to 0.93, respectively [14]. Tibial and patellar cartilage volumes were measured to the nearest 1 mm^3 using the software ImageJ (National Institutes of Health, USA) and Osiris (University Hospitals of Geneva, Switzerland), respectively [43]. Coefficients of variation (CVs) for cartilage volume measures were 3.4% for medial tibial, 2.0% for lateral tibial [43], and 2.6% for patellar cartilage [24]. Cross-sectional area of tibial plateau (see Figure 3) was measured to the nearest 1 mm^2 using Osiris from axial images [41]. Patellar bone volume (see Figure 3) was measured to the nearest 1 mm^3 by using the same method as for cartilage volume [24]. CVs for the medial and lateral tibial plateau areas, and patellar bone volume were 2.3%, 2.4% [43], and 2.2% [24], respectively. All measures were performed by independent trained observers, with independent random cross checks blindly performed by a different trained observer, all blinded to clinical and group status.

Statistical analysis

Statistical analyses were performed on the outcomes variables of prevalence of cartilage defects, cartilage volume, and bone area/volume. The prevalence of cartilage defects was a dichotomous variable, thus binary logistic regression was used. Cartilage volume and bone area/volume showed normal distribution, thus linear regression was used. Multivariate regression models were constructed to explore the relationship between meniscectomy-related variables and

knee cartilage and bone, adjusting for potential confounders of age, gender, BMI, MRI resource (different MR scanners), cartilage volume and bone size for cartilage defects, and bone size for cartilage volume. P-values < 0.05 were considered statistically significant. All analyses were performed using the SPSS statistical package (version 16.0, SPSS, Chicago, IL).

Results

The characteristics of study participants are presented in Table 1.

After adjustment for the confounders, APMM patients had an increased prevalence of medial tibiofemoral and patellar cartilage defects compared with the controls (Table 2). Time from APMM was positively associated with the prevalence of patellar cartilage defects, and weakly positively associated with the prevalence of medial tibiofemoral cartilage defects. No significant relationship existed between prevalence of lateral tibiofemoral cartilage defects and time from APMM (Table 2). Further adjustment for tibial plateau bone area or patellar bone volume did not alter the resultsTo determine if the patellar cartilage defects relationships with APMM and time from APMM were due to the confounding of medial tibial pathology, medial tibial cartilage volume was included in the multivariate analyses of patellar cartilage defects. APMM (odds ratio 14.86, 95% confidence interval 1.61-137.14, P=0.02) and time from APMM (odds ratio 1.04, 95% confidence interval 1.01-1.08, P=0.01) were still significantly associated with the risk of patellar cartilage defects.

APMM was not significantly associated with tibial or patellar cartilage volume after adjustment for confounders (Table 3). Time between APMM and MRI was negatively associated with lateral tibial cartilage volume, but not significantly related to medial tibial or patella cartilage volume after adjusting for confounders (Table 3).

After adjusting for confounders, APMM and time from APMM were significantly associated with medial tibial plateau bone area, but not lateral tibial plateau bone area or patellar

bone volume (Table 4). Since there was a tendency that patients with APMM had larger tibial and patellar bone size compared with the controls (Table 1), further adjustment for body height, a proxy measure for bone size of the knee was performed with no effect on the results.

When males and females were examined separately, similar results were observed and the direction of associations persisted for the above analyses, although due to the small numbers in each group some of the results were not significant (data not shown).

Discussion

The most important finding of this study was that APMM was related to early signs of OA in the patellofemoral as well as the tibiofemoral compartment. This study demonstrated that both APMM and time from APMM were positively associated with the prevalence of cartilage defects in the medial tibiofemoral and patellofemoral joints, independent of cartilage volume and bone size of the respective compartment, and medial tibial plateau bone area. Time from APMM was also negatively associated with lateral tibial cartilage volume. The relationship between APMM and time from APMM and patellar cartilage defects could not be explained by the concurrent disease in the medial tibiofemoral compartment since it was independent of medial tibial cartilage volume.

Previous studies have established partial meniscectomy as a risk factor for tibiofemoral OA [8,18,5,27,35,36,34]. These studies used radiographic knee OA as the outcome measure with most studies following up the meniscectomy population for at least 10 years. The use of radiography to assess the disease status of the knee has limited the capacity of these studies to identify the early effect of meniscectomy on articular cartilage and subchondral bone. Previous MRI studies have shown increased cartilage loss and cartilage defects and subchondral sclerosis in the tibiofemoral joint 2-8 years post-meniscectomy [9,42,29]. Consistent with these studies, this study showed APMM was associated with an increased risk of tibiofemoral cartilage defects,

independent of tibial cartilage volume and bone area. The study also found the risk of cartilage defects increased with time from APMM. Cartilage defects have been shown to be predictors of knee cartilage loss independent of cartilage volume in both asymptomatic and symptomatic populations [12,44], suggesting they are markers of early cartilage pathology. A negative relationship between time from APMM and lateral tibial cartilage volume was identified, which was independent of age at APMM. Previous studies have reported that medial meniscectomy affects both medial and lateral compartment architecture [31], and causes reduced compressive strains within the lateral tibia [6], which may contribute to the observed alterations in lateral compartment cartilage volume. While it would be expected to see reduction in the medial cartilage volume as well this was not apparent. It is unclear why this is the case. Further investigation of the tibiofemoral biomechanics is required to better understand this result.

