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CONFLICT OF INTEREST

No authors have a conflict of interest.

ABSTRACT

Purpose: Higher knee load and quadriceps weakness are potential factors involved in the pathogenesis of knee osteoarthritis following arthroscopic partial meniscectomy (APM). In people following APM, this study evaluated the association between external knee joint moments and quadriceps strength and 2-year change in indices of cartilage integrity in the medial tibiofemoral compartment and patella.

Methods: 70 people with medial APM were assessed 3-months following APM (baseline) and reassessed 2 years later (follow-up). At baseline, isokinetic quadriceps strength and the external knee adduction moment (peak and impulse), and knee flexion moment (peak) during walking were assessed. Magnetic resonance imaging was used to assess cartilage (cartilage volume and cartilage defects) in the medial tibial compartment and patella at baseline and follow-up.

Results: Increased peak knee adduction moment during fast pace walking at baseline was associated with onset or deterioration of medial tibiofemoral cartilage defects (OR = 2.06, 95% CI 1.03 to 4.12, p=0.042) over 2 years. Increased peak knee flexion moment during normal pace walking at baseline was associated with loss of patellar cartilage volume over 2 years (β = -0.24, 95% -0.47 to -0.01, p = 0.04). No significant association was observed for quadriceps strength.

Conclusion: In middle-aged adults following APM, a higher peak knee adduction moment and peak knee flexion moment at 3 months following medial APM may be associated with adverse structural changes at the medial tibia and patella over the subsequent 2 years. These preliminary findings warrant further investigation as interventions aimed at reducing these moments may be designed if appropriate. **Keywords:** knee joint load; quadriceps strength; arthroscopic partial meniscectomy; early knee osteoarthritis.

INTRODUCTION

Arthroscopic partial meniscectomy (APM) has been widely used to manage the symptoms associated with medial meniscal lesions. However, people following meniscectomy are at high risk to develop radiographic osteoarthritis in both the medial tibiofemoral and patellofemoral joint compartments (12). Despite this, little is known about contributing factors to the development of osteoarthritis in this population group. Higher knee joint loading, inferred though external knee moments during walking, and quadriceps weakness, are factors associated with the pathogenesis of knee osteoarthritis (4), and have been reported following APM (14, 31). In people following APM, the relationship between these factors and knee structural changes following APM are yet to be investigated.

Knee joint moments are often used as a proxy for knee joint loading and may be associated with structural knee pathology. Influenced by knee alignment (19), the knee adduction moment (KAM) is associated with adverse medial tibiofemoral compartment structural change in people with knee osteoarthritis (3, 25). In particular, the peak KAM is associated with radiographic disease progression (25) while KAM impulse, which is a measure that accounts for the duration of the magnitude of the KAM, is associated with medial tibial cartilage volume loss (3). In a recently published study, we found that 3-months following APM, the external peak KAM and KAM impulse during gait are higher in the operated leg compared to the contralateral leg and to a healthy control group (14). Furthermore, in the same study we observed a significant increase in the peak KAM over 2 years in the medial APM leg, albeit no different to the 2 year change in the contralateral limb or healthy control group (14). The external peak knee flexion moment (KFM) is also potentially associated with structural joint change given its ability to alter medial

tibiofemoral (35) and patellar contact forces (17). We have found that 3-months following medial APM, the external peak KFM was significantly higher in the operated limb compared to the contralateral limb (14) but was not different compared to healthy controls (14, 31). The peak KFM significantly increased over 2 years compared to controls (14). Exploring if higher knee joint moments following recent APM are associated with knee joint structural change is of clinical interest considering that knee moments increase over time (14) and are potentially modifiable with conservative interventions during rehabilitation.

Quadriceps weakness is also a suggested risk factor for knee osteoarthritis (4) with some evidence supporting its link with adverse structural change in the tibiofemoral joint (29) and at the patella (2), albeit inconsistently (28). Studies, including our own, report quadriceps weakness in the operated limb 3-months following APM compared to healthy controls (13,14) but no difference in quadriceps strength approximately 2-years following APM compared with healthy controls (14, 34) or the contralateral limb (34). It is of clinical interest to explore if quadriceps weakness in the APM leg following recent surgery is associated with structural knee joint change as quadriceps strength is modifiable during rehabilitation.

