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Repetitive knee bending and synovitis in people at risk and with knee osteoarthritis: Data from the FNIH Osteoarthritis Biomarkers Consortium

Running Head: Knee bending and synovitis in knee OA

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ABSTRACT

Objective To investigate associations between engagement in knee bending (stair climbing, kneeling, squatting, heavy lifting, getting in/out of a squatting position) and synovitis prevalence on non-contrast magnetic resonance imaging (MRI) in people at risk and with knee osteoarthritis (OA).

Methods We included baseline data from 594 participants (age: 61.5 ± 8.9 years; 61% Kellgren-Lawrence grade ≥2; 59% female; body mass index: 30.7 ± 4.8 kg/m^2) of the Osteoarthritis Biomarker Consortium Foundation for the National Institutes of Health project. Knee bending activities were queried by standard questionnaire and severity of Hoffa-synovitis and effusion-synovitis (surrogate outcomes of synovitis) graded utilizing the MRI OsteoArthritis Knee Scoring system. Logistic regression was used, unadjusted and adjusted for metabolic syndrome, physical activity level and sex. A grade ≥1 defined synovitis prevalence, with a grade ≥2 cut-off implemented in sensitivity analyses.

Results The prevalence of grade ≥1 Hoffa-synovitis and effusion-synovitis equaled 59% (n=353) and 62% (n=366), respectively. Adjusted for confounders, kneeling for ≥30 minutes during a single day was associated with grade ≥1 Hoffa-synovitis prevalence (odds ratio (OR) (95% confidence interval (CI)): 1.65 (1.11, 2.47)). Participants engaging in this activity one day or less per week had greater odds for prevalent Hoffa-synovitis, than those who did not perform the activity (OR (95% CI):1.88 (1.11, 3.18)). No other significant associations were found. Sensitivity analyses yielded similar findings.

Conclusions In this selected sample with a preponderance of grade ≥1 Hoffa- and/or effusion-synovitis on non-contrast MRI, only prolonged kneeling associated with Hoffa-synovitis prevalence. Replication in other samples is warranted.

SIGNIFICANCE AND INNOVATION

- In this sample of people at risk and with definite knee OA and the majority presenting with grade ≥1 synovitis on non-contrast MRI, participation in kneeling for 30 minutes or longer was significantly associated with a greater likelihood of ≥grade 1 Hoffa-synovitis.
- Specifically, participants who kneeled one day per week or less had significantly greater odds of Hoffa-synovitis prevalence compared with those reporting no such activity.
- No associations were found for stair climbing, squatting, heavy lifting or getting in/out of a squatting position and Hoffa-synovitis prevalence nor did any of the knee bending activities showed a significant association with effusion-synovitis prevalence.
- Sensitivity analyses utilizing a more restrictive cut-off to define synovitis prevalence (grade ≥2) and reducing interference from potential misclassification errors, yielded similar findings.

INTRODUCTION

Repetitive knee bending is a well-recognized risk factor of knee osteoarthritis (OA). Frequent squatting, kneeling and heavy lifting have been shown to increase the likelihood of worse cartilage defects both in men with symptomatic knee OA and healthy women.(1, 2) Although cartilage loss and radiographic disease severity are typically monitored ascertaining disease progression, synovial inflammation or synovitis has gained interest as a hallmark feature of OA pathogenesis.

Synovitis is common in knee OA, manifests across all stages of the disease and likely also acts as a precursor of disease rather than just a consequence of underlying structural damage.(3) That is, low-grade systemic inflammation and activation of synovial macrophages may also be induced by the metabolic syndrome, a comorbidity prevalent amongst people with knee OA.(4) In an exploratory study of 100 people with knee OA, however, Roze et al.(4) suggested that Hoffa-

synovitis as detected on non-contrast magnetic resonance imaging (MRI) was more prevalent in participants who were lean and physically active than in those with the metabolic syndrome. Additionally, effects of moderate-intensity knee bending loads, or exercise therapy, on inflammatory wet biomarkers appeared variable in people at risk or with knee OA.(5, 6) Thus, it remains unclear whether, and to what extent, repetitive knee bending is associated with the prevalence of synovitis in people at risk or with knee OA.

The purpose of this study was to investigate the association between repetitive knee bending and the prevalence of synovitis in people at risk and with definite knee OA.