APMM and time from APMM were found to be positively associated with medial tibial bone area. There is emerging evidence suggesting that subchondral bone plays an important role in the pathogenesis of OA, with changes in the trabecular structure and subchondral bone expansion seen in the early stages of OA [13,22,45,20]. In fact subchondral bone expansion has been shown to be an early response to biomechanical factors such as obesity and adduction moment, occurring before any effect is seen on knee cartilage [13,22]. The expansion of subchondral bone may reflect the architectural changes with the bone and therefore affect the mechanical properties of the subchondral bone which in turn increase the susceptibility of the overlying articular cartilage to damage [33,41]. Subchondral bone expansion has been shown to be associated with cartilage defects and considered to be an important element in the pathogenesis of knee OA [11,7,14].

Both APMM and time from APMM were found to be positively associated with the prevalence of patellar cartilage defects. Moreover, we showed that the association between

APMM and patellar cartilage defects, a more sensitive measure of early OA changes than radiographic joint space narrowing, was independent of patellar cartilage and bone volume. These findings support the results from the study by Englund and Lohmander showing that patellofemoral OA coexisted with tibiofemoral OA following meniscectomy [17]. In that study, patellofemoral cartilage changes were observed at the time of index surgery in many of the OA cases, suggesting that pre-radiographic or incipient OA was present at the time of surgery and that for many of their mostly middle aged subjects, the meniscal tear may merely have been a 'signal feature' of early OA. In contrast, participants with knee OA were excluded from our study. Furthermore, the association of APMM with patellar cartilage defects was independent of medial tibial cartilage volume, suggesting that APMM affects the patellofemoral joint independent of possible early OA changes in the tibiofemoral joint [23]. Our findings further support the notion that partial meniscectomy is a risk factor for the development of patellofemoral OA, and indicate that patellofemoral OA should be considered as an individual disease entity resulting from meniscectomy, independent of early tibiofemoral OA existence.

Biomechanical studies have demonstrated that partial meniscectomy results in a reduced tibiofemoral contact area and an increased contact pressure in the knee joint [39,26]. These changes may increase the susceptibility of cartilage to damage, thus increasing the risk of cartilage defects in the tibiofemoral joint. The APM population has been shown to exhibit increased external adduction moments during the stance phase of gait [38]. There is evidence that increased knee adduction moments are associated with increased tibial bone size in healthy women [22] and are predictive of progression of tibiofemoral OA [30]. Individuals who have undergone APM also have weaker quadriceps than healthy controls [37], and quadriceps strength is reduced in the meniscectomized leg compared with the non-operated leg [19]. Increased quadriceps strength appears to be protective against cartilage loss in the lateral patellofemoral

compartment [2]. There is evidence that medial patellofemoral OA is more likely to be associated with varus alignment, while lateral patellofemoral OA is more likely to be associated with valgus alignment [16]. Patients undergoing partial medial meniscectomy exhibit greater varus angulation on the side of surgery than the uninvolved side [25]. When coupled with quadriceps weakness seen in a meniscectomy population, a varus alignment may increase the force on the medial patellar facet and thus consequentially increase the risk of developing patellofemoral OA. Further work is needed to identify the relationships between biomechanical factors and the risk of OA in meniscectomy populations.

The control group exhibited some degree of early signs of knee joint OA, with 23% demonstrating medial knee cartilage defects, 32% lateral cartilage defects and one participant a patella cartilage defect. These values however, are reflective of those identified in apparently healthy cohorts of similar ages.[40,29] With regards to the findings presented, the early signs of knee joint OA in the control groups is likely to result in the controls being more similar to the APMM patients and thus diluting any effects we observed.