Knee structural changes can be measured reliably using magnetic resonance imaging (MRI) techniques (18) and accumulating MRI data indicate patients with APM present adverse cartilage morphology as early as 3 months following surgery (36). Reports include greater cartilage loss over 2 years following meniscectomy (8) and a greater prevalence of cartilage defects in patients with APM 3 months to 4 years following surgery compared to controls (36). These measures of

cartilage integrity enable assessment of osteoarthritic changes, as are both are related to increased risk of knee joint replacement (6, 9).

Following on from our previous findings, this exploratory prospective study aimed to evaluate the hypotheses that greater external knee joint moments and weaker quadriceps strength that in the limb that had undergone medial APM 3 months previously would be associated with i) loss of medial tibial and patellar cartilage volume, and ii) greater onset or deterioration in medial tibiofemoral and patellar cartilage defects, over 2 years as measured on MRI.

PATIENTS AND METHODS

This prospective cohort study used a convenience sample of people that participated in our previously described study (14). Eighty-two participants aged between 30 to 50 years old and who had undergone an isolated medial APM 3 months previously were recruited. People were excluded if they had: evidence of lateral meniscal resection; greater than one third of medial meniscus resected; >2 tibiofemoral cartilage lesions; a single tibiofemoral cartilage lesion > approximately 10mm in diameter as assessed at arthroscopy; previous knee or lower limb surgery (other than the recent APM); history of knee pain (other than that leading to APM); post-operative complications; cardiac, circulatory or neuromuscular conditions; diabetes; stroke; multiple sclerosis; and/or contraindication to MRI. Baseline measures included gait and strength assessment, and were performed at The University of Melbourne while an MRI was performed at The Epworth Hospital, Melbourne. Gait and strength were also assessed in 66 of these participants at follow-up and have previously been reported (14). Participants underwent a second MRI approximately two years following their baseline scan. Each participant provided

written informed consent and The University of Melbourne Human Research Ethics Committee approved this study.

Gait Analysis

At baseline, kinematic data (120Hz) were acquired using a Vicon motion capture system (Vicon, Oxford, UK) with eight M2/MX CMOS cameras (1280 x 1024) while kinetic data (1080Hz) were captured in synchrony using two 0R6-6-2000 force plates and one BP-600-900 force plate (Advanced Mechanical Technology, Watertown Massachusetts, USA). A custom seven-segment lower limb direct kinematics and inverse dynamics model written in Matlab (Mathworks, Natick, USA) and BodyBuilder (Vicon, Oxford, UK) was used to estimate lower limb joint kinematics and kinetics (5). First, hip joint centers and knee joint flexion/extension axes were defined (5). Participants then performed five barefoot walking trials at a self-selected normal and fast pace described as a 'natural and comfortable pace' and a pace 'you would walk in a hurry' respectively. The peak KAM, peak KFM, and positive KAM impulse were expressed as external moments applied to the distal segment and reported for the APM limb in this study. The peak KAM and KFM in the first half of stance, and the positive KAM impulse during the entire stance phase were recorded (14). The knee moment parameters were averaged over five trials, and normalised to the product of body weight (N) and height (m). The test-retest reliability for the external knee moments during walking have been previously reported ≥ 0.75 (coefficient of multiple determination, r^2) (5). Two photoelectric beams measured walking speed. For this cohort of 70 participants, the coefficient of variation for normal pace walking and fast pace walking is 2.7% and 3.2%, respectively.

Isokinetic Strength Assessment

A Kin-Com 125-AP dynamometer (Chattecx, Chattanooga, Tennessee, USA) was used to measure maximal isokinetic quadriceps muscle strength at baseline. For the leg that underwent APM, participants performed two sub-maximal warm-up efforts for familiarisation. Participants then performed five repetitions of reciprocal maximal concentric-concentric contractions of quadriceps and hamstrings at 60°/sec, followed by eccentric-eccentric contractions with 40 seconds separating the two bouts. Participants were encouraged to 'push as hard as you can'. From the five trials, peak concentric and eccentric torques were recorded, normalised to body mass (Nm/kg), and used in subsequent analysis. Concentric and eccentric contractions were performed to comprehensively characterise strength. Isokinetic strength test-retest reliability using is reportedly excellent (intraclass correlation coefficients ICC≥0.96) (24).

