



Kneeling as a risk factor of patellofemoral joint cartilage damage worsening: an exploratory analysis on the Osteoarthritis Initiative

Arya Haj-Mirzaian^{1,2} · Bahram Mohajer¹ · Ali Guermazi³ · Frank W. Roemer^{3,4} · Bashir Zikria⁵ · Shadpour Demehri¹

Received: 10 June 2020 / Revised: 21 August 2020 / Accepted: 22 September 2020 / Published online: 2 October 2020

© European Society of Radiology 2020

Abstract

Objectives To determine whether kneeling activity is associated with the MRI measures of patellofemoral (PF) joint cartilage damage worsening in subjects with/without patella alta (PA).

Methods Baseline and 24-month 3-T MR images and semi-quantitative MRI Osteoarthritis Knee Score (MOAKS) of PF joint of 600 subjects from the FNIH study, a nested study within the Osteoarthritis Initiative (OAI), were extracted. At baseline visit, subjects were asked how many days per week they participated in kneeling activities lasted ≥ 30 min. Insall-Salvati ratio (ISR) (patellar tendon/patellar height) was measured on baseline MRIs by a musculoskeletal radiologist; $ISR \geq 1.3$ was considered PA. Regression analysis adjusted for confounding variables was used to assess the impact of kneeling on worsening of MOAKS cartilage over 24 months. The potential moderating effect of PA was evaluated using adjusted regression analysis.

Results Six hundred subjects (58.8% female, years, $BMI = 30.7 \pm 4.8$ kg/m²) were included; 13.7%, 6.2%, and 5.5% of participants reported 1 day, 2–5 days, and ≥ 6 days of kneeling activities per week. A higher frequency of kneeling activity was associated with the increased risk of MOAKS cartilage score worsening (adjusted OR (95% CI): 2.33 (1.08–5.06)). Stratification analysis showed that only ≥ 6 days/week of kneeling activities was associated with the worsening of MOAKS cartilage scores (2.74 (1.03–7.27)). When we included the presence of PA in regression models, the OR (95% CI) for the association between kneeling and PF cartilage damage will decrease to 1.26 (0.78–2.04), suggesting the potential role of PA as the moderator variable.

Conclusion Extensive kneeling activity (≥ 6 days/week) may be associated with the MRI-based worsening of PF cartilage damage, specifically in subjects with an underlying patella alta.

Key Points

- Frequent daily kneeling activity is associated with a higher risk of patellofemoral cartilage damage resulting in patellofemoral osteoarthritis.
- The cartilage damage associated with extensive kneeling activity may be worse in subjects with an underlying patella alta (i.e., high-riding patella).

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00330-020-07337-z>) contains supplementary material, which is available to authorized users.

Keywords Patellofemoral joint · Magnetic resonance imaging · Cartilage · Osteoarthritis

✉ Arya Haj-Mirzaian
arya.mirzaian@gmail.com

¹ Russell H. Morgan Department of Radiology, Johns Hopkins University, Baltimore, MD, USA

² Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, 601 N Caroline St, JHOC 5165, Baltimore, MD 21287, USA

³ Department of Radiology, Boston University School of Medicine, Boston, MA, USA

⁴ Department of Radiology, University of Erlangen-Nuremberg, Erlangen, Germany

⁵ Department of Orthopaedic Surgery, Johns Hopkins University, Baltimore, MD, USA

Abbreviations

BMI	Body mass index
DMOADs	Disease-modifying OA drugs
FNIH	Foundation for the National Institute of Health study participants
JSN	Joint space narrowing
MOAKS	MRI Osteoarthritis Knee Score
OAI	Osteoarthritis Initiative
PA	Patella alta
PF	Patellofemoral

Introduction

A growing body of evidence has pointed out the clinical importance of patellofemoral (PF) osteoarthritis (OA), with a prevalence of ~25% among the adult population worldwide, and one of the leading causes of knee pain and disability [1–4]. Despite the high clinical importance and prevalence, the main risk factors of PF OA and impact of physical activities on the incidence/progression of this medical condition have not been comprehensively assessed [5–7].

A few studies reported an increased risk of tibiofemoral knee OA progression due to prolonged knee-bending activities. Among these activities, a causal relationship was observed between certain occupational activities that involve excessive kneeling with structural worsening of tibiofemoral OA [8–13]. However, it is doubtful whether the kneeling activity can be associated with the increased risk of PF OA progression as well. A limited number of researches have focused on this question with an overall conflicting finding. Among these studies, a few reports suggested a higher chance of having PF OA in subjects with frequent kneeling [8], whereas, others found no significant association between kneeling activity and PF OA development [9]. Moreover, all previous studies were performed using the cross-sectional design and defined their exposure as the general knee-bending activities including climbing, squatting, and kneeling (rather than only kneeling activity) [8–11]. Furthermore, the development of PF OA was mainly assessed using a knee radiograph which is not sensitive to early and subtle OA-related structural damage worsening [8–11]. Magnetic resonance imaging (MRI) has gained much attention in OA research as it provides a unique opportunity to study early changes of PF OA-related structural damages.