The limitation of this study is its cross-sectional nature. Pre-surgery MRI was not obtained, thus we were unable to address the changes in knee morphology prior to and after the APMM. At the time of surgery, the APMM patients had no evidence of knee OA, based on arthroscopic examination and radiography, thus it is unlikely that our findings were due to underlying knee OA. Furthermore, knee structural changes were associated with the time elapsed since APMM, suggesting an effect of the surgery itself rather than the underlying meniscal tear. Gender differences across the groups may be a potential confounder. We examined the effect of gender by both adjusting for gender in the analyses, where relationships between APMM and knee structure remained significant after the adjustment, and also sub-group analyses where males and females were examined separately. In the subgroup analyses the relationships between

APMM and knee structure persisted, although due to the smaller numbers some results were no longer significant. Ideally, it would be best to follow up the same APMM participants over the 4 year period and track changes in tibiofemoral and patellofemoral compartments. This would account for subject-specific confounding factors. However, by using strict inclusion criteria to retrospectively select our cohort the study accounted for many known confounding factors. Frontal plane knee alignment was not measured in the current study. However, whether this is a confounding variable or on the causal pathway warrants further examination. Using two different MRI scanners may also be a limitation. However this was factored into the statistical analysis as a covariate and this should have accounted for any clustering effects. Another limitation of the study is the lack of information regarding the preoperative status of the meniscus, such as whether it experienced a traumatic or degenerative tear, and the morphological characteristics of the tear. These features might have an effect on the morphological changes observed in our study. However we restricted our study population to those with isolated APMM to control for the confounding of arthroscopic partial lateral meniscectomy and excluded participants with moderate or severe cartilage lesions, concomitant knee ligament damage or signs of knee OA at APMM. This resulted in a more homogeneous population thus allowing a more accurate assessment of the impacts of APMM on knee cartilage and bone. The results from this study and that of Englund and Lohmander's retrospective cohort study suggest there is a need to undertake further longitudinal work to better understand the relationship between meniscectomy and OA development in all compartments of the knee.

In summary, MRI evidence of morphological changes in articular cartilage and subchondral bone appears in both the tibiofemoral and patellofemoral joints in patients with isolated APMM within 5 years post-surgery. Both APMM and increased time from APMM are associated with adverse effect on articular cartilage and subchondral bone. Moreover, the

association between APMM and patellar cartilage pathology was independent of cartilage morphology of the tibiofemoral joint. These findings suggest that partial meniscectomy plays a role in the pathogenesis of both tibiofemoral and patellofemoral OA. However additional prospective longitudinal studies are needed to better understand the influence of APMM on cartilage loss and bone morphology within the knee joint. Interventions aimed at preventing meniscal injury and therefore meniscectomy will be important for the prevention of both tibiofemoral and patellofemoral OA. In addition, if meniscectomy is necessary, strategies will need to be developed that focus on both the tibiofemoral and patellofemoral compartments in order to reduce the risk of subsequent OA.

Conclusions

Partial medial meniscectomy is associated with adverse effects on articular cartilage and subchondral bone, which are associated with subsequent OA, in both tibiofemoral and patellofemoral compartments. Clinicians designing rehabilitation or OA prevention programs for implementation following meniscectomy need to focus on both the patellofemoral and tibiofemoral compartments, rather than the tibiofemoral compartment in isolation.

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Conflict of Interest

No authors have a conflict of interest.