Static Knee Alignment

Static knee alignment was taken using a gravity inclinometer attached to callipers (Acuangle Iosmed, Portland, OR) (15). The angle of the tibia was measured with respect to vertical using an inclinometer as participants stood comfortably with their weight distributed equally on both lower limbs. This clinical measure of static knee alignment has been shown to be reliable (ICC 0.94) and to correlate with knee alignment measured from the gold standard long leg x-rays (correlation coefficient 0.80) (15).

Self-reported Function and Symptoms

Participants completed the Knee Injury Osteoarthritis Outcome Scores (KOOS) to determine knee-related pain and function. The KOOS is valid and reliable in people undergoing meniscectomy (26).

Physical activity

The mean daily step count was recorded using an Actigraph GT256 (Actigraph, Pensacola, FL, USA) physical activity monitor. Participants were instructed to wear the Actigraph for seven consecutive days on an adjustable belt that was secured firmly around their waist. The mean daily step count was analysed from the accelerometer and all included participants had at least 4 valid days of accelerometer data. The validity and reliability of the Actigraph accelerometer has been previously described (21).

Magnetic Resonance Imaging

Images of the operated knee were acquired with a 1.5-T whole-body magnetic resonance unit at 3 months following APM (baseline) and 2 years later (follow-up) using sequences and parameters previously described (3). Two MRI scanners were used in this study: Philips (Eindhoven, The Netherlands) initially, followed by GE (Signa Advantage HiSpeed GE Medical Systems, Milwaukee, Wisconsin, USA) due to the decommissioning of the Philips scanner. We have previously reported the comparable reproducibility between these two scanners (3).

Cartilage Volume and Bone Area

Medial tibial and patellar cartilage volume were assessed to the nearest $1mm^3$ on T1-weighted MR images using Osiris (University of Geneva, Geneva, Switzerland) as previously described (3, 23). The inter-observer reproducibility of the longitudinal change in the medial tibial and patellar cartilage volume was assessed in 60 randomly selected images and the ICC was 0.89 for medial tibial cartilage volume change and 0.84 for patellar cartilage volume change. The coefficient of variation (CV) has previously been shown to be 3.4% and 2.6% for the medial tibia (40) and patellar (20) cartilage volumes, respectively. The annual rate of cartilage volume change was determined as: [((follow-up cartilage volume – baseline cartilage volume)/baseline cartilage volume)/time between two scans in years) x 100] such that a negative value corresponded to a loss in cartilage volume. Baseline medial tibial bone cross-sectional area was assessed to the nearest $1mm^2$ on transformed axial T1-weighted MR images using Osiris as previously described (37). Similar to methods used to assess cartilage volume, patellar bone volume was assessed to the nearest $1mm^3$ (20). The CVs for medial tibial bone area and patellar bone volume have previously been shown to be 2.3% (39) and 2.2% (20), respectively.

Cartilage defects

Medial tibiofemoral and patellar cartilage defects were assessed on T1-weighted MR images using a previously reported classification system where grade 0 represents normal cartilage; grade 1 represents focal blistering and intracartilaginous low-signal intensity area with an intact surface and bottom; grade 2 represents surface irregularities and thickness loss less than 50%; grade 3 represents deep ulceration with thickness loss of more than 50%; and grade 4 reflects full thickness wear with exposure of subchondral bone (11). Previous intra- and inter-observer

reliability of this grading system has reported intraclass correlation coefficients 0.89 and 0.85 for the medial tibiofemoral and patellofemoral compartments, respectively (11). Cartilage defect onset or deterioration was defined as an increase in cartilage defect score of ≥ 1 from baseline to follow-up (3).