Several reports demonstrated that PF morphology abnormalities including patella alta (PA) as significant predictors of PF OA development [14]. PA is defined as a high-riding patella relative to the trochlear groove, which may result in the instability of the PF joint during knee extension and flexion movements [15, 16]. High-riding patella reduces the contact area between the patella and trochlea during knee motion. It can lead to increased articular surface contact pressure which subsequently may result in PF OA [17–19]. The Insall-Salvati ratio (ISR) is a validated measurement to determine PA using sagittal-plane MRI, CT, or lateral knee radiograph [20, 21]. Due to the relationship between the PA and biomechanical loading during knee motion as well as its relation to PF OA, it can be hypothesized that the presence of PA might mediate the association between PF OA development and excessive kneeling activities.

The Osteoarthritis Initiative (OAI) cohort provides the opportunity to evaluate the potential impact of kneeling activity on PF OA-related cartilage damage worsening. This study aims to assess whether kneeling activity is associated with

the worsening of MRI measures of PF cartilage damage in subjects with and without PA. Understanding how frequent kneeling activity may affect PF joint might provide further insights into the pathogenesis and primary prevention strategies for PF OA.

Methods

Study population

The OAI is an ongoing multicenter cohort of 4796 subjects with or at risk of knee OA (for details: <https://www.niams.nih.gov/grants-funding/funded-research/osteoarthritis-initiative>). The OAI is a HIPAA-compliant study and has been approved by the institutional medical ethics review boards of the OAI centers (approval number: 10-00532).

We used the data from the Foundation for the National Institute of Health (FNIH) OA biomarker consortium project in this study. The FNIH is a nested case-control of 600 subjects within the OAI. The FNIH study was primarily designed to assess the role of baseline/24-month knee MRI findings in predicting 48-month symptomatic/radiographic knee OA progression (for details: <https://oai.epi-ucsf.org/datarelease/FNIH.asp>). FNIH biomarker consortium data contains MRI-based OA-related structural damage measurements for PF joint and provides the opportunity to study risk factors of PF OA. In the present study, we included all participants of the FNIH project (one index knee per subject). Demographic characteristics of included participants (age, sex, body mass index (BMI)), the frequency/duration of kneeling activity, 3-T MRI of knee, and MRI-based measurements were extracted and assessed at baseline and 24 months. The timeline of the study is presented in Fig. 1.

Magnetic resonance imaging pulse sequence protocols

MRI was performed using the same 3-T scanners at four OAI site centers (Trio, Siemens Healthcare). Briefly, the MRI protocol included sagittal three-dimensional (3D) dual-echo at steady state (DESS), a coronal two-dimensional (2D) intermediate-weighted (IW) turbo spin-echo (TSE), sagittal IW fat-saturated TSE sequences, and coronal and axial multiplanar reformations of the 3D DESS [22, 23].

Semi-quantitative assessment of patellofemoral joint

OA-related cartilage damage worsening in PF joints was scored by two experienced musculoskeletal radiologists (A.G. and F.W.R.; with 16 and 14 years of experience) using the validated MRI Osteoarthritis Knee Scoring (MOAKS) method, which is a semi-quantitative scoring system of OA-

related features [23, 24]. MOAKS cartilage scores (cartilage surface and full-thickness scores) were evaluated in the patellar and trochlear regions (medial and lateral; 4 subregions total). Cartilage surface area and extent of full-thickness articular damage were determined using the same scale, where 0 was the absence of any damage, and 1, 2, and 3 showed damages involving < 10%, 10–75%, and > 75% of cartilage surface or full-thickness areas, respectively (Fig. 2). Previous studies reported the intra-rater and inter-rater reliability of moderate-perfect (0.64–1.0) and moderate-strong (0.62–0.93) for MOAKS measures, respectively [23, 24].

To assess the worsening of cartilage damage, we used the worsening criteria defined by Runhaar et al [25]. Briefly, scores of cartilage were reported as worsened if interval (baseline to 24 months); increase was reported in surface and/or full-thickness damage scorings (Fig. 2). Minor within-grade changes were also considered worsening. A region was categorized into the worsening group if any of its subregions demonstrated worsening. We categorized knees with any worsening in cartilage damage into the PF cartilage worsening group.

Assessment of kneeling activity

At baseline visit, all FNIH subjects were asked, “How many days per week, you participated in the activities with kneeling ≥ 30 minutes?” Subjects reported the average frequency of their kneeling activities which last more than 30 min. All self-reported data were extracted from the OAI database and subjects were categorized into four groups of (A) controls, who had no kneeling activities during week; (B) 1 day of kneeling activities during week; (C) 2 to 5 days of kneeling activities during week; (D) frequent activity which is defined as 6 to 7 days of kneeling activities per week. It is pertinent to note that we followed the same concept of intention to treat (ITT) analysis and analyzed the results of our prospective study according to the study groups that were originally assigned at baseline visit. To minimize the possibility of attrition bias (i.e., changing frequency of kneeling activity over time), all clinical data regarding kneeling activity at 12-month

and 24-month visits were also extracted and compared with baseline data, which showed no significant difference.

