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a prospective cohort study

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1	Changes in	knee joint load	l indices from	before to 12 m	onths after arth	roscopic partial

2 meniscectomy: A prospective cohort study

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6

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15	Running head: Changes in knee joint loading following APM
16	

1 ABSTRACT

2 *Objective*: Patients undergoing arthroscopic partial meniscectomy (APM) are at increased risk of

3 knee osteoarthritis. Meniscal damage and/or surgery may alter knee joint loading to increase

4 osteoarthritis risk. We investigated changes in knee joint loading following medial APM surgery,

5 compared with the contra-lateral leg.

6 *Methods:* We estimated indices of knee joint loading (external peak knee adduction moment 7 (KAM), KAM impulse and peak knee flexion moments) normalized to body size (i.e. body mass 8 (BM) and height (HT)) using 3D gait analysis in 23 patients (17 men, mean (SD) 46.2 (6.4) years, 9 BMI 25.8 (3.4) kg/m²) without radiographic knee osteoarthritis before and 12 months after medial 10 APM. Static alignment was assessed by radiography and self-reported outcomes by Knee Injury and 11 Osteoarthritis Outcome Score (KOOS).

12 *Results:* Peak KAM and KAM impulse increased in the APM leg compared to the contra-lateral leg

13 from before to 12 months after surgery (change difference: 0.38 Nm/BM*HT% 95% CI 0.01 to

14 0.76 (p=0.049) and 0.20 Nm*s/BM*HT% 95% CI 0.10 to 0.30 (p<0.001)). Patients self-reported

15 improvements on all KOOS subscales (KOOS pain improvement: 22.8 95% CI 14.5 to 31.0

16 (p<0.01)).

Conclusions: A relative increase in indices of medial compartment loading was observed in the leg
undergoing APM compared with the contra-lateral leg from before to 12 months after surgery. This
increase may contribute to the elevated risk of knee OA in these patients. Randomized trials
including a non-surgical control group are needed to determine if changes in joint loading following
APM are caused by surgery or by changes in symptoms.

22

23 Keywords: Osteoarthritis, Meniscectomy, joint load, knee adduction moment, arthroscopy,

24 biomechanics

1 INTRODUCTION

Biomechanical factors play an important role in the initiation and progression of knee osteoarthritis
(OA)¹. One such factor is dynamic loading during walking. The external knee adduction moment
(KAM), calculated from gait analysis, is considered a valid and reliable estimate of medial
tibiofemoral compartment loading^{2 3} and studies have shown that increased KAM is related to
disease severity⁴, disease progression⁵⁻⁷ and structural joint changes⁸ in patients with knee OA.

Meniscectomized patients have a high risk of developing knee OA⁹ and have knee 7 arthroplasty at a younger age compared to patients without prior knee surgery¹⁰. Arthroscopic 8 9 partial meniscectomy (APM) is one of the most frequently performed orthopedic procedures¹¹, even 10 though surgery is not superior to non-operative interventions in relieving pain in middle-aged and older patients¹². Patients who have undergone medial meniscectomy show increased KAM. 11 12 indicative of an increase in the medial tibiofemoral compartment loading compared to healthy controls^{13 14}. Furthermore, a higher KAM is predictive of structural knee joint changes in these 13 patients¹⁵. Collectively, these findings indicate that increased knee joint loading may contribute to 14 15 the increased risk of knee OA in meniscectomized patients.

16 The KAM is primarily determined by the magnitude of the ground reaction force vector and the degree of varus alignment⁸, and removal of medial meniscus tissue could increase 17 joint loading via an increase in the varus alignment of the knee. Indeed, one cross-sectional study 18 19 reported increased varus alignment 5 years after medial meniscectomy, with the increase in varus alignment dependent on the amount of meniscus tissue resected¹⁶. On the other hand, change in gait 20 speed, which is often affected by pathology or symptoms, could also affect the ground reaction 21 force and elicit changes in the KAM¹⁷¹⁸. To our knowledge, no studies have investigated in vivo 22 changes in medial compartment knee joint loading from before to after arthroscopic partial medial 23 24 meniscectomy.