Statistical Analysis

Independent variables included the peak KAM, KAM impulse and peak KFM assessed during self-selected normal pace gait and fast pace gait; in addition to peak quadriceps torque assessed during concentric and eccentric contractions. Dependent variables included change in cartilage volume and cartilage defect onset or deterioration (yes or no) in the medial tibiofemoral compartment and patella. Multiple linear regression models were constructed to investigate change in medial tibial cartilage volume and change in patellar cartilage volume as these variables were normally distributed and there was no evidence that multiple linear regression assumptions were violated. Shapiro-wilk tests and plot inspections confirmed that regression residuals were normally distributed. Multiple linear regression models were performed unadjusted as well as adjusted for age, gender body mass index, MRI scanner and static alignment (3, 38). Binary logistic regression was used to investigate the dichotomous variable; cartilage defect onset or deterioration. Binary logistic models were performed unadjusted as well as adjusted for age, gender, body mass index, MRI scanner, baseline medial tibiofemoral defect score, and bone area (3, 38). Using accepted guidelines with a ratio of one predictor variable per 10 participants (22), this study was adequately powered to develop stable regression models. Paired t-tests were used to determine if medial tibial cartilage volume and patellar cartilage volume changed significantly from baseline to follow-up. Statistical analyses were performed

using SPSS 21.0 (SPSS Inc. Chicago, Illinois, USA) and a significance level was set at alpha 0.05 (2 sided significance).

RESULTS

Seventy of the 82 (85%) participants completed both MRI assessments and were included in the analyses. Baseline participant characteristics are described in Table 1. At baseline, 3 participants opted not to have an MRI, and one person had the wrong leg imaged. Eight participants did not return for follow-up MRI for various reasons including; relocation and no longer being interested in participating in the study. The average time to follow-up was 2.06 years (SD 0.12, range 1.82-2.38). Participants who had complete data sets had a statistically significantly higher peak KAM during normal pace walking at baseline (mean±SD peak KAM, Nm/(BW×HT)% 2.39±0.98) compared to the 12 participants who had incomplete data sets (mean±SD peak KAM, Nm/(BW×HT)% 1.78±0.57, p=0.039), but no other statistically significant differences were observed for any other study variables. Forty-seven participants (67%) had their baseline and follow-up MRI on a different scanner.

From the 68 participants available for medial tibial cartilage volume analysis, there was a 3.5% statistically significant reduction in medial tibial cartilage volume over 2 years (mean±SD, cm^3 -0.07±0.11; 95% CI -0.10 to -0.05, p<0.001). No statistically significant relationships between the annual percentage change in medial tibial cartilage volume and joint moments or quadriceps strength were found (Table 2). For 70 participants, there was a 2.8% statistically significant reduction in patellar cartilage volume over 2 years (mean±SD, cm^3 -0.10±0.10; 95%CI -0.12 to -0.08, p<0.001). The adjusted results (Table 2) demonstrated that a higher KFM during normal

walking at baseline was associated with statistically significantly greater patellar cartilage loss over 2 years. Male gender (odds ratio = -1.57; 95%CI [-2.54 to -0.60], p = 0.002) and a higher BMI (odds ratio = -0.08; 95%CI [-0.16 to 0.00], p = 0.042) significantly contributed to cartilage volume loss in the adjusted model.

Medial cartilage defect onset or deterioration was found in 17 participants (24%). The adjusted results (Table 3) showed that peak KAM during fast pace walking at baseline was positively associated with medial cartilage defect onset or deterioration over 2 years. Notably, higher BMI (odds ratio = 1.38; 95%CI [1.11 to 1.71], p = 0.04) and smaller bone area (odds ratio = 0.65; 95%CI [0.44 to 0.96], p = 0.03) were also statistically significant predictors in this model. No other statistically significant relationships were observed for the onset or deterioration of medial cartilage defects. As onset or deterioration in patellar cartilage defects and bone marrow lesions was found in only five and seven participants respectively, subsequent regression analysis was not performed due to the small sample size.

DISCUSSION

This exploratory longitudinal study assessed the relationship of peak knee joint moments and quadriceps strength assessed 3-months following APM with subsequent 2-year change in structural knee joint indices from MRI in people following medial APM. The findings suggest that the peak KAM during fast pace walking and peak KFM during normal pace walking are associated with medial tibiofemoral cartilage defect onset or deterioration and patellar cartilage volume loss, respectively. We found no evidence to support an association between maximal isokinetic quadriceps strength and structural changes in the medial tibiofemoral compartment or

patella over 2 years. Further research is required to confirm these preliminary findings that potentially provide insight into the pathogenesis of osteoarthritis both in the medial tibiofemoral compartment and patella following a medial APM.