Insall-Salvati ratio measurement

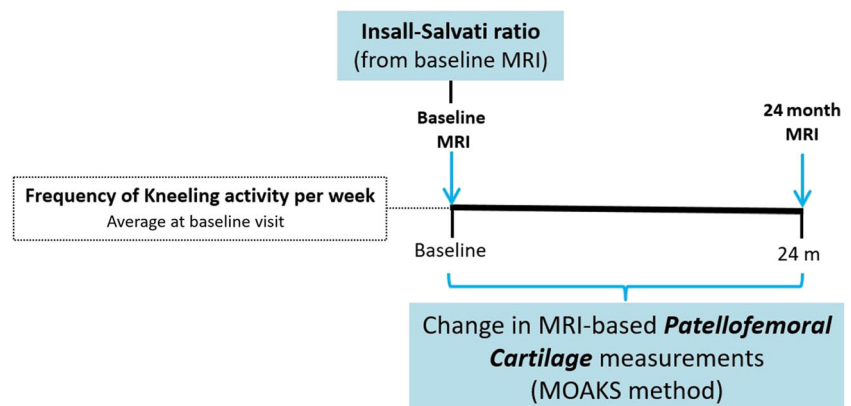
We calculated the ISR on MRI as the length of the patellar tendon (PT) divided by the height of the patella (PH) (PT/PH) (Fig. 2). We defined the length of PT as the distance between the inferior poles of the patella to the insertion of the patellar tendon to the tibial tuberosity. PH was measured using the sagittal plane with the greatest diameter of the patella [26].

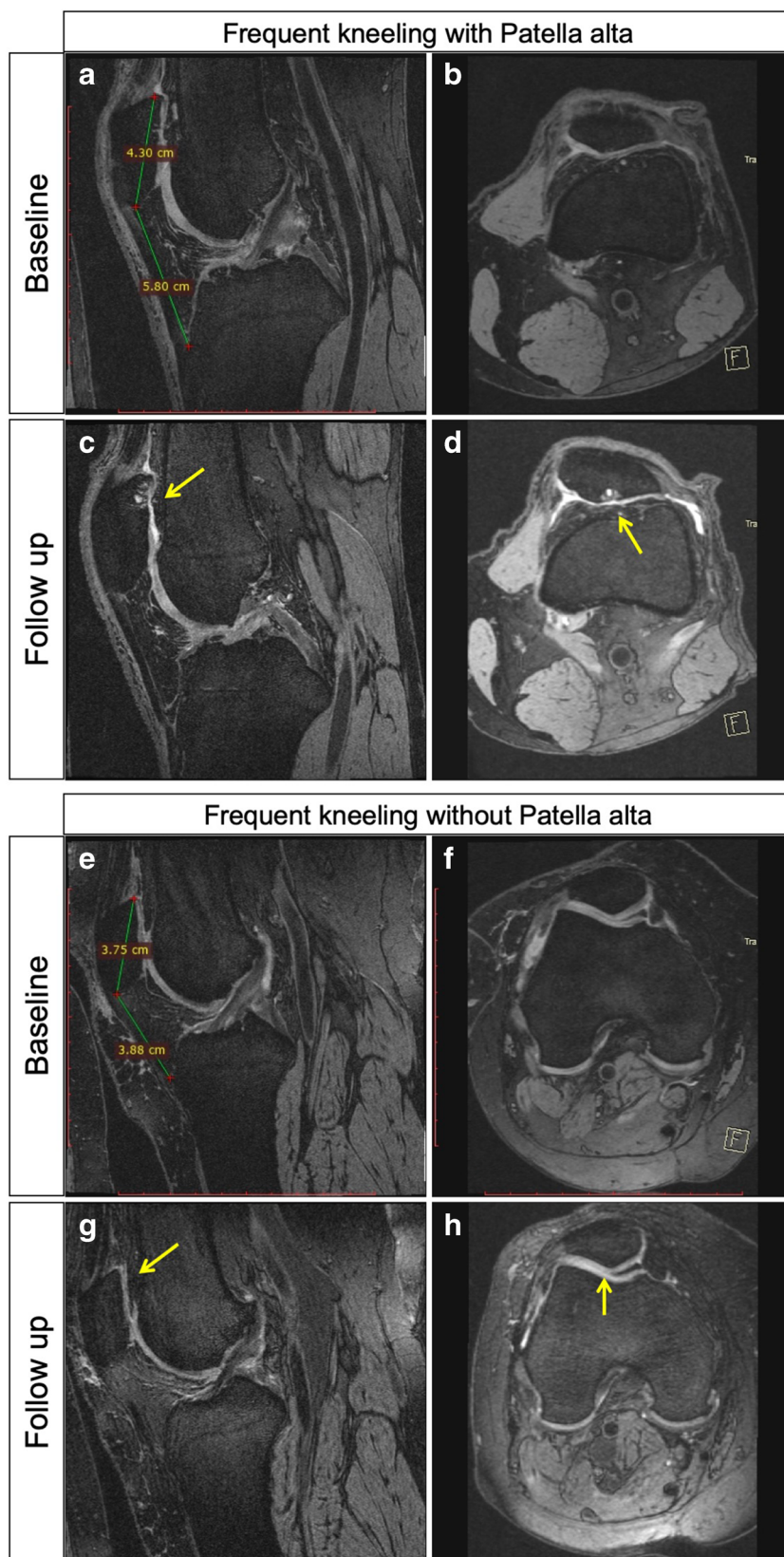
Two musculoskeletal radiologists (M.H. and C.S.) with more than 3 years of experience performed the measurements using baseline MRIs (sagittal MRIs, fully extended knees, IW fat-saturated TSE sequences); readers were blinded to the all outcomes. The intra-rater and inter-rater reliability of moderate-strong (0.6–0.85) for MRI-derived ISR were reported by previous studies [27]. Using MRI-derived ISR, knees were categorized into PA positive (+) with ISR of ≥ 1.3 and PA negative (-) group with ISR < 1.3 [26, 28].

