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Is the Association between Knee Injury and Knee Osteoarthritis Modified by the Presence of General Joint Hypermobility

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Abstract

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Competing Interest Statement

None of the authors have any competing interests in relation to this work.

Objective.—To evaluate whether joint hypermobility modifies the association between knee joint injury and knee osteoarthritis (OA) among adults.

Methods.—Data were from three studies: Genetics of Generalized Osteoarthritis (GOGO; N=2,341), Genetics of Osteoarthritis (GO; N=1,872), and the population-based Johnston County Osteoarthritis Project (JoCoOA; N=1,937). Knee injury was defined as a self-report of prior fracture or severe injury to either knee. OA was defined using three variables: knee pain (pain, aching, or stiffness of the knee on most days), radiographic OA (rOA; Kellgren-Lawrence grade 2–4), and symptomatic OA (sxOA; knee rOA with knee pain). Joint hypermobility was defined as Beighton score ≥4. For each study, separate logistic regression models, stratified by joint hypermobility, were used to estimate the association of knee injury with knee pain, rOA, and sxOA, adjusting for age, sex, body mass index, and race (JoCoOA only); statistical interactions between injury and hypermobility were assessed (p-value<0.10).

Results.—In all three studies, knee injury was associated with OA variables of knee pain, rOA, and sxOA (adjusted odds ratios [aOR] range 1.83–3.75). The association of knee injury with rOA and sxOA was magnified among individuals with vs. without joint hypermobility in GOGO: rOA aOR 11.0, 95% confidence interval [CI] 4.0–30.1 vs. 2.7, 95% CI 2.0–3.6, p=0.009; sxOA aOR 9.2, 95% CI 3.5–24.3 vs. 3.3, 95% CI 2.4–4.4, p=0.032. Interactions were not statistically significant in GO or JoCoOA.

Conclusions.—In a general adult population, the presence of joint hypermobility may not modify the strong association between knee injury and OA.

Keywords

Osteoarthritis; Joint Hypermobility; Cohort; Pain; Injury

INTRODUCTION

Osteoarthritis (OA) is a leading cause of disability; the escalating prevalence of this condition is largely driven by the aging of the population and the rise in obesity[1]. Factors that alter joint biomechanics, such as injury, may accelerate progression to OA. The knee is one of the most commonly injured joints in the body. Anterior cruciate ligament (ACL) injury, meniscal tear, and direct injury to the articular cartilage are all associated with knee OA[2]. The risk of OA 10 or more years following knee injury has been estimated to be 13% among individuals with isolated ACL injuries and 21–48% among those with both ACL and meniscal injuries[3]. Knee injury may initiate or accelerate changes in joint metabolism that lead to the degeneration of cartilage and the formation of osteophytes[4–9].

Joints that are hypermobile present with a range of motion that is considered greater than normal, and this excessive motion and associated laxity of joint tissues could increase a joint's vulnerability to injury and may lead to degenerative changes in joint tissues over time. Current evidence suggests that joint hypermobility is a risk factor for both knee joint injury[10] and knee OA[11–13]. For the knee, both generalized joint hypermobility (hypermobility at more than one joint) and knee-specific hypermobility have been linked to knee injury in young athletes[14,15], but associations between joint hypermobility and injury in non-athletes or in adults have not been reported. The combination of joint hypermobility

and knee injury, which both may aberrantly alter joint tissues, could plausibly amplify the susceptibility to knee OA, although no prior large cohort study has examined the interaction of joint hypermobility and injury in relation to OA.

The purpose of this study was to evaluate whether joint hypermobility modifies the association of knee joint injury and knee OA among adults from three large studies that included participants with and without OA and comprised identical ascertainment of the exposure, outcomes, and covariates. Our hypothesis was that the occurrence of knee OA would be magnified for participants with a history of knee injury and with vs without joint hypermobility.

METHODS

Participants

This study included existing data from participants with and without OA from three large studies: the Genetics of Generalized Osteoarthritis (GOGO) Study, the Genetics of Osteoarthritis (GO) Study, and the Johnston County Osteoarthritis Project (JoCoOA). Participants in each study were sampled without regard to the presence of knee OA, knee injury, joint pain, or joint hypermobility. The study has been approved by the University of North Carolina Institutional Review Board (IRB# 14–3219).