References

1. Aglietti P, Buzzi R, Bassi PB, Pisaneschi A (1986) Results of arthroscopic meniscectomy. Ital J Orthop Traumatol 12 (3):315-325.
2. Amin S, Baker K, Niu J, Clancy M, Goggins J, Guermazi A, Grigoryan M, Hunter DJ, Felson DT (2009) Quadriceps strength and the risk of cartilage loss and symptom progression in knee osteoarthritis. Arthritis Rheum 60 (1):189-198.
3. Appleyard RC, Ghosh P, Swain MV (1999) Biomechanical, histological and immunohistological studies of patellar cartilage in an ovine model of osteoarthritis induced by lateral meniscectomy. Osteoarthritis Cartilage 7 (3):281-294.
4. Bernstein J (2000) Meniscal tears of the knee: diagnosis and individualized treatment. Phys Sportsmed 28 (3):83-90.
5. Bolano LE, Grana WA (1993) Isolated arthroscopic partial meniscectomy. Functional radiographic evaluation at five years. Am J Sports Med 21 (3):432-437.
6. Bourne RB, Finlay JB, Papadopoulos P, Andreae P (1984) The effect of medial meniscectomy on strain distribution in the proximal part of the tibia. J Bone Joint Surg Am 66 (9):1431-1437.
7. Burr DB (1998) The importance of subchondral bone in osteoarthrosis. Curr Opin Rheumatol 10 (3):256-262.
8. Chatain F, Adeleine P, Chambat P, Neyret P (2003) A comparative study of medial versus lateral arthroscopic partial meniscectomy on stable knees: 10-year minimum follow-up. Arthroscopy 19 (8):842-849.
9. Cicuttini FM, Forbes A, Yuanyuan W, Rush G, Stuckey SL (2002) Rate of knee cartilage loss after partial meniscectomy. J Rheumatol 29 (9):1954-1956.
10. Conaghan PG, Felson D, Gold G, Lohmander S, Totterman S, Altman R (2006) MRI and non-cartilaginous structures in knee osteoarthritis. Osteoarthritis Cartilage 14 Suppl A:A87-94.
11. Ding C, Cicuttini F, Jones G (2007) Tibial subchondral bone size and knee cartilage defects: relevance to knee osteoarthritis. Osteoarthritis Cartilage 15 (5):479-486.
12. Ding C, Cicuttini F, Scott F, Boon C, Jones G (2005) Association of prevalent and incident knee cartilage defects with loss of tibial and patellar cartilage: a longitudinal study. Arthritis Rheum 52 (12):3918-3927.
13. Ding C, Cicuttini F, Scott F, Cooley H, Jones G (2005) Knee Structural Alteration and BMI: A Cross-sectional Study. Obes Res 13 (2):350-361.
14. Ding C, Garnero P, Cicuttini F, Scott F, Cooley H, Jones G (2005) Knee cartilage defects: association with early radiographic osteoarthritis, decreased cartilage volume, increased joint surface area and type II collagen breakdown. Osteoarthritis Cartilage 13 (3):198-205.
15. Eckstein F, Cicuttini F, Raynauld JP, Waterton JC, Peterfy C (2006) Magnetic resonance imaging (MRI) of articular cartilage in knee osteoarthritis (OA): morphological assessment. Osteoarthritis Cartilage 14 Suppl A:A46-75.
16. Elahi S, Cahue S, Felson DT, Engelman L, Sharma L (2000) The association between varus-valgus alignment and patellofemoral osteoarthritis. Arthritis Rheum 43 (8):1874-1880.
17. Englund M, Lohmander LS (2005) Patellofemoral osteoarthritis coexistent with tibiofemoral osteoarthritis in a meniscectomy population. Ann Rheum Dis 64 (12):1721-1726.
18. Englund M, Roos EM, Lohmander LS (2003) Impact of type of meniscal tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. Arthritis Rheum 48 (8):2178-2187.

19. Ericsson YB, Roos EM, Dahlberg L (2006) Muscle strength, functional performance, and self-reported outcomes four years after arthroscopic partial meniscectomy in middle-aged patients. Arthritis Rheum 55 (6):946-952.
20. Gomoll AH, Madry H, Knutsen G, van Dijk N, Seil R, Brittberg M, Kon E (2010) The subchondral bone in articular cartilage repair: current problems in the surgical management. Knee Surg Sports Traumatol Arthrosc 18 (4):434-447.
21. Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S (2007) Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. Knee Surg Sports Traumatol Arthrosc 15 (4):393-401.
22. Jackson BD, Teichtahl AJ, Morris ME, Wluka AE, Davis SR, Cicuttini FM (2004) The effect of the knee adduction moment on tibial cartilage volume and bone size in healthy women. Rheumatology (Oxford) 43 (3):311-314.
23. Jones G, Ding C, Scott F, Glisson M, Cicuttini F (2004) Early radiographic osteoarthritis is associated with substantial changes in cartilage volume and tibial bone surface area in both males and females. Osteoarthritis Cartilage 12 (2):169-174.
24. Jones G, Glisson M, Hynes K, Cicuttini F (2000) Sex and site differences in cartilage development: a possible explanation for variations in knee osteoarthritis in later life. Arthritis Rheum 43 (11):2543-2549.
25. Jones RE, Smith EC, Reisch JS (1978) Effects of medial meniscectomy in patients older than forty years. J Bone Joint Surg Am 60 (6):783-786.
26. Lee SJ, Aadalen KJ, Malaviya P, Lorenz EP, Hayden JK, Farr J, Kang RW, Cole BJ (2006) Tibiofemoral contact mechanics after serial medial meniscectomies in the human cadaveric knee. Am J Sports Med 34 (8):1334-1344.
27. Maletius W, Messner K (1996) The effect of partial meniscectomy on the long-term prognosis of knees with localized, severe chondral damage. A twelve- to fifteen-year followup. Am J Sports Med 24 (3):258-262.
28. Menetrey J, Unno-Veith F, Madry H, Van Breuseghem I (2010) Epidemiology and imaging of the subchondral bone in articular cartilage repair. Knee Surg Sports Traumatol Arthrosc 18 (4):463-471.
29. Mills PM, Wang Y, Cicuttini FM, Stoffel K, Stachowiak GW, Podsiadlo P, Lloyd DG (2008) Tibio-femoral cartilage defects 3-5 years following arthroscopic partial medial meniscectomy. Osteoarthritis Cartilage 16 (12):1526-1531.
30. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S (2002) Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. Ann Rheum Dis 61 (7):617-622.
31. Petersen MM, Olsen C, Lauritzen JB, Lund B, Hede A (1996) Late changes in bone mineral density of the proximal tibia following total or partial medial meniscectomy. A randomized study. J Orthop Res 14 (1):16-21.
32. Radin EL, Burr DB, Caterson B, Fyhrie D, Brown TD, Boyd RD (1991) Mechanical determinants of osteoarthrosis. Semin Arthritis Rheum 21 (3 Suppl 2):12-21.
33. Radin EL, Paul IL, Rose RM (1972) Role of mechanical factors in pathogenesis of primary osteoarthritis. Lancet 1 (7749):519-522.
34. Rangger C, Klestil T, Gloetzer W, Kemmler G, Benedetto KP (1995) Osteoarthritis after arthroscopic partial meniscectomy. Am J Sports Med 23 (2):240-244.
35. Rockborn P, Gillquist J (1996) Long-term results after arthroscopic meniscectomy. The role of preexisting cartilage fibrillation in a 13 year follow-up of 60 patients. Int J Sports Med 17 (8):608-613.