Statistical analysis

Baseline characteristics were compared between the study groups using the ANOVA test (all normally distributed) and chi-square test. We assessed the association between the frequency of kneeling activities and longitudinal PF OA-related cartilage damage worsening (PF cartilage worsening) using a multivariable regression model. We defined the exposure as four grades of kneeling activities (groups A–D, explained earlier). We defined the outcomes as PF surface, full-thickness, or any cartilage worsening over 24 months (both for medial and lateral sides). We considered kneeling activity an “ordered categorical” variables with levels ranging from no kneeling activity to ≥ 6 days/week, and fitted the multivariable regression models. Then, to determine the kneeling level/threshold associated with the worsening of cartilage score, we fitted separate multivariate regression models with separate levels of kneeling activity (categories A–D, described above) as

Fig. 1 Timeline of the study. Before study: Average frequency of kneeling activity (≥ 30 min) per week was evaluated in all enrolled subjects. Baseline: Insall-Salvati ratio (ISR) measurement, baseline MRI assessments for patellofemoral osteoarthritis (OA) including MRI Osteoarthritis Knee Score (MOAKS). 24-month: follow-up MRI assessments of patellofemoral OA





exposure. We adjusted all models for potentially confounding variables including age, sex, and BMI in model 1 and additional adjustment for predefined radiographic progression in

the medial joint space narrowing (JSN) over 48-month follow-up of the FNIH study, in model 2. In order to assess the potential role of PA as the moderating variables, we

◀ **Fig. 2** Insall-Salvati ratio and MRI Osteoarthritis Knee Score (MOAKS) assessment in patients with frequent kneeling (≥ 6 days/week), with and without patella alta. Sagittal IW fat-saturated TSE sequence from the left knee MRI of a 59-year-old female with patella alta and frequent kneeling activity. **a** The Insall-Salvati ratio was measured by dividing the patellar tendon length by the length of the patella on baseline MRI, which is ≥ 1.3 . Baseline sagittal (**a**) and axial (**b**) MRI showed minimal-moderate PF cartilage defect with surface and full-thickness score of 2 (10–75% of cartilage surface and thickness involved) in semi-quantitative MRI Osteoarthritis Knee Score (MOAKS). Follow-up sagittal (**c**) and axial (**d**) MRI of the same patient at 24-month visit showing PF cartilage damage worsening for both surface and thickness scores. New subchondral bone marrow lesion is also detected on follow-up images. Baseline sagittal (**e**) and axial (**f**) IW fat-saturated TSE sequence right knee MRI of a 56-year-old female with frequent kneeling but without patella alta (Insall-Salvati ratio < 1.3) in baseline axial MRI (**e**). The 24-month follow-up, sagittal (**g**) and axial (**h**) MRI of the same patient showing no PF cartilage damage worsening in MOAKS scores

performed two sets of regression analyses which include the presence/absence of PA as a covariate. By comparing the results of each fully adjusted regression model, we aimed to assess whether the association between kneeling activity and PF OA is different between subjects with and without PA. We separately calculated odds ratios of 95% confidence interval (ORs 95% CI) of the association between the frequency of kneeling activities and 24-month PF cartilage worsening in each model with (+) and without (-) PA as a covariate. We used SPSS statistical software, version 24 and the R platform (v.3.2.5) to conduct analysis (easyreg and erl packages). Two-way *p* values lower than 0.05 were assumed to be statistically significant.

Results

The mean \pm standard deviation (SD) of age and BMI in enrolled FNIH subjects was 61.6 ± 8.9 and 30.7 ± 4.8 , respectively, and 58.8% of subjects were female. In all FNIH participants, 447 (74.5%) subjects had no kneeling activities during the week, whereas 82 (13.7%), 37 (6.2%), and 33 (5.5%) subjects reported less 1 day, 2–5 days, and ≥ 6 days of kneeling activities during the week, respectively. Table 1 shows the baseline characteristics of the study population. The analysis showed that a higher proportion of subjects with frequent kneeling activity are female (*p* value: 0.049). However, we detected no significant differences regarding the age and BMI between the study populations (Table 1).