Genetics of Generalized Osteoarthritis (GOGO) Study.—The GOGO Study was a cohort study of 2,756 participants in the United States and United Kingdom that aimed to identify regions of the human genome that were associated with generalized (multi-joint) rOA[16]. During 2000–2002, participants were recruited from rheumatology clinics, hospital databases of OA patients, pre-existing OA cohorts, and the community. Participants were included if they were White, fulfilled clinical GOGO hand rOA criteria (bony enlargement of ≥3 joints bilaterally, including bony enlargement of ≥1 distal interphalangeal joint and no more than 3 swollen metacarpophalangeal joints), and had ≥1 sibling with similar hand OA who agreed to participate in the study. Additional nuclear family members were invited to participate in families qualified on the basis of two hand OA-affected siblings.

Genetics of Osteoarthritis (GO) Study.—Genetic differences of people with and without OA were investigated in this case-control study conducted at the University of North Carolina. A total of 1,122 cases and 1,032 controls were enrolled from 2002–2005 and were considered eligible if they were White, weighed <300 pounds, and were unrelated by blood to any other participants. Cases were 45+ years old and fulfilled clinical GOGO hand rOA criteria. Controls were 60+ years old and had no rOA in hips, knees, or hands. Cases and controls did not have other types of arthritis, hemochromatosis, or ankylosing spondylitis. All participants from GO were included in the present analysis without regard to their original case/control status.

Johnston County Osteoarthritis Project (JoCoOA).—The JoCoOA is a longitudinal community-based study of African American and White civilian, non-institutionalized residents aged 45+ years living in the predominantly rural Johnston County, North Carolina. Participants did not need to have rOA or OA pain to be eligible for the JoCoOA. The

original cohort was enrolled during 1991–1997 (n=3,187)[17], and an enrichment cohort was enrolled during 2003–2004 (n=1,015)[18], Follow-up data collection visits occurred roughly every 5 years.

Measures

The measures listed below were available for all three studies and were consistently collected. Questionnaire and clinic data analyzed in the present study were attained at a single study time point in each of the three studies; thus, all analyses were cross-sectional.

Knee Injury.—Participants were asked two questions about their history of a knee injury: "Has a doctor ever told you that you broke or fractured your [right/left] knee?" and "Other than a fracture, have you injured your [right/left] knee enough to require a cane, cast, or crutch for two weeks or longer?" History of knee injury was defined as an affirmative response to at least one of the questions for either knee.

Knee Pain and Osteoarthritis.—OA was assessed using three separate variables: knee pain, radiographic OA (rOA), and symptomatic OA (sxOA). Participants were asked: "On most days, do you have pain, aching, or stiffness in your [right/left] knee?", with the presence of knee pain defined separately for each knee based on an affirmative response to this question. Bilateral weight-bearing posteroanterior fixed-flexion knee radiographs were acquired for all participants. For all three studies, radiographs were read by a single expert musculoskeletal radiologist (JBR; weighted kappa for interrater reliability 0.9; kappa for intrarater reliability 0.9)[19]. Knee rOA was defined as a Kellgren Lawrence grade (KLG) of ≥2, and sxOA of the knee was considered to be present if an individual had both knee pain and knee rOA in the same joint.

Joint Hypermobility.—Joint hypermobility was assessed using the Beighton criteria[20]. Participants were asked to complete 9 maneuvers for the Beighton criteria: forward trunk flexion with the knees extended and palms on the floor, right and left knee hyperextension ≥10 degrees, right and left elbow hyperextension ≥10 degrees, right and left fifth finger passive dorsiflexion ≥90 degrees, and right and left thumb passive apposition to the forearm. The participant received one point for each maneuver they were able to complete, with the total score for the Beighton criteria ranging from 0 to 9 (unable to perform any maneuver and able to perform all maneuvers, respectively). A Beighton score of ≥4 was classified as joint hypermobility[21–24]. Participants in GO and GOGO completed the Beighton maneuvers at the baseline visit, and Beighton data were collected during the 2003–2004 and 2006–2010 study visits for JoCoOA[12]. Because the Beighton criteria were collected at more than one time point for some participants in JoCoOA, the first study visit with available Beighton data was used in the present analyses.