The aim of this study was to investigate changes in indices of medial compartment
 knee joint loading in the leg undergoing surgery from before to 12 months after medial APM, as
 compared with the contra-lateral leg. We hypothesized that indices of knee joint loading would
 increase in the leg undergoing surgery compared to the contra-lateral leg.
 METHOD
 The "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE)

8 Statement was used as guideline for reporting this observational study¹⁹.

9

10 Patients

11 Patients aged 35-55 years at time of enrollment and assigned for partial meniscectomy by an 12 orthopedic specialist on suspicion of a medial meniscal tear were recruited. We included patients 13 from April 2012 to September 2013 from two public hospitals (Odense University Hospital, Odense 14 and Lillebaelt Hospital, Kolding) and one private clinic in the city of Odense with self-reported 15 gradual symptom onset or symptom onset caused by a minor incident like bending/twisting of the knee during daily activities (i.e. tears of degenerative origin). Exclusion criteria were: clear 16 17 traumatic symptom onset (i.e. caused by a sports injury, crash or collision); tibiofemoral and/or 18 patellofemoral OA defined as having Kellgren and Lawrence (K/L) grades 2 or higher in either 19 knee; previous knee surgery in either knee; back pain within last 30 days limiting physical activity; other injuries limiting physical activity within last 30 days; BMI above 36 kg/m²; very low physical 20 21 activity level (indoors walking only). After meniscectomy, patients were given a leaflet with 22 standard rehabilitation exercises, which they were encouraged to perform at home. Information on 23 compliance with the exercise recommendation was not collected. All patients gave their written 24 informed consent and the Ethics Committee for the Region of Southern Denmark approved the

1 study (ID: 20120006).

2

3 *Radiographs*

4 Standardized fixed-flexion posteroanterior and skyline x-ray examinations were made at baseline 5 prior to surgery to assess degree of radiographic tibiofemoral and patellofemoral OA according to Kellgren and Lawrence²⁰. For standardization of x-ray examinations of the tibiofemoral 6 compartments the Synaflexer frame was used²¹. Anatomical knee alignment was estimated from the 7 8 short film x-ray examinations at both baseline and 12 months follow-up using a conversion of anatomical femorotibial axis to mechanical axis²² with lower values representing varus alignment. 9 All x-ray images were scored by a resident specializing in radiology (GMJ) (ICC_{3.1} 0.99 for 10 11 assessment of alignment).

12

13 Gait analysis

14 Gait analysis was performed before and 12 months after APM. A six-camera (100 Hz) 3D motion 15 analysis system (Nexus version 1.8.5, Vicon, Oxford, UK) was used to estimate the knee joint 16 moments during walking. The standard plug-in-gait marker set was used and ground reaction forces 17 were measured (1000 Hz) in synchrony with the kinematic data using two force plates (AMTI, 0R6-18 7 Series Inc., Watertown, MA, US) imbedded in the floor. Patients walked barefoot at self-selected 19 speed. If patients walked more than 5% faster or slower at the follow-up assessments we collected 20 data from additional trials matching the baseline speed (+/- 5%) as walking speed is known to affect joint moments¹⁷. Knee joint moments were estimated using inverse dynamics and normalized to 21 22 body mass (BM) and height (HT). Subsequently, the following variables of interest were extracted: external peak KAM (Nm/BM*HT%), KAM impulse (Nm*s/BW*HT%) and peak knee flexion 23 24 moment (KFM; Nm/BM*HT%). We included the KFM since it has been reported to contribute to