Our analysis considering kneeling activity as an ordered categorical variable showed a significant association between the frequency of kneeling activity and cartilage damage worsening over 24 months (model 2 OR 95% CI of 2.33 (1.08–5.06)) (Table 2). Furthermore, multivariable regression model stratified for different levels of kneeling activity (model 2: adjusted for age, sex, BMI, and JSN progression) showed only

frequent kneeling activity, which was defined as ≥ 30 min of kneeling activities ≥ 6 days/week, and was associated with the higher odds of PF joint full-thickness (OR 95% CI of 2.95 (1.06–8.19)) and any cartilage worsening (OR 95% CI of 2.74 (1.03–7.27)) over 24 months when compared with subjects with < 6 days/week or no kneeling activities. Despite the trend, 2–5 days/week of kneeling activity was not associated with the worsening of PF cartilage damage worsening when compared with less kneeling activity (< 2 days/week) (Table 2). Assessment of each covariate in the models showed that progression in radiographic JSN is not significantly associated with the cartilage damage worsening (Supplementary Table 1).

The possible role of PA in moderating impact of kneeling activity on PF joint cartilage damage was assessed in the last part. Overall, 139 (23.2%) patients had PA on baseline MRI (i.e., ISR of ≥ 1.3). Results showed that PA+ patients were more female (66.2% of PA+ and 56.6% of PA- were female; *p* value = 0.049). However, no significant difference was observed between PA+ and PA- groups regarding age (PA+ mean age = 60.3 ± 8.5 , PA- = 61.9 ± 8.9 ; *p* value = 0.126) and BMI (PA+ mean BMI = 31.5 ± 5.0 , PA- = 30.5 ± 4.7 ; *p* value = 0.433). Two sets of regression models (1: without PA and 2: with PA as the covariate) were performed (Table 3). As noted above, regression analysis showed a significant association between frequent kneeling activity and PF joint cartilage damage worsening over 24 months (Tables 2 and 3). When we added the presence of PA as an additional variable to our model, the OR (95% CI) will significantly decrease to 1.26 (0.78–2.04) (Table 3). This result suggested the potential role of PA as the moderator variable.

Discussion

We showed that frequent kneeling activity is associated with an increased risk of PF joint cartilage damage worsening, especially in subjects with an underlying PA. We also quantified this risk factor and demonstrated that ≥ 6 days/week of ≥ 30 -min kneeling activities is associated with a higher risk of MRI-based PF cartilage damage worsening. Therefore, we could suggest that PA-positive subjects with obligated occupational or sport kneeling activity could reduce the frequency of their kneeling activity as a behavioral modification for primary prevention of PF OA.

Regarding the previously published study on this topic, Rytter et al showed that there are no significant differences regarding radiographic-based PF OA progression between occupations involving high versus low amount of kneeling activities [9]. Another study demonstrated that frequent generalized knee-bending activities (including but not limited to kneeling) are associated with the higher odds of having PF cartilage lesions worsening [8]. It should be noted that all

Table 1 Baseline characteristics of the study population

	Kneeling frequency (at least 30 min per week)				<i>p</i> value
	No kneeling	1 day or less	2–5 days	6–7 days	
Number (knees)	447	82	37	33	
Age (years)	61.6 ± 8.8	62.3 ± 9.3	62.1 ± 8.1	59.0 ± 9.9	0.334
Gender (% female)	281 (62.9%)	33 (40.2%)	17 (45.9%)	21 (63.6%)	<i>0.049</i>
BMI	31.0 ± 4.8	30.2 ± 4.4	29.6 ± 5.2	29.9 ± 5.4	0.149
Medial JSN narrowing in FNIH groups	219 (49.0%)	43 (52.4%)	27 (52.9%)	8 (42.1%)	0.805

Data were presented as mean ± standard deviation. Groups were compared using the ANOVA test or chi-square test. *BMI*, body mass index; *JSN*, joint space narrowing

Italicized number: *p* value < 0.05

these previous studies utilized a cross-sectional design, relied on radiographic measurements rather than MRI, and not focused on kneeling and its frequency/duration as a “potential dose-dependent and modifiable risk factor” for longitudinal PF OA progression [8–11].

Current treatment approaches for knee OA include palliative therapies with analgesics with no established protective

effects in slowing OA progression, and knee replacement surgery for end-stage disease. To date, existing treatments for knee OA demonstrated controversial or little disease-modifying efficacy, and no therapy can be labeled as disease-modifying OA drugs (DMOADs) [29, 30]. Therefore, it has been suggested to minimize the risk factors of knee OA, especially among the at-risk population, to prevent disease

Table 2 Frequency of kneeling activity and MRI-derived patellofemoral cartilage damage worsening over 24 months