Covariates.—Potential confounders included sex, age (years), and body mass index (BMI, kg/m^2; based on height and weight measured with stadiometer and balance beam scale). Race was considered a covariate for JoCoOA only (African American vs. White), and family membership was included as a covariate for GOGO only.

Statistical Analysis

For each study, means and standard deviations (continuous variables) and frequencies and percentages (categorical variables) were calculated for demographic and clinical characteristics. The frequency of knee injury and knee OA variables by joint hypermobility was also calculated for each study. Separate logistic regression models for each study were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association of knee injury with pain, rOA, and sxOA at the knee. Given the occurrence of knee pain, OA, joint hypermobility, and injury can differ by age, one set of models was adjusted for age only. A second set of models was further adjusted for sex and BMI; additionally, race was added to JoCoOA models and family membership was added to models using GOGO data. Statistical interaction between knee injury and joint hypermobility were assessed for each of the knee OA variables through the inclusion of an interaction term in each regression model, with p-value <0.10 considered statistically significant. Given that the purpose of this study was to explore whether joint hypermobility modifies the association of knee joint injury and knee OA, stratum-specific ORs were calculated regardless of statistical significance of the interaction. Statistical analyses were completed using SAS System Software 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Within the GOGO, GO, and JoCoOA studies, there were respectively 2,341, 1,872, and 1,987 total participants included for analysis (Figure 1). Demographic and clinical characteristics of study participants are presented in Table 1. Mean age across the three studies was similar, though participants in GO were slightly older. Each study consisted primarily of women, with the highest proportion observed in the GOGO cohort (78%). JoCoOA was the only study that recruited African-American participants (34%). Compared with GO and GOGO, JoCoOA participants had a greater mean BMI (28, 29, and 31 kg/m^2, respectively).

Of the three OA variables, evidence of knee pain was more frequent than evidence of either knee rOA or knee sxOA in each of the three study cohorts. A majority of GOGO participants reported knee pain (66%), which was more common than in JoCoOA (45%) or GO (33%) participants. The proportion of participants with radiographic evidence of knee OA was similar between GOGO and JoCoOA (42% and 39%, respectively), though greater than the proportion of participants with rOA in GO (32%). Fewer than one-third of participants across the three cohorts had knee sxOA. Regarding joint hypermobility, a Beighton score ≥ 4 was relatively uncommon, but was recorded most frequently in the GO study (11%), followed by JoCoOA (7%), then GOGO (3%). Prior knee injury was reported in 16% of JoCoOA participants, a greater proportion than the 10% and 11% of GO and GOGO participants, respectively.

Association of Knee Injury and Knee OA Variables by Joint Hypermobility

Evidence of associations between prior knee injury and the knee OA variables are presented in Tables 2–4, with separate tables for knee pain, knee rOA, and knee sxOA. Each table includes frequencies and adjusted ORs (aORs) for the estimated association between

the respective knee OA variable and knee injury, both overall and stratified by joint hypermobility. Given the aORs from the age-adjusted and fully-adjusted (age, sex, BMI, race, family membership) models were not substantially different, only the fully-adjusted aORs are presented here.

In each of the three studies, the presence of knee pain, knee rOA, and knee sxOA was consistently more common in participants with prior knee injury than in participants without prior knee injury (aORs for total study samples ranging from 1.83 to 3.75). Specifically with respect to knee pain (Table 2), the positive association with prior knee injury was the greatest in JoCoOA participants (aOR=3.75, 95% CI: 2.85–4.94), whereas the associations of knee injury with rOA (Table 3) and sxOA (Table 4) were both strongest in GOGO (respectively, aOR=2.82, 95% CI 2.12–3.75 and aOR=3.41, 95% CI 2.54–4.58).