medial compartment contact force²³. Variables were calculated for individual trials and averaged 1 2 over 5 trials. Test-retest reliability in our laboratory for peak KAM, KAM impulse and peak knee 3 flexion moment is 0.84, 0.95 and 0.77 (ICC_{3,1}), respectively. 4 5 Knee injury and Osteoarthritis Outcome Score (KOOS) 6 Patient reported symptoms, pain, function and quality of life were collected using the KOOS 7 questionnaire prior to meniscectomy and at the 12 month follow-up. A normalized score was 8 calculated for each subscale (0 indicating extreme symptoms and 100 indicating no symptoms). The 9 KOOS score has been validated for meniscectomy patients and has shown high test-retest reproducibility^{24 25}. 10 11 Collection of surgery information 12 13 All surgeries were carried out under general anesthesia. Information regarding the location of tear 14 within the medial compartment (anterior, mid body or posterior) and amount of tissue resected (in 15 %) was collected using the International Society of Arthroscopy, Knee Surgery and Orthopaedic 16 Sports Medicine - Classification of meniscal tears questionnaire (ISAKOS) filled out by the 17 operating surgeon. We report amount of resection as 0-25%, 26-50%, or more than 50%. The ISAKOS questionnaire has moderate reliability for reporting of such structural/surgical features²⁶. 18 19 20 Statistical analysis 21 The main outcomes were change in peak KAM, KAM impulse and peak knee flexion moment from 22 before to 12 month after APM. All outcomes were checked for normality by inspection of 23 histograms and Shapiro Wilk test for normality prior to analysis. Difference in change between the

24 operated and contra-lateral leg was evaluated using a students paired t-test. To account for the

1 potential effect of changes in gait speed from baseline to the 12 months follow-up all analyses were 2 repeated in additional gait trials conducted at speeds similar to baseline. A priori we calculated that 3 including 20 patients would enable us to detect a difference in change in peak KAM between the 4 operated and contra-lateral leg of 7% using the formula smallest detectable change (SDC)/ \sqrt{n} (assuming a SDC_{95%} of 0.80 Nm/BM*HT% or an SDC of about 25% of the mean)²⁷. All analyses 5 6 were conducted using STATA (version 13.1, Statacorp, College Station, Texas, US) with a 7 significance level set to 0.05, and all tests were two-tailed. P-values were not adjusted for multiple 8 testing due to the observational design of this study.

9

10 **RESULTS**

Twenty-three patients had medial APM and participated in the baseline assessment. One patient declined to participate at the follow-up assessment, leaving 22 patients at the 12-month follow-up (Figure 1). No between leg differences were observed at baseline except for peak KFM, which was lower in the leg scheduled for APM compared with the contra-lateral leg (Table 1).

At surgery, surgeons reported that meniscal tears were located in the posterior horn in 16 16 patients, posterior and mid body in 5 patients, mid body in 1 patient and in the anterior part in 1 17 patient. Fifteen patients had a resection involving 25% or less of the meniscus and 7 had a resection 18 involving between 26 and 50% of the meniscus (data on amount of resection missing for one 19 patient).

The patients self-reported improvements on all KOOS sub scales from baseline to 12 months after APM (Figure 2). All indices of knee joint loading increased within the APM leg from baseline to 12 month. In contrast, a decrease in KAM impulse was observed within the contralateral leg (Table 2). Both peak KAM and KAM impulse increased in the APM leg compared with the contra-lateral leg from baseline to 12 months follow-up (Table 2). This resulted in a 12% higher KAM impulse at 12 months in the APM leg compared to the contra-lateral leg (p=0.008) but no
significant difference was found for peak KAM (p=0.130) and KFM (p=0.353) between legs at 12
months. No difference in change in static alignment was observed between the APM leg and the
contra-lateral leg (Table 2).

Gait speed increased by 0.08 m/s (95% CI 0.04 to 0.13) to 1.34 m/s (95% CI 1.28 to
1.40) at the 12 months follow-up. Secondary analyses where patients walked at speeds similar to
baseline at the 12 months follow-up did not change the interpretation for peak KAM and KAM
impulse but a significant increase in KFM was observed in the APM leg compared with the contralateral leg (Supplementary Table 1).

10

11 **DISCUSSION**

Arthroscopic partial medial meniscectomy was associated with significant differences in changes in indices of medial compartment knee joint loading between the APM leg and the contra-lateral leg (i.e. peak KAM and KAM impulse) from before to 12 months after surgery, resulting in a 12% higher KAM impulse in the APM leg compared with the contra-lateral leg. This increase is consistent with an increase in the loading of the medial knee compartment following partial removal of the meniscus. Concomitantly, patients self-reported improvements on all KOOS subscales.