	Number of days with ≥ 30-min kneeling in a week (an ordinal categorical variable)		
	OR (95% CI), <i>p</i> value	Adjusted 1	Adjusted 2
Worsening in cartilage MOAKS scores	Crude	Adjusted 1	Adjusted 2
Surface (medial/lateral)	1.19 (0.36–3.91), 0.774	1.13 (0.34–3.74), 0.841	1.14 (0.34–3.78), 0.829
Thickness (medial/lateral)	2.15 (0.94–4.97), 0.068	2.21 (0.95–5.12), 0.065	2.27 (0.98–5.27), 0.056
Any	2.28 (1.07–4.88), 0.033	2.29 (1.06–4.97), 0.035	2.33 (1.08–5.06), 0.032
	Kneeling 1 day or less per week vs. controls (no kneeling)		
	OR (95% CI), <i>p</i> value	Adjusted 1	Adjusted 2
Surface (medial/lateral)	0.47 (0.16–1.34), 0.156	0.57 (0.20–1.68), 0.309	0.54 (0.19–1.57), 0.259
Thickness (medial/lateral)	0.63 (0.29–1.37), 0.246	0.77 (0.35–1.71), 0.524	0.77 (0.35–1.71), 0.527
Any	0.62 (0.31–1.26), 0.189	0.81 (0.39–1.69), 0.578	0.75 (0.37–1.55), 0.438
	Kneeling 2–5 days per week vs. less kneeling or controls		
	Crude	Adjusted 1	Adjusted 2
Surface (medial/lateral)	1.09 (0.41–2.86), 0.869	1.20 (0.41–2.96), 0.854	1.18 (0.44–3.13), 0.747
Thickness (medial/lateral)	0.99 (0.43–2.28), 0.980	1.21 (0.51–2.84), 0.668	1.16 (0.49–2.71), 0.741
Any	1.17 (0.57–2.42), 0.675	1.25 (0.59–2.67), 0.557	1.34 (0.64–2.82), 0.435
	Kneeling 6–7 days per week vs. Less kneeling or controls		
	Crude	Adjusted-1	Adjusted-2
Surface (medial/lateral)	1.17 (0.26–5.18), 0.841	1.10 (0.24–5.04), 0.900	1.09 (0.24–4.91), 0.909
Thickness (medial/lateral)	2.87 (1.06–7.78), 0.038	2.99 (1.06–8.44), 0.039	2.95 (1.06–8.20), 0.038
Any	2.76 (1.056–7.17), 0.038	2.95 (1.08–8.07), 0.035	2.74 (1.03–7.27), 0.043

Association between the worsening of patellofemoral cartilage damages (worsening change in MOAKS cartilage surface and full-thickness variables over 24 months) and frequency of kneeling activity (days per week, 30 min or more in each day). Analyses were performed using multivariable logistic regression models. Adjustments are regarding age, sex, and body mass index (adjusted 1 as well as adjusted 2), and predefined progression in the joint space narrowing (JSN) in 48-month follow-up of the FNIH study. *OR*, odds ratio; *CI*, confidence interval; *MOAKS*, MRI Osteoarthritis Knee Score

Italicized numbers: *p* value < 0.05

Table 3 Role of patella alta in moderating impact of kneeling activity on longitudinal MRI-derived patellofemoral cartilage damage worsening

	Association with worsening of MOAKS cartilage scores (any worsening)	
	OR (95% CI), <i>p</i> value	
	Model 1 (without patella alta)	Model 2 (adjusted with patella alta)
Number of days with \geq 30 min kneeling in week (ordinal categorical variable)	2.35 (1.08–5.08), <i>p</i> :0.031	1.24 (0.77–2.02), <i>p</i> :0.376
	Model 1 (without patella alta)	Model 2 (adjusted with patella alta)
Kneeling 6–7 days per week vs. less kneeling or controls (binary variable)	2.78 (1.045–7.35), <i>p</i> :0.040	1.26 (0.78–2.04), <i>p</i> :0.346

Knees with Insall-Salvati ratio (patellar tendon/patellar height) of ≥ 1.3 in baseline MRI examinations were considered PA+. We separately calculated odds ratios of 95% confidence interval (ORs 95% CI) of the association between the frequency of kneeling activities and 24-month PF cartilage worsening in two adjusted regression models: with (model 1) and without (model 2) PA as a covariate. Regression models were also adjusted for age, sex, BMI, and JSN progression. The difference between the calculated ORs in the two models was assessed. Italicized numbers: *p* value < 0.05

progression. However, there are several issues in knee OA risk modifying and prevention. First, the main risk factors of knee OA, especially PF OA, were not established [31, 32]. For instance, the proven predictors of tibiofemoral OA, such as obesity and female gender, were not shown to be the main risk factors of PF OA [5–7]. Second, nearly all knee OA risk factors are non-modifiable. For instance, a large body of evidence demonstrated that older age, female gender, some races, positive family history of OA, presence of Heberden's node, etc. are significant predictors of knee OA (all are not modifiable). Among all these factors, obesity is the only one that can be labeled as a knee OA modifiable risk factor. Therefore, it has been recommended to all patients who are at risk or early-stages of knee OA, to reduce their BMI to prevent OA incidence and/or progression [33].

All taken together, due to the high importance of determining PF OA risk factors and applying behavioral modification, we aimed to evaluate the possible association between PF OA and frequency of kneeling activity, as the potential modifiable risk factor. Our results demonstrated that frequent kneeling activity (≥ 6 days/week of ≥ 30 min) is associated with an increased risk of PF cartilage damage worsening over 24 months. Therefore, for the first time, we introduced kneeling activity as a “potential dose-dependent and modifiable risk factor” for PF OA cartilage worsening. All subjects who are at-risk of PF knee OA worsening, especially patients with daily occupational or sport kneeling activities, could be recommended to reduce their kneeling activity to prevent PF OA worsening.