36. Roos H, Lauren M, Adalberth T, Roos EM, Jonsson K, Lohmander LS (1998) Knee osteoarthritis after meniscectomy: prevalence of radiographic changes after twenty-one years, compared with matched controls. Arthritis Rheum 41 (4):687-693.
37. Sturnieks DL, Besier TF, Hamer PW, Ackland TR, Mills PM, Stachowiak GW, Podsiadlo P, Lloyd DG (2008) Knee strength and knee adduction moments following arthroscopic partial meniscectomy. Med Sci Sports Exerc 40 (6):991-997.
38. Sturnieks DL, Besier TF, Mills PM, Ackland TR, Maguire KF, Stachowiak GW, Podsiadlo P, Lloyd DG (2008) Knee joint biomechanics following arthroscopic partial meniscectomy. J Orthop Res 26 (8):1075-1080.
39. von Lewinski G, Stukenborg-Colsman C, Ostermeier S, Hurschler C (2006) Experimental measurement of tibiofemoral contact area in a meniscectomized ovine model using a resistive pressure measuring sensor. Ann Biomed Eng 34 (10):1607-1614.
40. Wang Y, Ding C, Wluka AE, Davis S, Ebeling PR, Jones G, Cicuttini FM (2006) Factors affecting progression of knee cartilage defects in normal subjects over 2 years. Rheumatology 45 (1):79-84.
41. Wang Y, Wluka AE, Cicuttini FM (2005) The determinants of change in tibial plateau bone area in osteoarthritic knees: a cohort study. Arthritis Res Ther 7 (3):R687-693.
42. Williams RJ, 3rd, Warner KK, Petrigliano FA, Potter HG, Hatch J, Cordasco FA (2007) MRI Evaluation of Isolated Arthroscopic Partial Meniscectomy Patients at a Minimum Five-Year Follow-up. Hss J 3 (1):35-43.
43. Wluka AE, Davis SR, Bailey M, Stuckey SL, Cicuttini FM (2001) Users of oestrogen replacement therapy have more knee cartilage than non-users. Ann Rheum Dis 60 (4):332-336.
44. Wluka AE, Ding C, Jones G, Cicuttini FM (2005) The clinical correlates of articular cartilage defects in symptomatic knee osteoarthritis: a prospective study. Rheumatology (Oxford) 44 (10):1311-1316.
45. Wolski M, Stachowiak GW, Dempsey AR, Mills PM, Cicuttini FM, Wang YY, Stoffel KK, Lloyd DG, Podsiadlo P (2011) Trabecular bone texture detected by plain radiography and variance orientation transform method is different between knees with and without cartilage defects. J Orthop Res 29 (8):1161-1167.

Table 1. Characteristics of study population

	Control	Time from APMM		
	(n = 38)	3 months	2 years	4 years
		(n = 54)	(n = 63)	(n = 41)
Age at MRI, years	42.4 ± 6.5	42.9 ± 5.8	43.1 ± 5.4	46.2 ± 6.2
Age at APMM, years	--	42.5 ± 5.7	40.7 ± 5.4	41.8 ± 6.3
Time from APMM to MRI, months	--	3.8 ± 1.2	28.1 ± 1.6	52.9 ± 9.6
Female, n (%)	18 (47)	10 (19)	8 (13)	8 (20)
Height (m)	1.75 ± 0.09	1.77 ± 0.09	1.75 ± 0.08	1.77 ± 0.09
Body mass (kg)	77.1 ± 14.7	83.9 ± 12.1	83.1 ± 14.2	86.0 ± 16.4
Body mass index, kg/m^2	25.2 ± 4.1	26.7 ± 3.0	27.0 ± 4.2	27.2 ± 3.7
Medial tibial cartilage volume, mm^3	1819 ± 352	1891 ± 411	1849 ± 378	1907 ± 398
Lateral tibial cartilage volume, mm^3	2157 ± 492	2540 ± 535	2360 ± 580	2252 ± 547
Patella cartilage volume, mm^3	3459 ± 813	3671 ± 768	3891 ± 789	3788 ± 818
Medial tibial plateau area, mm^2	2193 ± 316	2424 ± 270	2454 ± 303	2529 ± 349
Lateral tibial plateau area, mm^2	1353 ± 180	1471 ± 212	1443 ± 205	1486 ± 217
Patella bone volume, mm^3	16866 ± 3884	18946 ± 3965	20322 ± 4138	18874 ± 3340
Medial tibiofemoral cartilage defects, n (%)	8 (21)	23 (43)	30 (48)	24 (59)
Lateral tibiofemoral cartilage defects, n (%)	12 (32)	24 (44)	24 (38)	18 (44)
Patella cartilage defects, n (%)	1 (3)	5 (9)	12 (19)	10 (24)