Stratified by Beighton score, the proportion of participants with knee pain, knee rOA, and knee sxOA remained greater in those with a history of knee injury, though the presence of joint hypermobility did not consistently modify this association by study. In only the GOGO cohort, joint hypermobility magnified the association between knee injury and the three OA variables. For rOA (Table 3), the aOR for GOGO participants with hypermobility was 11.02 (95% CI 4.03–30.1) compared to an aOR of 2.67 (95% CI 1.99–3.58) in those without hypermobility. Similarly, for sxOA (Table 4), the aORs (95% CIs) comparing GOGO participants with vs. without joint hypermobility were 9.16 (3.46–24.3) and 3.25 (2.40–4.41), respectively. Though estimates were imprecise, particularly for rOA, the interaction between knee injury and joint hypermobility was statistically significant in GOGO for both rOA (p=0.009) and sxOA (p=0.032). In both the GO and JoCoOA studies, the interactions between knee injury and joint hypermobility in relation to knee pain, knee rOA, and knee sxOA were generally not statistically significant.

DISCUSSION

Knee pain, knee rOA, and knee sxOA were consistently and strongly associated with knee injury in all three studies. Joint hypermobility modified this association in some but not all of our studies. In particular, joint hypermobility amplified the association of knee injury with knee rOA and sxOA in the GOGO study. Overall, differences in the knee injury-OA association by hypermobility status were not statistically significant in GO and JoCoOA.

The association of knee injury and knee OA from this study are consistent with the broader literature and in particular, larger population-based studies[25–31]. Joint hypermobility has been shown to contribute to a higher incidence of musculoskeletal injury[32], and it may be associated with more severe injuries that could ultimately lead to OA. For example, time to return to play and period of disability have been noted to be longer in professional soccer players with than without joint hypermobility[33]. Results for GOGO support a potential linkage of knee injury and joint hypermobility which is associated with knee OA, although this connection was not observed in the other two studies.

Differences in the results by study may be due to differences in how participants were recruited. Because GOGO participants were recruited from families with at least one sibling

pair with hand OA, findings of magnified associations of knee injury and knee OA among those with joint hypermobility may be unique to that population. Further, the results from GO may also be unique, given that specific criteria were imposed for enrollment into the case and control arms of this cohort. JoCoOA is the only one of these three studies that is community-based in which both White and African American individuals were enrolled without regard to OA status, and thus, this cohort may be more representative of a general population than the other two studies. Further, results from a sensitivity analysis restricting the JoCoOA cohort to White participants were similar to those observed for the full study, but with stronger associations overall. Accordingly, the JoCoOA results may provide the best indication of the role joint hypermobility has as a modifier of the association of knee injury and knee OA in the general population.

Considering the imprecision of the estimates across all three studies, which was largely driven by the low frequency of joint hypermobility, caution is warranted in the interpretation of these differences. Most likely, results from JoCoOA suggest that the presence of joint hypermobility in middle-aged to older adults may not have much of an influence on the knee injury-OA association. Since knee injury is strongly associated with knee OA, the additional presence of general joint hypermobility may not provide a notably increased risk for OA.

An important strength of the current analysis is that all three data sources have identical measures of knee injury, OA, pain, joint hypermobility, and covariates, which allowed for a descriptive comparison of results of the knee injury-OA association. Further, JoCoOA provided community-based estimates that may be more generalizable to an adult population than the other two studies. However, a limitation is that misclassification of injury and joint hypermobility is possible. An individual's recall of injury may not be reliable, including the timing of the injury. Participants in these studies who had joint hypermobility in youth could be classified as "not hypermobile" at the time of study assessment if they experienced joint stiffening with age or following an injury. The present analyses were cross-sectional, which limits our understanding of the sequence of events in the joint hypermobility, injury, and OA relationships. Differences in sampling (recruiting specifically based on presence or absence of OA [GO, GOGO] vs. population-based [JoCoOA]) and designs (cohort and case-control) across the studies may partly explain variation in study results.

In summary, the presence of joint hypermobility may not intensify the already robust association between knee injury and knee OA in a general population of adults. Longitudinal studies may clarify whether joint hypermobility is an initial factor that contributes to an increased risk of injury, and in turn, an increased risk for posttraumatic OA.