Joint injury is a well-known risk factor for knee OA and patients with meniscal pathology not undergoing surgery have been reported to be at increased risk of knee OA. However, surgery has the potential to further influence the mechanical environment in the knee joint. Thus, partial resection of medial meniscal tissue may increase varus alignment and thus increase medial compartment knee joint load measured as the KAM. One previous study reported peak KAM to increase from 3 to 24 months following APM¹⁴, and a higher peak KAM post APM has been shown

to be predictive of subsequent degenerative structural knee joint changes¹⁵, indicating a link to knee 1 2 OA development. However, these studies did not include assessments of indices of knee joint 3 loading prior to surgery and therefore did not provide any information about the potential impact of 4 surgery on joint loads. To the best of our knowledge only one small study (n=10) has investigated knee joint loading before and after meniscal surgery²⁸, the analysis however was limited to sagittal 5 6 plane moments. In the present study we included both frontal plane (KAM) and sagittal plane 7 moments (KFM) as both have been reported to be important for estimating medial compartment joint loading^{3 23 29}. We observed increased peak KAM and KAM impulse from before to 12 months 8 after APM in the leg having undergone surgery as compared to the contra-lateral leg. This resulted 9 10 in 12% higher KAM impulse in the APM leg compared to the contra-lateral leg at 12 months after surgery, whereas the 9% higher peak KAM in the operated leg compared to the contra-lateral leg at 11 12 12 month did not reach statistical significance. The minimal clinically relevant difference and 13 change in KAM in relation to risk of knee OA development and pain is not known. However, 14 interventions to reduce the KAM peak and impulse such as insoles or orthotics have reduced KAM by 2 to $9\%^{30}$, and knee braces by 5 to $14\%^{30 31}$. A study using a variable stiffness shoe reduced the 15 16 peak KAM by 6.6%, accompanied by a larger proportion of patients in the intervention group having a clinically important improvement in pain³². Both orthotics and knee braces are 17 recommended in clinical guidelines for non-surgical treatment of knee OA to reduce joint loading 18 and symptoms³³. The observed increases in joint loading observed in the present study are of the 19 20 same magnitude as the reductions observed with orthotics and knee braces, suggesting that the 21 observed changes in KAM in the present study may be clinically important.

A previous study reported increased varus alignment in the operated leg 5 years after meniscectomy, with the magnitude of increase being dependent on amount of meniscus resected¹⁶. However, we did not observe any changes in static alignment in the present study. Malalignment 1 assessed by radiographs may take several years to develop, thus the lack of change may not be all 2 that surprising since we only followed patients for 1 year. Nevertheless, altered *dynamic* alignment 3 assessed by 3D motion analysis during walking may contribute to the observed increase in KAM in 4 the present study. Indeed, a recent study reported increased dynamic varus alignment together with 5 an increase in the magnitude of the ground reaction force contributed to the observed increases in KAM from 3 to 24 months after meniscectomy³⁴. Other factors such as changes in toe-out angle and 6 7 trunk lean may also affect the KAM. It was beyond the scope of this study to analyze these potential 8 contributors in detail.

9 Walking speed is known to influence knee joint loading. Our patients were asked to 10 walk at their own self-selected speed at baseline. If a patient changed his/her walking speed at the 11 12 month follow-up assessment, additional gait trials with the same speed as the baseline 12 assessment were conducted as the appropriateness of statistically adjusting for walking speed has been questioned¹⁷. We observed a 6% increase in gait speed from baseline to 12 month. However, 13 14 the overall interpretation of increased KAM in the APM leg compared to the contra-lateral leg from 15 baseline to 12 months did not change in the analysis using speeds normalized to baseline. Rather, 16 the sensitivity analysis using normalized speeds displayed a significant increase in peak KFM in the 17 APM leg compared to the contra-lateral leg, which was not observed at self-selected walking speed. This indicates that the relative increase in knee joint loading indices reflect an actual altered knee 18 19 load distribution and not merely increased gait speed following surgery. Furthermore, sagittal plane loading is more sensitive to changes in gait speed than frontal plane loading³⁵. 20