Specifically, we found that a higher peak KAM during fast pace gait may relate to adverse cartilage changes in the medial tibiofemoral compartment. No previous study has examined the effect of KAM on cartilage integrity in a non-osteoarthritic population. Nonetheless, this result is consistent with findings that a higher KAM is associated with structural change in people with established knee osteoarthritis (3, 25). The association between peak KAM and medial cartilage defect onset or deterioration is of clinical relevance as cartilage defects are associated with reduced cartilage volume (10), increased rates of cartilage loss (11), and ultimately knee joint replacement (6). The 3.5% medial tibial cartilage loss in our cohort is relatively consistent with a previous study that reported a 4.1% reduction in tibial cartilage volume in APM patients over 2 years (8). However, in contrast to findings in people with established knee osteoarthritis (3) we did not find a significant relationship between KAM parameters and medial tibial cartilage volume loss in APM patients. It is possible that a longer follow-up time is required to observe a significant relationship between KAM parameters and cartilage volume loss, as disease progresses.

While knee cartilage defects have been observed in people with meniscal pathology (16) and without known knee pathology (11) they are nonetheless informative measures of adverse structural change (10,11,6). In this study we found that the risk of cartilage defect onset or deterioration was increased by more than two-fold for a 1% unit increase in the peak KAM

(BWxHT%) during fast walking. Although a 1% unit increase in peak KAM is relatively high, given that we observed an approximate 0.2 BWxHT% increase in peak KAM for this cohort over the 2 year period (14), the estimated doubling of risk is also potentially substantial. Further research is required to substantiate these findings as interventions aimed at reducing peak KAM at 3-months following APM may reduce the risk of early structural changes in the medial tibiofemoral compartment. This may have a considerable impact on the risk of development of knee osteoarthritis given the 14-fold increased risk of developing knee osteoarthritis 21 years following meniscectomy (27).

People following a medial meniscectomy are 2.6 times more likely to develop patellofemoral osteoarthritis compared to controls (12), although the mechanisms are unclear. Our data implicate that a higher peak KFM during normal pace walking is associated with patella cartilage loss following a medial APM. We observed that a 1% unit increase in peak KFM (BWx HT%) during normal pace walking was associated with a 0.24% increase in the annual rate of patellar cartilage volume loss. Given that we have previously found an increase in peak KFM over 2 years up to 1.0 BWxHT% in this cohort (14), the current findings are potentially concerning. However, without cartilage volume measures from a comparable control group we cannot speculate further on the potential implications of this finding. Furthermore, the amount of patellar cartilage loss associated with pain and loss of function is unknown. As such, the magnitude of reduction in peak KFM required to prevent patellar cartilage volume loss by a clinically meaningful amount also remains unknown. These preliminary findings implicating a higher peak KFM during normal pace walking as a potential mechanism for patellofemoral osteoarthritis following APM require further investigation.

Evidence suggests that static knee malalignment increases the incident risk and progression of tibiofemoral (32) and patellofemoral osteoarthritis (33). The relationships between the peak KAM during pace walking and medial tibiofemoral cartilage defect onset or deterioration remained even after adjusting for static knee alignment suggesting that peak KAM during fast pace walking is an independent risk factor for structural knee joint change. However, the relationship between peak KFM during normal pace walking and patellar cartilage loss just failed to reach significance (p=0.051) when adjusting for static knee alignment, highlighting the potential influence of alignment on peak KFM.

Normal and fast pace walking were assessed to increase the generalisability of our findings as it is typical to walk at both paces. We observed a significant relationship between medial tibiofemoral cartilage defect onset or deterioration and peak KAM during fast pace walking, but not for peak KAM during normal pace walking. This may reflect that higher loads are associated with faster walking speed. Discordant findings for walking speeds were also observed for patellar cartilage volume loss where we found a significant relationship between peak KFM during normal pace walking but not fast pace walking. It remains unclear why these relationships are not statistically consistent for both walking speeds. However, it should be noted that similar results albeit non-significant, were observed for the association between normal pace walking and medial tibiofemoral cartilage defect onset or deterioration (p=0.054) and between fast pace walking and patellar cartilage volume loss (p=0.051).