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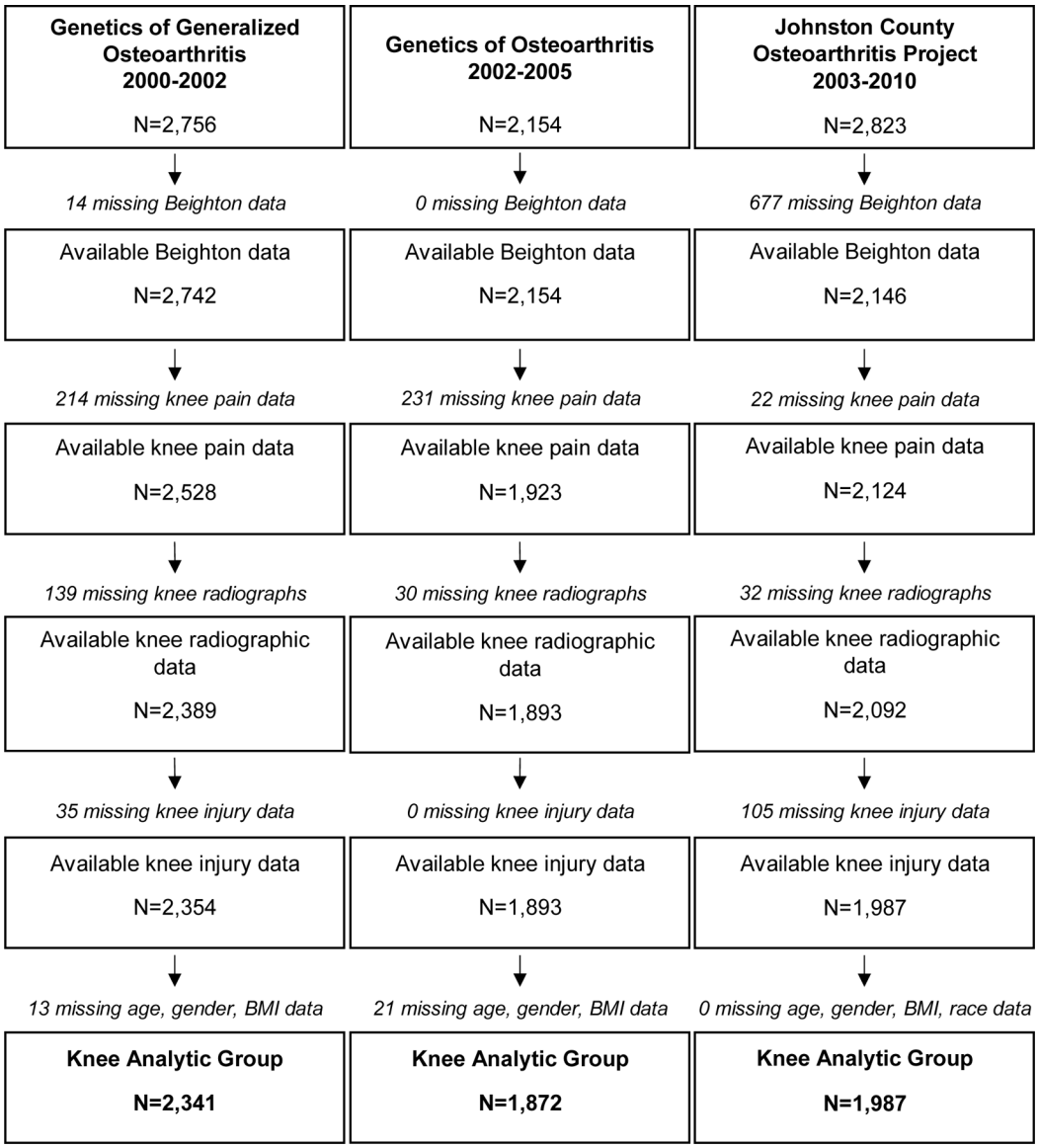

Figure 1.
Participants available for analyses.

Table 1.

Participant characteristics and conditions of those included in analyses from the three studies.

	Genetics of Generalized OA (GOGO) n (%) or mean ± SD N=2,341	**Genetics of OA (GO) n (%) or mean ± SD N=1,872**	**Johnston County OA Project (JoCoOA) n (%) or mean ± SD N=1,987**
Age (years)	66 ± 10	69 ± 8	65 ± 11
Women	1,828 (78.1)	1,335 (71.3)	1,322 (66.5)
African American	0 (0.0)	0 (0.0)	670 (33.7)
Body Mass Index, kg/m^2	29 ± 6	28 ± 5	31 ± 7
Knee Pain	1,541 (65.8)	610 (32.6)	889 (44.7)
Knee rOA	988 (42.2)	590 (31.5)	766 (38.6)
Knee sxOA	763 (32.6)	251 (13.4)	460 (23.2)
Beighton ≥4	78 (3.3)	197 (10.5)	138 (6.9)
Prior Knee Injury	249 (10.6)	192 (10.3)	323 (16.3)

OA=osteoarthritis, SD=standard deviation, rOA=radiographic osteoarthritis, sxOA=symptomatic osteoarthritis

Table 2.