We also found a higher level of association between the frequent kneeling activity and PF OA in subjects with PA. High-riding patella in PA might lead to the lower contact area between patella and trochlea during knee bending, and prone subjects to PF OA development [17–19]. It should be noted that although PA can be easily measured using a lateral radiograph or CT scan, we used MRI in our study since this imaging is only available in the OAI dataset. Therefore, it can be

suggested to perform a lateral knee radiograph and evaluate the presence of PA in subjects with frequent kneeling activities and recommend them to reduce the frequency of their activities if evidence of PA is detected.

Several limitations existed in our study. First, the FNIH study outcomes were primarily designed based on tibiofemoral OA. We used available data of the FNIH study and performed ISR measurements. To minimize this limitation, we adjusted regression models for all known confounding variables. However, a more sophisticated analysis of cohort studies which is mainly designed to assess the main risk factors of PF OA should be performed in future works to confirm our initial observation. Second, the sample size and duration of follow-up may not be adequate, and the relationship between kneeling (especially in PA⁺ subjects) and PF OA needs to be further explored using more extensive databases with more extended follow-up data. Third, PF joint radiograph (lateral knee radiograph) and PF joint-specific symptom outcomes were not available using the OAI dataset. Therefore, PF joint cartilage damage and ISR were assessed using baseline and follow-up MR images of fully extended knees. Fourth, the frequency of kneeling activity was assessed at baseline visit which may lead to attrition bias since the frequency of activities varies over time. Considering the main concept of intention to treat analysis, we defined our exposed and non-exposed groups at baseline visit and analyzed prospectively collected data according to the study groups that were originally assigned. However, changing the frequency of kneeling activity over time may lead to underestimation for the impact of kneeling activity on PF cartilage damage and the overall association might be stronger than our reported estimates. To address this limitation and validate our findings, we have extracted follow-up clinical data regarding kneeling activity over 24 months which showed no significant difference when compared with baseline records.

Finally, our findings are the first exploratory observational report on the association between kneeling activity and MRI-

based PF joint cartilage damage worsening using a longitudinal study design. Further studies are needed to be performed to clarify this association and evaluate the role of kneeling activity as a modifiable risk factor for PF OA development and/or worsening.

Acknowledgments The authors would be thankful to participants and staff involved in FNIH and OAI projects. Several grants and direct or in-kind contributions provide the publically available data from the FNIH OA Biomarkers Consortium Project, including AbbVie, Amgen, Arthritis Foundation, Artialis; Bioiberica, BioVendor, DePuy, Flexion Therapeutics, GSK, IBEX, IDS, Merck Serono, Quidel, Rottapharm | Madaus, Sanofi, Stryker, the Pivotal OAI MRI Analyses (POMA) study, NIH HHSN2682010000 21C, and the Osteoarthritis Research Society International. The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health. This manuscript was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Dr. Shadpour Demehri.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in the osteoarthritis initiative (OAI) study.

Written informed consent was not directly required for this study, since we have used the data of OAI study.

Ethical approval Institutional Review Board approval was obtained.

The study has received ethics board approval by the institutional review board at the University of California, San Francisco (OAI Coordinating Center; Approval Number: 10-00532), and all enrolled subjects gave informed consent.

Study subjects or cohorts overlap Osteoarthritis Initiative (OAI) is a well-known publicly available dataset. Some study subjects or cohorts have been previously reported in in studies published using the OAI and/or FNIH study.

List of studies on OAI dataset can be found in the online address of <https://nda.nih.gov/oai/publications>.