MATERIALS AND METHODS

Study design

We conducted a cross-sectional analysis with baseline data from the Foundation for the National Institutes of Health (FNIH) Osteoarthritis Biomarkers Consortium project.(7, 8) This project investigated biomarkers of knee OA progression over 48 months in a nested case-control design utilizing public data and images from the Osteoarthritis Initiative (OAI).(7) Briefly, 600 participants were selected from the OAI cohort and grouped based on whether persistent pain and/or radiographic disease progression had occurred in the index knee, with one index knee identified per subject. A pre-specified number of participants was selected across strata and frequency-matched for radiographic disease severity and body mass index. (Figure 1)

Participants

The OAI is a multi-center observational cohort study of knee OA consisting of males and females between 45 and 79 years old, including all ethnic minorities and subdividing participants into 3 sub-cohorts; the progression sub-cohort with symptomatic tibiofemoral OA (n=1390), the incidence sub-cohort at risk of OA (n=3284), and a non-exposed control group (n=122). Main exclusion criteria were the presence of inflammatory arthritis, contra-indications to 3Tesla MRI and bilateral end-stage knee OA. The detailed eligibility criteria for each of the sub-cohorts can be consulted elsewhere (https://data-archive.nimh.nih.gov/oai/). To qualify for the FNIH sub-study in particular, participants had at least one knee with a Kellgren-Lawrence grade of 1, 2 or 3 at baseline and complete data at all relevant time points. This included biochemical as well as imaging biomarker data such as knee radiographs and MR images suitable for analysis, and clinical data.(7) Participants were excluded from the FNIH dataset if they had (i) knee/hip replacements or metallic bone implants from baseline to 24 months, (ii) minimum medial joint space width of <1.0mm and/or Western Ontario McMasters Universities Osteoarthritis Index (WOMAC) pain score of >91 (0-100 scale) at baseline indicating ceiling effects of disease progression, (iii) radiographic and pain progression by the 12 month follow-up, (iv) predominant lateral joint space narrowing at baseline or during follow-up, and (v) insufficient follow-up times to ascertain persistent pain progression.(7) Finally, from a total of 600 participants in the FNIH project selected as such, we retained 594 participants with complete data on knee bending activities (99% of the original FNIH sample) for the present analyses.

MRI

The OAI consortium used 3 Tesla MRI Trio systems (Siemens Healthcare, Erlangen, Germany). The pulse sequences consisted of sagittal and coronal intermediate-weighted turbo spin-echo sequences, a sagittal 3D dual-echo in the steady state sequence with water excitation, and the axial

and coronal multi-planar reformats of the latter.(7) The semi-quantitative MRI Osteoarthritis Score (MOAKS) system was implemented to grade the severity of Hoffa- and effusion-synovitis, as surrogate outcomes of synovial thickening or synovitis.(9) Images were read sequentially by two experienced musculoskeletal radiologists not blinded to time points, but unaware of clinical characteristics and disease progression status.(7, 9)

Hoffa-synovitis was evaluated ascertaining the presence of signal alterations in the intercondylar region of the Hoffa's fat pad and scored from 0 (normal) to 3 (severe). Similarly, the degree of effusion-synovitis was determined estimating the distention of the synovial cavity, with grade 0 representing a normal physiologic amount of joint effusion and grade 3 a large effusion with evidence of capsular distention.(9) Intra-rater and inter-rater reliability for Hoffa-synovitis have been reported to both equal a weighted kappa of 0.68 (95% CI 0.38, 0.99) whilst reliability estimates for effusion-synovitis attained 0.95 (95% CI 0.61, 1.00) and 0.91 (95% CI 0.57, 1.00), respectively.(7, 8) We used a grade ≥1 cut-off to define Hoffa- and/or effusion-synovitis prevalence as well as a more restrictive cut-off of grade ≥2 to reduce interference from potential misclassification errors in sensitivity analyses.(8)

Repetitive knee bending

Occupational and non-occupational knee bending activities were queried at enrollment using a standard questionnaire adapted from the literature.(10) Questions assessed whether participants had performed the following activities over the past 30 days and during a single day (yes/no): (i) taking a flight of stairs ≥10 times, (ii) kneeling for ≥30 minutes, (iii) squatting or deep knee bending ≥30 minutes, (iv) lifting or moving weights of ≥25 pounds, and (v) getting in or out a squatting position ≥10 times. Additionally, the frequency by which each activity occurred in a typical week was

categorized as “none”, “one day per week or less”, “2-3 days per week”, “4-5 days per week”, or “(nearly) every day”.