Values expressed as mean ± SD, or number (%)

Table 2. Relationship between arthroscopic partial medial meniscectomy and prevalence of cartilage defects

	Odds ratio (95% CI)	P value
APMM (yes/no)*		
Medial tibiofemoral cartilage defects	3.17 (1.24, 8.11)	0.02
Lateral tibiofemoral cartilage defects	1.46 (0.63, 3.40)	n.s.
Patella cartilage defects	13.76 (1.52, 124.80)	0.02
Time between APMM and MRI (months)**		
Medial tibiofemoral cartilage defects	1.02 (1.00, 1.03)	0.09
Lateral tibiofemoral cartilage defects	1.00 (0.99, 1.02)	n.s.
Patella cartilage defects	1.04 (1.01, 1.07)	0.02

*Adjusted for age at MRI, gender, body mass index, MRI resource, cartilage volume and tibial plateau bone area/patella bone volume;

**Adjusted for age at APMM, gender, body mass index, MRI resource and cartilage volume and tibial plateau bone area/patella bone volume

Table 3. Relationship between arthroscopic partial medial meniscectomy and cartilage volume

	Regression coefficient (95% CI)	P value
APMM (yes/no)*		
Medial tibial cartilage volume (mm^3)	-75.8 (-211.0, 59.4)	n.s.
Lateral tibial cartilage volume (mm^3)	42.1 (-132.3, 216.5)	n.s.
Patella cartilage volume (mm^3)	-11.6 (-256.5, 233.3)	n.s.
Time between APMM and MRI (months)**		
Medial tibial cartilage volume (mm^3)	-1.5 (-4.3, 1.2)	n.s.
Lateral tibial cartilage volume (mm^3)	-4.9 (-8.4, -1.5)	< 0.01
Patella cartilage volume (mm^3)	2.0 (-2.9, 6.8)	n.s.

*Adjusted for age at MRI, gender, body mass index, MRI resource, and tibial plateau bone area/patella bone volume; **Adjusted for age at APMM, gender, body mass index, MRI resource and tibial plateau bone area/patella bone volume

Table 4. Relationship between arthroscopic partial medial meniscectomy and bone area/volume

	Regression coefficient (95% CI)	P value
APMM (yes/no)*		
Medial tibial plateau bone area (mm^2)	140.5 (41.3, 239.8)	0.01
Lateral tibial plateau bone area (mm^2)	51.8 (-18.7, 122.3)	n.s.
Patella bone volume (mm^3)	682.2 (-628.9, 1993.4)	n.s.
Time between APMM and MRI (months)**		
Medial tibial plateau bone area (mm^2)	2.2 (0.2, 4.2)	0.03
Lateral tibial plateau bone area (mm^2)	0.7 (-0.8, 2.1)	n.s.
Patella bone volume (mm^3)	5.3 (-21.2, 31.8)	n.s.

*Adjusted for age at MRI, gender, body mass index, and MRI resource; **Adjusted for age at APMM, gender, body mass index, and MRI resource