Methodology

- retrospective
- case-control
- multicenter study

References

1. Davies A, Vince A, Shepstone L, Donell S, Glasgow MJ (2002) The radiologic prevalence of patellofemoral osteoarthritis. *Clin Orthop Relat Res* 402:206–212
2. Kobayashi S, Pappas E, Fransen M, Refshauge K, Simic M (2016) The prevalence of patellofemoral osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 24:1697–1707
3. Utting MR, Davies G, Newman JH (2005) Is anterior knee pain a predisposing factor to patellofemoral osteoarthritis? *Knee* 12:362–365
4. Crossley KM (2014) Is patellofemoral osteoarthritis a common sequela of patellofemoral pain? *Br J Sports Med* 48:409–410
5. McAlindon T, Zhang Y, Hannan M et al (1996) Are risk factors for patellofemoral and tibiofemoral knee osteoarthritis different? *J Rheumatol* 23:332–337
6. Englund M, Lohmander LS (2005) Patellofemoral osteoarthritis coexistent with tibiofemoral osteoarthritis in a meniscectomy population. *Ann Rheum Dis* 64:1721–1726
7. Neuman P, Kostogiannis I, Fridén T et al (2009) Patellofemoral osteoarthritis 15 years after anterior cruciate ligament injury—a prospective cohort study. *Osteoarthritis Cartilage* 17:284–290
8. Virayavanich W, Alizai H, Baum T et al (2013) Association of frequent knee bending activity with focal knee lesions detected with 3 T magnetic resonance imaging: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)* 65:1441–1448
9. Rytter S, Egund N, Jensen LK, Bonde JP (2009) Occupational kneeling and radiographic tibiofemoral and patellofemoral osteoarthritis. *J Occup Med Toxicol* 4:19
10. Cooper C, McAlindon T, Coggon D, Egger P, Dieppe P (1994) Occupational activity and osteoarthritis of the knee. *Ann Rheum Dis* 53:90–93
11. Dulay GS, Cooper C, Dennison EM (2015) Knee pain, knee injury, knee osteoarthritis & work. *Best Pract Res Clin Rheumatol* 29:454–461
12. Kajaks T, Costigan P (2015) The effect of sustained static kneeling on kinetic and kinematic knee joint gait parameters. *Appl Ergon* 46:224–230
13. Van Ginckel A, Wittoek R, De Mits S, Calders P (2019) Repetitive knee bending and synovitis in individuals at risk of and with knee osteoarthritis: data from the Foundation for the National Institutes of Health Osteoarthritis Biomarkers Consortium. *Arthritis Care Res (Hoboken)* 71:1372–1378
14. Haj-Mirzaian A, Guermazi A, Pishgar F et al (2019) Association of patella alta with worsening of patellofemoral osteoarthritis-related structural damage: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 27:278–285
15. Simmons JE, Cameron JC (1992) Patella alta and recurrent dislocation of the patella. *Clin Orthop Relat Res* 274:265–269
16. Venkatesan S, van Kampen A (2014) Patellofemoral arthrodesis as pain relief in extreme patella alta. *Knee Surg Sports Traumatol Arthrosc* 22:2551–2553
17. Luyckx T, Didden K, Vandenneucker H, Labey L, Innocenti B, Bellemans J (2009) Is there a biomechanical explanation for anterior knee pain in patients with patella alta? Influence of patellar height on patellofemoral contact force, contact area and contact pressure. *J Bone Joint Surg Br* 91:344–350
18. Ward SR, Terk MR, Powers CM (2005) Influence of patella alta on knee extensor mechanics. *J Biomech* 38:2415–2422
19. Singerman R, Davy D, Goldberg VM (1994) Effects of patella alta and patella infera on patellofemoral contact forces. *J Biomech* 27:1059–1065
20. Shabshin N, Schweitzer ME, Morrison WB, Parker L (2004) MRI criteria for patella alta and baja. *Skeletal Radiol* 33:445–450

21. Chhabra A, Subhawong TK, Carrino JA (2011) A systematised MRI approach to evaluating the patellofemoral joint. *Skeletal Radiol* 40:375–387
22. Collins JE, Losina E, Nevitt MC et al (2016) Semiquantitative imaging biomarkers of knee osteoarthritis progression: data from the Foundation for the National Institutes of Health Osteoarthritis Biomarkers Consortium. *Arthritis Rheumatol* 68:2422–2431
23. Hunter DJ, Guermazi A, Lo GH et al (2011) Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis Cartilage* 19:990–1002
24. Podlipská J, Guermazi A, Liukkonen E et al (2015) Diagnostic performance of semi-quantitative knee ultrasonography—comparison with magnetic resonance imaging osteoarthritis knee score (MOAKS): data from the Oulu osteoarthritis study. *Osteoarthritis Cartilage* 23:A76–A77
25. Runhaar J, Schiphof D, van Meer B, Reijman M, Bierma-Zeinstra SM, Oei EH (2014) How to define subregional osteoarthritis progression using semi-quantitative MRI osteoarthritis knee score (MOAKS). *Osteoarthritis Cartilage* 22:1533–1536
26. Biedert RM, Tscholl PM (2017) Patella alta: a comprehensive review of current knowledge. *Am J Orthop (Belle Mead NJ)* 46:290–300
27. Yılmaz B, Ozdemir G, Sirin E et al (2017) Evaluation of patella alta using MRI measurements in adolescents. *Indian J Radiol Imaging* 27:181
28. Yılmaz B, Ozdemir G, Sirin E, Cicek ED, Anil BS, Bulbun G (2017) Diagnosis and characterization of patellofemoral instability: review of available imaging modalities. *Sports Med Arthrosc Rev* 25:64–71
29. Qvist P, Bay-Jensen A-C, Christiansen C, Dam EB, Pastoureau P, Karsdal MA (2008) The disease modifying osteoarthritis drug (DMOAD): is it in the horizon? *Pharmacol Res* 58:1–7
30. Karsdal M, Michaelis M, Ladel C et al (2016) Disease-modifying treatments for osteoarthritis (DMOADs) of the knee and hip: lessons learned from failures and opportunities for the future. *Osteoarthritis Cartilage* 24:2013–2021
31. van Middelkoop M, Bennell KL, Callaghan MJ et al (2018) International patellofemoral osteoarthritis consortium: consensus statement on the diagnosis, burden, outcome measures, prognosis, risk factors and treatment seminars in arthritis and rheumatism. *Semin Arthritis Rheum* 47:666–675
32. Neal BS, Lack SD, Lankhorst NE, Raye A, Morrissey D, van Middelkoop M (2019) Risk factors for patellofemoral pain: a systematic review and meta-analysis. *Br J Sports Med* 53:270–281
33. Christensen R, Astrup A, Bliddal H (2005) Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. *Osteoarthritis Cartilage* 13:20–27

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.