Our hypothesis that quadriceps strength would be associated with indices of structural joint change was refuted. While some evidence supports an association between quadriceps weakness

and development or progression of medial tibiofemoral osteoarthritis (29) our findings appear to concur with a previous study that did not observe a relationship between quadriceps weakness and medial compartment cartilage volume loss over 30 months in people with symptomatic knee osteoarthritis (2). Similarly, in this study we found no evidence to support a relationship between quadriceps strength and change in patellar cartilage volume, despite previous research supporting a relationship (2). One possible explanation for our observation relates to our previously published finding in this same cohort, that increases in quadriceps strength over the 2 years (14) may have attenuated the predictive value of strength measures 3-months post-APM. A second consideration is that we only assessed maximal isokinetic quadriceps strength and it is possible that other interrelated aspects of muscle function such as muscle activity patterns (4) and proprioceptive acuity (4) may influence the integrity of the joint structure. Indeed, both muscle activity patterns (30) and proprioceptive acuity (1) are reportedly altered following APM. Third, our cohort included people with and without cartilage defects at baseline. Given that there may be a different relationship between strength and cartilage defect onset versus deterioration, combining those with and without cartilage defects may have obscured any relationships. However, as we adjusted for baseline cartilage defect score, the results are independent of whether or not there were cartilage defects at baseline.

Strengths of our study include its prospective cohort study design, homogenous patient group at high knee osteoarthritis risk (12), and comprehensive assessment of knee joint moments and quadriceps strength. However, this study also has several limitations. First, the use of two MRI scanners for follow-up assessments in 67% of participants may have increased the error in measuring structural change. Nonetheless, our previous cross-calibration and repeatability studies confirmed that cartilage volume showed excellent agreement and was not significantly

different between the two scanners (3). Second, the significant reductions in medial tibial (3.5%) and patella (2.8%) cartilage volume are similar to the CV values of these measurements (3.4% and 2.6%, tibia and patella respectively). It should be noted that the paired t-test used to determine change in cartilage volume includes any measurement error. Thus, even taking into account measurement error, the cartilage volume significantly reduces in both the media tibial compartment and at the patella. Third, our significant findings may be due to random chance, as we did not correct for the multiple statistics employed. However, we opted not to apply corrections given the exploratory nature of this study. Fourth, restricting the longitudinal study to two years may have limited our ability to identify significant relationships, especially at early stages in the disease process. A larger sample size may be needed to detect significant associations. This was evidenced by relatively small changes across the indices of structural change on MRI, as previously discussed. Finally, it is a limitation that information on the type of meniscal injury and whether or not participants underwent post-operative rehabilitation was not recorded and therefore cannot be accounted for in this study.

Identifying risk factors for knee osteoarthritis onset and progression following APM is integral to treat and ultimately prevent the personal and socio-economic burden of knee osteoarthritis. These preliminary findings suggest the peak KAM during fast pace walking and peak KFM during normal pace walking 3-months post-APM, are possible risk factors in the onset or progression of structural joint change in this population at high risk for osteoarthritis. Future research is needed to confirm our findings as interventions aimed at reducing these moments may be designed if appropriate.

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Conflict of Interest

No authors have a conflict of interest.

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Table 1 Baseline description of study participants