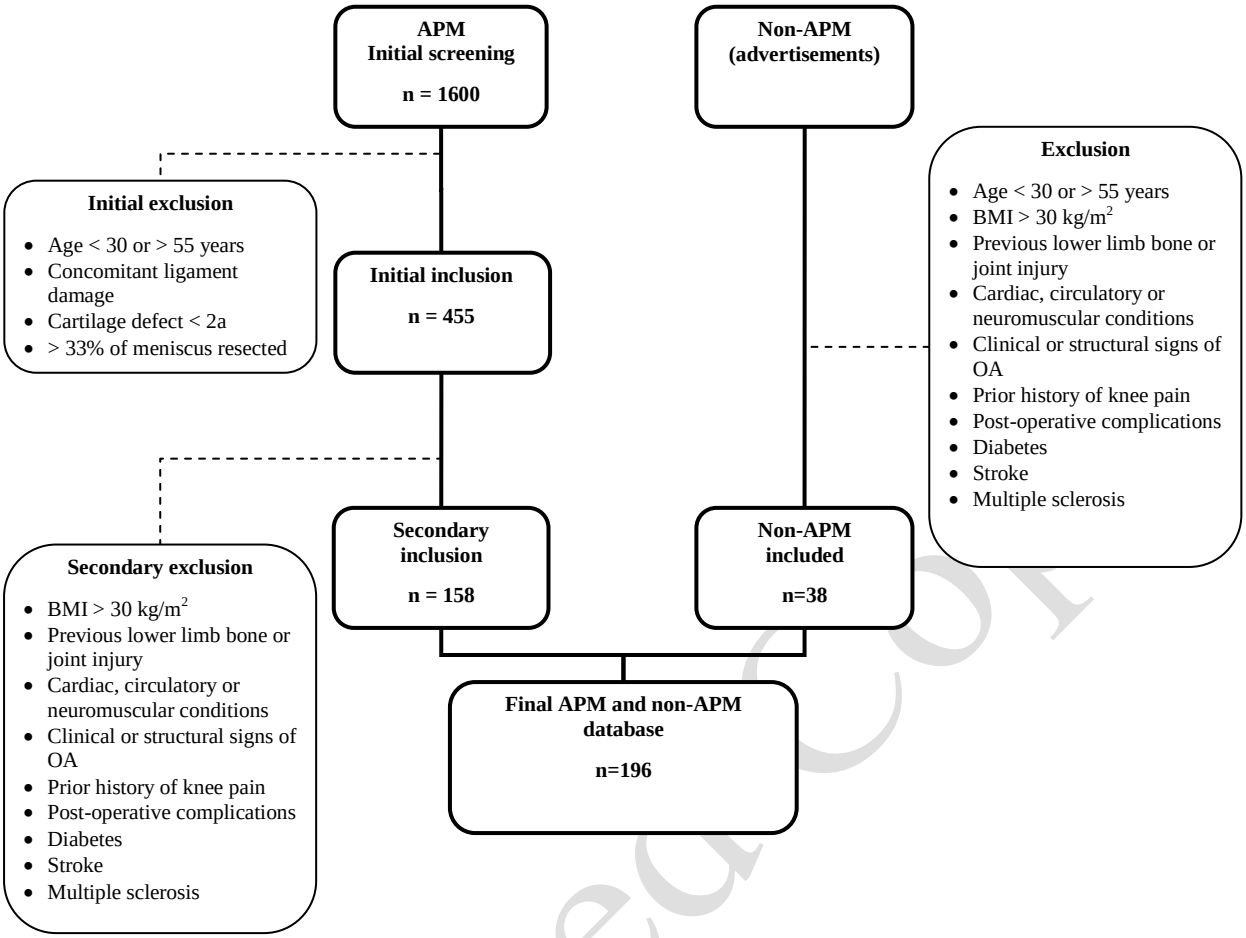

Figure 1 Participant selection flow chart.