Participant characteristics

Data of age, sex, radiographic disease severity, physical activity level, knee pain severity, and metabolic syndrome were collected at screening or enrollment using standardized measurements and/or questionnaires. Specifically, we used scores from the Physical Activity Scale for the Elderly assessing the level of physical activity as well as from the knee-specific WOMAC pain subscale reporting knee pain. Finally, as per Roze et al.(4), the International Diabetes Federation diagnostic criteria were used to generate a surrogate marker for the metabolic syndrome. Participants with signs of central obesity (abdominal circumference of 88 cm in women and 102 cm in men and/or a body mass index of >30 kg/m^2), were classified as having metabolic syndrome if at least any two of the following criteria were also present: (i) drug treatments for raised triglycerides, (ii) drug treatments for cholesterol abnormalities, (iii) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or anti-hypertensive drug treatments, (iv) type 2 diabetes and/or treatment, as per the Charlson Comorbidity Index.

Statistical analysis

Descriptive statistics were calculated, and baseline comparability assessed using chi-square tests (for categorical variables) and independent *t* test (for continuous variables) as appropriate.

To investigate the association between engagement in, and frequency of, knee bending activities (exposures) and either the prevalence of Hoffa- or effusion-synovitis (outcomes), unadjusted and adjusted multi-variate logistic regression was performed calculating crude and adjusted odds ratios (OR) and 95% confidence intervals (CI) accordingly. Analyses were adjusted for presence of metabolic syndrome, physical activity level and sex as potential confounders. Confounders were selected considering causal diagrams as well as changes in ORs of the exposure variables when adding confounders separately to the models. The Hosmer-Lemeshow test was implemented to evaluate model calibration ($p>0.05$). Sensitivity analyses were performed utilizing an alternative definition of synovitis prevalence (≥grade 2) according to a similar statistical approach. All analyses were performed in Stata 15.1 (Stata Corp, TX, USA) with level of significance set at $p<0.05$.

RESULTS

Participants were 61.5 (± 8.9) years old and 59% (n=348) were female. Approximately 60% (n=364) had evidence of radiographic tibiofemoral OA and features of metabolic syndrome appeared common (n=490, 83%). Similarly, presence of grade ≥1 Hoffa-synovitis (n=353, 59%) and/or effusion-synovitis (n=366, 62%) was established in two thirds of the sample. Whilst stair climbing (n=352, 59%) and heavy lifting (n=414, 70%) were frequently performed, only up to one quarter on average reported squatting (n=82, 14%), kneeling (n=151, 25%) or getting in/out of a squatting position (n=160, 27%). Participants with effusion-synovitis exhibited significantly worse WOMAC pain ($p=0.007$) and greater proportion of definite knee OA ($p=0.042$) compared with those without effusion-synovitis, whilst no such differences were established between participants with and without Hoffa-synovitis. (Table 1)

Hoffa-synovitis

Amongst people with Hoffa-synovitis (n=353), the majority (n=301, 85%) was assigned mild grade 1 Hoffa-synovitis. Of all activities studied, kneeling for ≥30 minutes was associated with grade ≥1 Hoffa-synovitis prevalence, both in unadjusted and adjusted analyses.(Table 2) Adjusted for confounders, kneeling was associated with 65% greater odds of Hoffa-synovitis (OR (95% CI): 1.65 (1.11, 2.47), p=0.014). When compared with participants who did not kneel for ≥30 minutes during a single day, participants who had engaged in this activity one day or less per week had significantly greater odds for prevalent Hoffa-synovitis on MRI (adjusted OR (95% CI): 1.88 (1.11, 3.18), p=0.018). No other significant associations were found between frequency of knee bending activities and Hoffa-synovitis prevalence (data not shown). Sensitivity analyses yielded similar findings.(Supplementary Table 1)

Effusion-synovitis

Of the participants with prevalent effusion-synovitis (n= 366), 68% (n=249) presented with small grade 1 effusion. There were no significant associations between any of the knee bending activities and prevalence of effusion-synovitis, either in unadjusted or adjusted analyses.(Table 2) Frequency of knee bending activities also did not significantly associate with prevalence of effusion-synovitis (data not shown). Results remained unchanged in sensitivity analyses. (Supplementary Table 1)

DISCUSSION

In people at risk and with knee OA and a considerable proportion presenting with surrogate markers of synovitis on non-contrast MRI, we found that kneeling for at least 30 minutes during a single day was the only knee bending activity to associate with a greater likelihood of grade ≥1 Hoffa-synovitis.