Characteristics	n=70
Age, years	41.4 ± 5.5
Male, n (%)	61 (87)
Body mass index, kg/m^2	27.2 ± 4.1
Varus alignment,º	0.3 ± 2.6
Self-reported pain (KOOS)	86.6 ± 11.4
Self-reported function (KOOS)	91.5 ± 10.3
†Average number of steps per day	11,531 ± 2,920
Structural Measures	
¥Medial tibial cartilage volume, cm^3	1.95 ± 0.38
§Patellar cartilage volume, cm^3	3.71 ± 0.74
Medial tibiofemoral cartilage defects, n (%)	
Grade 0	7 (10)
Grade 1	45 (64)
Grade 2	13 (19)
Grade 3	4 (6)
Grade 4	1 (1)
Patellar cartilage defects, n (%)	
Grade 0	54 (77)
Grade 1	13 (19)
Grade 2	2 (3)
Grade 3	1 (1)
Grade 4	0 (0)
Normal Pace Walking	
Self-selected walking speed, ms	1.37 ± 0.16
Peak KAM, Nm/(BW×HT)%	2.39 ± 0.98
KAM Impulse, Nm.s/(BW×HT)%	0.88 ± 0.33
Peak KFM, Nm/(BW×HT)%	4.54 ± 1.43
Fast Pace Walking	
Self-selected walking speed, ms	1.88 ± 0.27
Peak KAM, Nm/(BW×HT)%)	2.93 ± 1.23
KAM Impulse, Nm.s/((BW×HT)%)	0.76 ± 0.28
Peak KFM, Nm/(BW×HT)%	6.86 ± 1.88
Isokinetic strength	
Concentric quadriceps, Nm/kg	1.71 ± 0.49
Eccentric quadriceps, Nm/kg	2.22 ± 0.70

† data available for 56 participants
¥ Medial tibial cartilage volume at follow-up, mean± SD, 1.86 ± 0.37cm^3
§Patellar cartilage volume at follow-up, mean± SD, 3.60 ± 0.75cm^3

Values are reported as mean ± SD, or n (%).
KOOS, Knee injury Osteoarthritis Outcome Score ranges 0-100; 100 is the best possible score
KAM, knee adduction moment
KFM, knee flexion moment
BW, body weight
HT, height

Table 2 Relationships between annual percentage change in cartilage volume and baseline indices of knee moments and quadriceps strength

Annual % change in cartilage volume	Simple linear regression		Multiple linear regression[1]		Multiple linear regression[2]	
	Regression coefficient (95%CI)	p Value	Regression coefficient (95%CI)	p Value	Regression coefficient (95%CI)	p Value
Medial tibia						
Normal Pace Walking						
Peak KAM (Nm/(BW×HT)%)	-0.32 (-0.97 to 0.33)	0.323	-0.44 (-1.11 to 0.24)	0.198	-0.29 (-1.02 to 0.44)	0.433
KAM Impulse (Nm.s/(BW×HT)%)	-0.70 (-2.61 to 1.21)	0.465	-1.20 (-3.17 to 0.78)	0.230	-0.72 (-2.88 to 1.44)	0.509
Peak KFM (Nm/(BW×HT)%)	0.02 (-0.41 to 0.46)	0.912	0.05 (-0.43 to 0.52)	0.844	0.11 (-0.37 to 0.58)	0.654
Fast Pace Walking						
Peak KAM (Nm/(BW×HT)%)	-0.04 (-0.57 to 0.48)	0.870	-0.12 (-0.67 to 0.43)	0.667	0.01 (-0.56 to 0.59)	0.963
KAM Impulse (Nm.s/(BW×HT)%)	-0.13 (-2.42 to 2.15)	0.907	-0.68 (-3.07 to 1.71)	0.572	0.15 (-2.49 to 2.79)	0.908
Peak KFM (Nm/(BW×HT)%)	0.24 (-0.10 to 0.58)	0.164	0.23 (-0.14 to 0.60)	0.213	0.23 (-0.14 to 0.60)	0.217
Isokinetic Strength (Nm/kg)						
Concentric quadriceps strength	1.10 (-0.19 to 2.39)	0.094	0.72 (-0.76 to 2.21)	0.335	0.68 (-0.80 to 2.15)	0.363
Eccentric quadriceps strength	0.80 (-0.09 to 1.69)	0.077	0.73 (-0.21 to 1.68)	0.127	0.76 (-0.16 to 1.70)	0.109
Patella						
Normal Pace Walking						
Peak KAM (Nm/(BW×HT)%)	0.17 (-0.17 to 0.51)	0.320	0.08 (-0.27 to 0.42)	0.647	0.13 (-0.24 to 0.50)	0.494
KAM Impulse (Nm.s/(BW×HT)%)	0.65 (-0.34 to 1.65)	0.195	0.26 (-0.76 to 1.27)	0.615	0.48 (-0.61 to 1.57)	0.380
Peak KFM (Nm/(BW×HT)%)	-0.12 (-0.35 to 0.11)	0.306	-0.24 (-0.47 to -0.01)	0.043	-0.24 (-0.48 to 0.01)	0.051
Fast Pace Walking						
Peak KAM (Nm/(BW×HT)%)	0.10 (-0.17 to 0.36)	0.483	0.02 (-0.25 to 0.30)	0.859	0.05 (-0.23 to 0.34)	0.731
KAM Impulse (Nm.s/(BW×HT)%)	0.50 (-0.68 to 1.67)	0.402	-0.02 (-1.21 to 1.18)	0.978	0.18 (-1.15 to 1.52)	0.785
Peak KFM (Nm/(BW×HT)%)	-0.05 (-0.22 to 0.13)	0.596	-0.18 (-0.36 to 0.00)	0.054	-0.18 (-0.36 to 0.00)	0.054
Isokinetic Strength (Nm/kg)						
Concentric quadriceps strength	0.21 (-0.49 to 0.90)	0.557	-0.25 (-1.01 to 0.51)	0.514	-0.26 (-1.02 to 0.51)	0.502
Eccentric quadriceps strength	0.14 (-0.34 to 0.62)	0.572	-0.09 (-0.59 to 0.40)	0.702	-0.09 (-0.59 to 0.40)	0.404