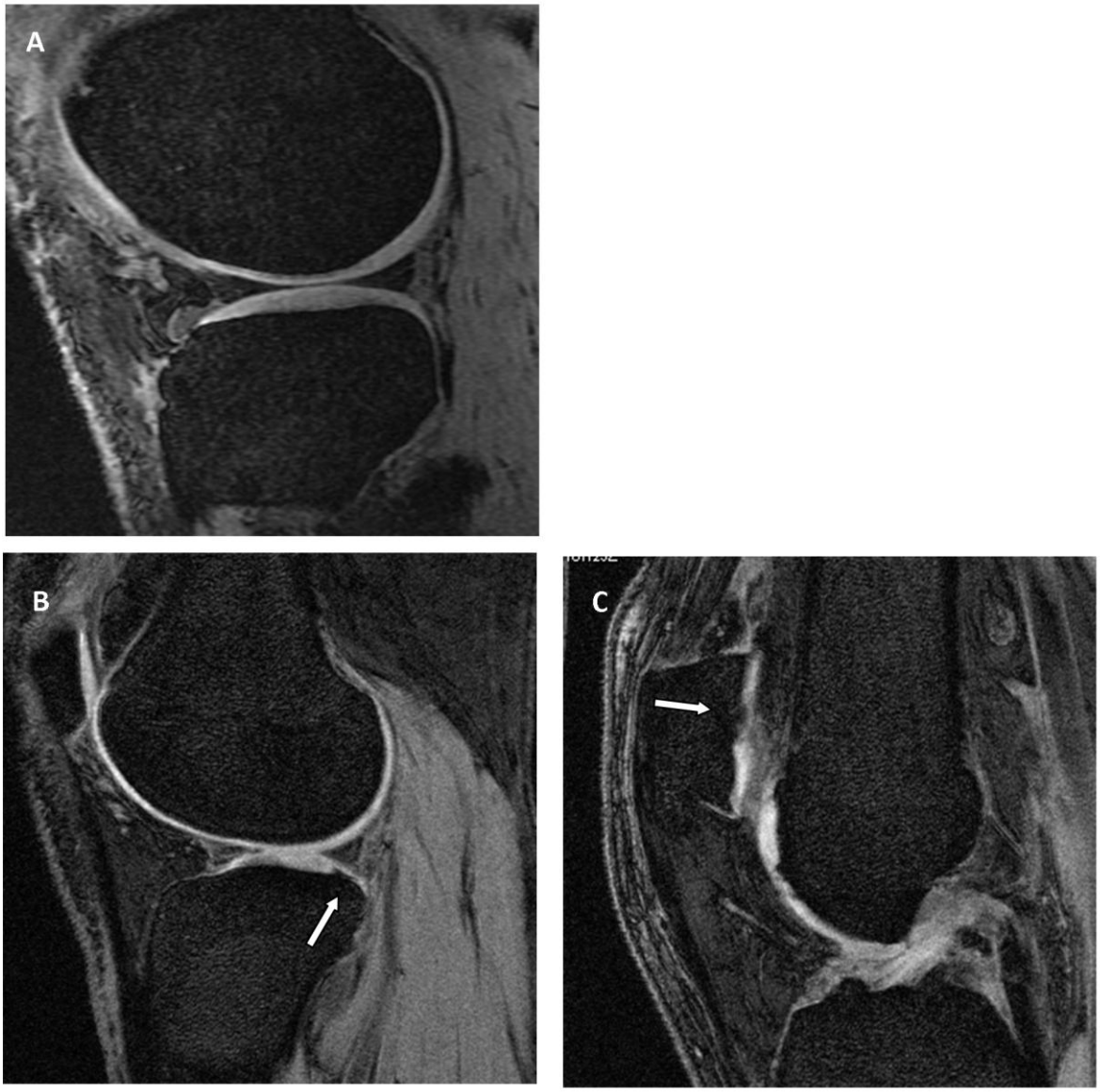

Figure 2 MRI images of A) a healthy knee, B) a knee with a tibial cartilage defect indicated by the arrow, and C) a knee with a patella cartilage defect indicated by the arrow.

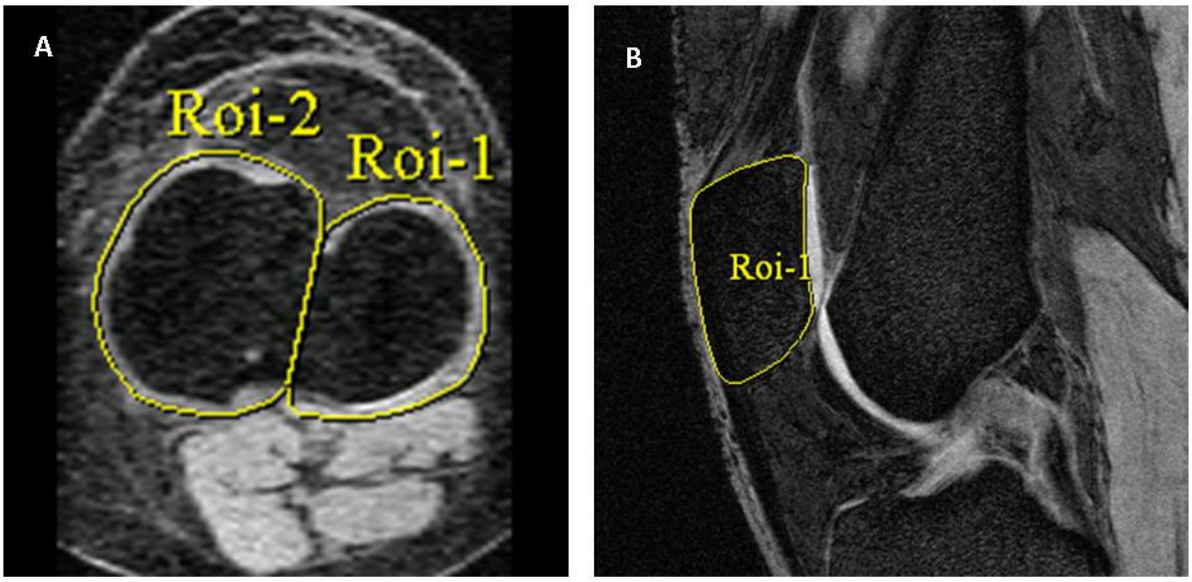

Figure 3 MRI images showing the regions used to calculate A) tibial plateau bone area, and B) patella bone volume.