To our knowledge we were the first to investigate the association between specific knee bending activities and synovitis prevalence in a relatively large sample of knee OA. Our observation partly agrees with Roze et al.(4) showing a greater prevalence of Hoffa-synovitis in active and lean people with knee OA than in those with metabolic syndrome. Although prolonged kneeling associated with a surrogate MRI outcome of synovitis, Hoffa-synovitis readings in particular are known to be non-specific also portraying other pathologies, such as e.g. Hoffa disease.(9) Indeed, knee bending beyond 90° of flexion causes increased pressures within the infra-patellar (Hoffa) fat pad.(11) Thus, prolonged deep knee flexion during kneeling may have induced fat pad inflammation increasing signal on fluid-sensitive MRI.(9, 12) Although crosstalk between the infra-patellar fat pad and cartilage/synovium likely exists furthering inflammatory processes in OA, we cannot conclusively discern synovitis from Hoffa-disease due to the lack of contrast-enhanced imaging or biopsy.(9, 12) Furthermore, semi-quantitative assessments of Hoffa-synovitis are also known to be less reliable than measurements of effusion-synovitis.(8, 9) Given it is challenging to dissociate grade 0 from grade 1 synovitis,(8) it is possible analyses were prone to misclassification errors (likely independent from exposure status) and may have underestimated, rather than overestimated, associations observed. Notably, however, reliability estimates from the FNIH sub-study were improved compared with previous endeavors (8, 9) and sensitivity analyses revealed similar findings overall.

Kneeling for one day or less per week increased the likelihood of Hoffa-synovitis prevalence compared with no such activity at all. Whilst only few participants (n=70, 12%) indicated prolonged kneeling for more than 1 day per week, one may argue that a risk of misclassification existed, particularly between categories indicating engagement for one day per week or less or none at all. Although impossible to clearly apprehend the extent of such errors, the probability of misclassification was unlikely conditional on synovitis prevalence. Nevertheless, bias of this nature, if any, may have exaggerated the respective effect estimate. Replication in other samples is needed to better understand the relationship between knee bending frequency and synovitis prevalence.

We were unable to support any other associations between knee bending activities and the prevalence of either Hoffa-synovitis or effusion-synovitis. Our findings agree with a study by Helmark et al.(5) reporting that, in 11 people with knee OA, no changes were observed in synovial fluid concentrations of pro-inflammatory cytokines following a moderate-intensity weight-bearing knee bending exercise. Indeed, depending on the duration and type of muscle contractions as well as the amount of activated muscle mass, quadriceps muscle contractions, as required during knee bending activities, may induce a significant release of muscle IL-6 with a net anti-inflammatory, rather than pro-inflammatory, effect as a result.(13)

Our results overall suggest that knee bending may not play a significant role in synovitis prevalence in people at risk and with knee OA. Yet, issues of selection bias should be considered when interpreting these findings. Indeed, we analyzed baseline data from the FNIH sub-study, a selected sample drawn from the OAI cohorts. Briefly, participants with severe joint space narrowing and high levels of pain at baseline were excluded from the study. Firstly, this may partly explain the relatively small proportion of people with moderate and severe synovitis on MRI as well as our inability to establish significant differences in pain severity between people with and without Hoffa-synovitis. Secondly, selection as such may have indirectly influenced the extent to which people engaged in knee bending and exhibited synovitis on MRI. Notably, however, 75% (n=441) of the current sample reported ≥1 knee bending activity over the past 30 days, similar to that of the main OAI cohort serving as a model for the target population of people at risk and with knee OA (73%, n=3460). Additionally, the current prevalence of Hoffa- and effusion-synovitis (59% and 62, respectively) lies within ranges reported previously using data from cohorts other than the OAI that investigated people at risk (8-11%)(14) or with symptomatic knee OA (69-79%)(15). However, exploration of our data revealed that 63% and 57% of the people at risk of knee OA presented with Hoffa- and effusion-synovitis (data not shown), respectively, much higher than previously reported.(14, 15) Partly due to

our definition of synovitis prevalence (grade ≥1) prone to misclassification errors, it may indeed be argued that people without synovitis were under-sampled potentially attenuating associations investigated. Notably, sensitivity analyses utilizing a grade ≥2 cut-off for synovitis prevalence led to increased proportions of people without synovitis and generally greater effect size estimates but with similar findings overall. Finally, due to availability of relevant data, we, as well as others (4), implemented a proxy definition for the presence of the metabolic syndrome potentially underestimating its true impact in the associations under study.(4)

In conclusion, in people at risk and with definite knee OA and a preponderance showing grade ≥1 Hoffa- and/or effusion-synovitis on non-contrast MRI, only kneeling for at least 30 minutes during a single day was associated with a greater likelihood of Hoffa-synovitis. As this was a selected sample, replication is warranted to better understand the role of repetitive knee bending in synovitis prevalence.