We observed large improvements in self-reported outcomes from baseline to 12 months follow-up. These improvements are similar to what has been observed in randomized trials investigating the effect of APM in patients with degenerative medial meniscal tears without radiographic knee OA^{36 37}. Importantly, improvements of the same size were observed in the non-

surgical control arm of these studies. Thus, this improvement may be due to the large placebo effect
associated with APM³⁷ and other orthopedic procedures³⁸. Nevertheless, patient reported
improvements in pain may influence the observed changes in knee joint loading indices and hence
not be caused by the surgery *per se*. We observed increased KAM impulse in the APM leg from
baseline to 12 months follow-up, but at the same time KAM impulse decreased in the contra-lateral
leg. This might indicate a shifting of load from the contra-lateral leg to the APM leg, which may be
elicited by reduced pain in the treated leg.

8 Some limitations apply to the present study. We did not include a non-surgical control 9 group (i.e. sham surgery, exercise therapy or no treatment group) but compared indices of knee 10 joint loading to the contra-lateral leg of the patients. As this is the first study to investigate changes 11 in knee joint loading in APM patients from before to after surgery we felt it would be unethical to 12 investigate this in a randomized trial requiring a much larger sample size. We therefore conducted a 13 prospective observational study using the contra-lateral leg as control as this required a much 14 smaller sample size to test the premise of this hypothesis and minimize patient's time and resources. 15 As the aim of the present mechanistic study was to investigate potential changes in knee joint 16 loading following APM, strict inclusion and exclusion criteria were applied, resulting in high 17 internal validity. However, a large proportion of screened patients were excluded, with the main 18 reason being previous knee surgery in either knee, limiting generalizability (i.e. external validity) of 19 this study to APM patients in general. Static alignment was assessed from short film radiographs 20 using a correction factor for transformation to mechanical axis. This method is less precise than 21 using long film radiographs, which may have affected the chance of detecting changes in alignment. 22 In conclusion, we observed a relative increase in medial compartment loading, 23 measured as the KAM, in the leg undergoing APM for a degenerative medial meniscal tear

compared with the contra-lateral leg from before to 12 months after surgery, resulting in a 12%

higher KAM impulse in the APM leg at 12 months after surgery. This increase may be an important
contributor to the high risk of knee OA development in patients undergoing APM. Further
randomized controlled trials are needed to determine if this is caused by the surgery *per se* or is
influenced by a change in patient symptom status.

5

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11

12 CONTRIBUTIONS

13 JBT, AHL, MWC, LSL conceived and designed the study. NN and AHL participated in the data

14 collection. JBT, AHL, GM, LSL, ME and MWC participated in the analysis and/or interpretation.

15 All authors helped in drafting the manuscript and gave their final approval of the submitted version.

16

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21

22 COMPETING INTERESTS

23 LSL is the editor in chief of Osteoarthritis and Cartilage. The remaining authors have no competing

24 interests to declare in relation to this work.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1: Biomechanical outcomes at 12 months after arthroscopic partial medial meniscectomy <u>matched to gait speed at</u> <u>baseline</u>.

			Change from baseline		
					Between-leg
	APM leg	<u>Contra-lateral leg</u>	APM leg	Contra-lateral leg	difference
Peak KAM (Nm/BM*HT%)	3.26 (2.91 to 3.62)	3.02 (2.64 to 3.40)	0.20 (-0.03 to 0.43)	-0.14 (-0.33 to 0.05)	0.34 (-0.01 to 0.70)
KAM impulse (Nm*s/BM*HT%)	1.31 (1.15 to 1.47)	1.18 (1.01 to 1.35)	0.16 (0.06 to 0.25)	-0.04 (-0.10 to 0.03)	0.19 (0.09 to 0.30)
Peak KFM (Nm/BM*HT%)	2.47 (2.05 to 2.90)	2.66 (2.14 to 3.18)	0.20 (-0.14 to 0.53)	-0.23 (-0.51 to 0.06)	0.42 (0.03 to 0.81)
Values are mean (95% confidence intervals). APM=Arthroscopic Partial Meniscectomy, BM=Body Mass, CON=Contra-lateral, HT=Height,					
KAM=Knee Adduction Moment, KFM=Knee Flexion Moment, Nm=Newton meters					