Multiple linear regression analysis[1] adjusted for age, gender, BMI, MRI scanner,
Multiple linear regression analysis[2] adjusted for age, gender, BMI, MRI scanner, static alignment.
Abbreviation: BW, body weight; HT, height

Table 3 Relationships between change in medial tibiofemoral cartilage defects over 2 years and baseline indices of knee moments and quadriceps strength

	Simple logistic regression		Multiple logistic regression[1]		Multiple logistic regression[2]	
Deterioration of cartilage defects, yes/no	**OR (95%CI)**	**p Value**	**OR (95%CI)**	**p Value**	**OR (95%CI)**	**p Value**
Medial tibiofemoral cartilage defects						
Normal Pace Walking						
Peak KAM (Nm/(BW×HT)%)	1.11 (0.65 to 1.94)	0.690	2.26 (0.99 to 5.21)	0.052	2.40 (0.98 to 5.89)	0.056
KAM Impulse (Nm.s/(BW×HT)%)	1.72 (0.33 to 8.86)	0.516	7.11 (0.78 to 65.09)	0.082	8.16 (0.73 to 91.98)	0.089
Peak KFM (Nm/(BW×HT)%)	0.86 (0.57 to 1.31)	0.862	1.08 (0.68 to 1.71)	0.758	1.07 (0.67 to 1.72)	0.770
Fast Pace Walking						
Peak KAM (Nm/(BW×HT)%)	1.12 (0.72 to 1.74)	0.629	2.06 (1.03 to 4.12)	0.042	2.10 (1.01 to 4.34)	0.047
KAM Impulse (Nm.s/(BW×HT)%)	1.38 (0.20 to 9.68)	0.745	8.32 (0.59 to 117.20)	0.116	9.47 (0.52 to 173.73)	0.130
Peak KFM (Nm/(BW×HT)%)	0.88 (0.65 to 1.20)	0.425	1.07 (0.73 to 1.57)	0.729	1.07 (0.73 to 1.57)	0.746
Isokinetic Strength (Nm/kg)						
Concentric quadriceps strength	1.00 (0.32 to 3.13)	0.997	2.30 (0.50 to 10.68)	0.284	2.33 (0.50 to 10.88)	0.283
Eccentric quadriceps strength	0.81 (0.37 to 1.80)	0.605	1.38 (0.51 to 3.71)	0.524	1.38 (0.51 to 3.74)	0.530

Multiple linear regression analysis[1] adjusted for age, gender, BMI, MRI scanner, baseline medial tibiofemoral defect score, baseline bone area
Multiple linear regression analysis[2] adjusted for age, gender, BMI, MRI scanner, baseline medial tibiofemoral defect score, baseline bone area, static alignment
Abbreviations: BW, body weight; HT, height