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FIGURE LEGENDS

Figure 1. Participant Flow Diagram. Adapted from Osteoarthritis Biomarkers Consortium FNIH Project: Study Design version 1.0

Table 1. Participant characteristics. Data are presented as n (%) unless stated otherwise.

	All n=594	No Hoffa-Synovitis (grade ≥1) n=241	Hoffa-Synovitis (grade ≥1) n=353	No Effusion-Synovitis (grade ≥1) n=228	Effusion-Synovitis (grade ≥1) n=366
Demographics and symptoms					
Age (yrs), mean ± SD	61.5 ± 8.9	60.8 ± 9.1	62.0 ± 8.7	61.2 ± 8.7	61.8 ± 9.0
Sex (% females)	348 (59%)	149 (62%)	199 (56%)	127 (56%)	221 (60%)
WOMAC pain (0-20), mean ± SD[2]	2.4 ± 3.1	2.12 ± 2.85	2.60 ± 3.28	1.97 ± 2.84	2.68 ±3.26 [b]
Metabolic syndrome	490 (83%)	203 (84%)	287 (81%)	181 (79%)	309 (84%)
Body Mass Index (kg/m^2), mean ± SD	30.7 ± 4.8	31.0 ± 4.7	30.5 ± 4.8	30.5 ± 4.8	30.9 ± 4.8
Structural parameters					
KL grade ≥2	364 (61%)	155 (64%)	209 (59%)	128 (56%)	236 (65%)[c]
Hoffa-synovitis					
- Grade 0	241 (41%)	241 (100%)	0 (0%)[a]	117 (51%)	124 (34%)[c]
- Grade 1	301 (51%)	0 (0%)	301 (85%)[a]	104 (46%)	197 (54%)[c]
- Grade 2	47 (8%)	0 (0%)	47 (13%)[a]	7 (3%)	40 (11%)[c]
- Grade 3	5 (1%)	0 (0%)	5 (1%)[a]	0 (0%)	5 (1%)[c]
Effusion-synovitis					
- Grade 0	228 (38%)	117 (49%)	111 (31%)[a]	228 (100%)	0 (0%)[c]
- Grade 1	249 (42%)	102 (42%)	147 (42%)	0 (0%)	249 (68%)[c]
- Grade 2	97 (16%)	21 (9%)	76 (22%)[a]	0 (0%)	97 (27%) [c]
- Grade 3	20 (3%)	1 (0%)	19 (5%)[a]	0 (0%)	20 (6%)[c]
Knee bending and physical activity					
Engaged in ≥1 frequent knee bending activity	441 (75%)	174 (73%)	267 (76%)	168 (74%)	273 (75%)
Stair climbing (≥10 flights)[1]	352 (59%)	141 (59%)	211 (60%)	140 (61%)	212 (58%)
- none	242 (41%)	100 (42%)	142 (40%)	88 (39%)	154 (42%)
- 1 day per week or less	20 (3%)	7 (3%)	13 (%)	4 (2%)	16 (4%)
- 2-3 days per week	54 (9%)	25 (10%)	29 (%)	21 (9%)	33 (9%)
- 4-5 days per week	49 (8%)	21 (9%)	28 (8%)	18 (8%)	31 (9%)
- (nearly) every day	229 (39%)	88 (37%)	141 (40%)	97 (43%)	132 (36%)

Kneeling (≥30 minutes)[1]	151 (25%)	47 (20%)	104 (30%)[a]	63 (28%)	88 (24%)
- none	443 (75%)	194 (81%)	249 (71%)[a]	165 (72%)	278 (76%)
- 1 day per week or less	81 (14%)	23 (10%)	58 (16%)[a]	33 (15%)	48 (13%)
- 2-3 days per week	37 (6%)	12 (5%)	25 (7%)[a]	14 (6%)	23 (6%)
- 4-5 days per week	14 (2%)	7 (3%)	7 (2%)[a]	6 (3%)	8 (2%)
- (nearly) every day	19 (3%)	5 (2%)	14 (4%)[a]	10 (4%)	9 (3%)
Squatting (≥30 minutes)[1]	82 (14%)	29 (12%)	53 (15%)	30 (13%)	52 (14%)
- none	512 (86%)	212 (88%)	300 (85%)	198 (87%)	314 (86%)
- 1 day per week or less	33 (6%)	10 (4%)	23 (7%)	11 (5%)	22 (6%)
- 2-3 days per week	34 (6%)	13 (5%)	21 (6%)	14 (6%)	20 (6%)
- 4-5 days per week	8 (1%)	4 (2%)	4 (1%)	3 (1%)	5 (1%)
- (nearly) every day	6 (1%)	2 (1%)	4 (1%)	2 (1%)	4 (1%)
Lifting/moving objects of ≥25 pounds[1]	414 (70%)	161 (67%)	253 (72%)	164 (72%)	250 (68%)
- none	180 (30%)	80 (33%)	100 (28%)	64 (28%)	116 (32%)
- 1 day per week or less	132 (22%)	54 (22%)	78 (22%)	50 (22%)	82 (22%)
- 2-3 days per week	152 (26%)	65 (27%)	87 (25%)	58 (25%)	94 (26%)
- 4-5 days per week	61 (10%)	19 (8%)	42 (12%)	26 (11%)	35 (10%)
- (nearly) every day	69 (12%)	23 (10%)	46 (13%)	30 (13%)	39 (11%)
Getting in/out squatting position ≥10 times[1]	160 (27%)	60 (25%)	100 (28%)	60 (26%)	100 (27%)
- none	434 (73%)	181 (75%)	253 (72%)	168 (74%)	266 (73%)
- 1 day per week or less	39 (7%)	16 (7%)	23 (7%)	10 (4%)	29 (8%)
- 2-3 days per week	64 (11%)	22 (9%)	42 (12%)	28 (12%)	36 (10%)
- 4-5 days per week	32 (5%)	15 (6%)	17 (5%)	12 (5%)	20 (6%)
- (nearly) every day	25 (4%)	7 (3%)	18 (5%)	10 (4%)	15 (4%)
Physical activity score (0-400), mean ± SD[3]	163.9 ± 83.0	159.8 ± 84.1	166.6 ± 82.3	165.5 ± 79.7	162.8 ± 85.2

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. KL: Kellgren-Lawrence grade.

[1]Participation in knee bending activity during a single day, over the past 30 days.

[2]Higher scores indicate worse pain

[3]Higher scores indicate greater physical activity levels

[a]significantly different at p<0.05 compared with participants without Hoffa-synovitis in a chi-square test.

[b]significantly different at p<0.05 compared with participants without Effusion-synovitis in an independent t test.

[c]significantly different at p<0.05 compared with participants without Effusion-synovitis in a chi-square test.

Table 2. Association between knee bending activities and prevalence of Hoffa-synovitis (grade ≥1) and effusion-synovitis (grade ≥1). Data are presented as odds ratios (OR) and 95% confidence intervals (CI: lower bound, upper bound), unadjusted and adjusted for confounders. Model fit is expressed using the p-value from the Losmer-Hemeshow test (LH-test)

	Unadjusted OR (95% CI)	Adjusted[1] OR (95% CI)	LH-test
Hoffa-synovitis			
Stair climbing ≥10 flights[2]	1.05 (0.76, 1.47)	1.01 (0.72, 1.41)	0.58
Kneeling ≥30 minutes[2]	1.72 (1.16, 2.55)[a]	1.65 (1.11, 2.47)[a]	0.95
Squatting ≥30 minutes[2]	1.29 (0.79, 2.09)	1.23 (0.75, 2.01)	0.62
Lifting/moving objects of ≥25 pounds[2]	1.26 (0.88, 1.79)	1.17 (0.80, 1.70)	0.50
Getting in/out squatting position ≥10 times[2]	1.19 (0.82, 1.73)	1.13 (0.76, 1.67)	0.49
Effusion-synovitis			
Stair climbing ≥ 10 flights[2]	0.87 (0.62, 1.21)	0.90 (0.64,1.27)	0.83
Kneeling ≥30 minutes[2]	0.83 (0.57,1.21)	0.87 (0.60, 1.27)	0.92
Squatting ≥ 30 minutes[2]	1.09 (0.67,1.77)	1.15 (0.70, 1.88)	0.86
Lifting/moving objects of ≥25 pounds[2]	0.84 (0.58, 1.21)	0.89 (0.61, 1.31)	0.93
Getting in/out squatting position ≥10 times[2]	1.05 (0.72, 1.53)	1.13 (0.76, 1.68)	0.89

[1]Adjusted for presence of metabolic syndrome, physical activity level, and sex.

[2] Participation in knee bending activity during a single day, over the past 30 days.

[a] Significant at $p<0.05$.