Association between knee injury and knee pain, overall and by joint hypermobility status.

	Genetics of Generalized OA (GOGO)		Genetics of OA (GO)		Johnston County OA Project (JoCoOA)	
Total Sample	**N=2,341**		**N=1,872**		**N=1,987**	
	Prior Knee Injury 249 (10.6%)	No Prior Knee Injury 2,092 (89.4%)	Prior Knee Injury 192 (10.3%)	No Prior Knee Injury 1,680 (89.7%)	Prior Knee Injury 323 (16.3%)	No Prior Knee Injury 1,664 (83.7%)
Knee Pain, n (%)	206 (82.7)	1,335 (63.8)	99 (51.6)	511 (30.4)	229 (70.9)	660 (39.7)
aOR[†] (95% CI)	2.67 (1.87–3.80)		2.51 (1.83–3.45)		3.75 (2.85–4.94)	
By Joint Hypermobility Status						
Beighton ≥ 4	**N=78**		**N=197**		**N=138**	
	Prior Knee Injury 11 (14.1%)	No Prior Knee Injury 67 (85.9%)	Prior Knee Injury 11 (5.6%)	No Prior Knee Injury 186 (94.4%)	Prior Knee Injury 22 (16.3%)	No Prior Knee Injury 116 (83.7%)
Knee Pain, n (%)	10 (90.9)	29 (43.3)	5 (45.5)	48 (25.8)	14 (63.6)	42 (36.2)
aOR[†] (95% CI)	5.05 (0.67–38.2)		3.48 (0.99–12.25)		3.10 (1.13–8.48)	
Beighton < 4	**N=2,263**		**N=1,675**		**N=1,849**	
	Prior Knee Injury 238 (10.5%)	No Prior Knee Injury 2,025 (89.4%)	Prior Knee Injury 181 (10.8%)	No Prior Knee Injury 1,494 (89.2%)	Prior Knee Injury 301 (16.3%)	No Prior Knee Injury 1,548 (83.7%)
Knee Pain, n (%)	196 (82.4)	1,306 (64.5)	93 (51.4)	463 (31.0)	215 (71.4)	618 (39.9)
aOR[†] (95% CI)	2.48 (1.73–3.54)		2.41 (1.75–3.33)		3.83 (2.87–5.11)	
p-value for interaction [§]	0.105		0.580		0.813	

OA=osteoarthritis, aOR=adjusted odds ratio, CI=confidence interval

[†]Adjusted for age, gender, and body mass index; additional adjustment for race in the Johnston County OA Project and for family membership in the Genetics of Generalized OA study

[§]Interaction between prior knee injury and joint hypermobility in relation to knee pain

Table 3.

Association between knee injury and knee radiographic OA, overall and by joint hypermobility status.

	Genetics of Generalized OA (GOGO)		Genetics of OA (GO)		Johnston County OA Project (JoCoOA)	
Total Sample	**N=2,341**		**N=1,872**		**N=1,987**	
	Prior Knee Injury 249 (10.6%)	No Prior Knee Injury 2,092 (89.4%)	Prior Knee Injury 192 (10.3%)	No Prior Knee Injury 1,680 (89.7%)	Prior Knee Injury 323 (16.3%)	No Prior Knee Injury 1,664 (83.7%)
Knee rOA, n (%)	160 (64.3)	828 (39.6)	101 (52.6)	489 (29.1)	142 (44.0)	624 (37.5)
aOR† (95% CI)	2.82 (2.12–3.76)		2.54 (1.82–3.55)		1.83 (1.38–2.42)	
By Joint Hypermobility Status						
Beighton ≥ 4	**N=78**		**N=197**		**N=138**	
	Prior Knee Injury 11 (14.1%)	No Prior Knee Injury 67 (85.9%)	Prior Knee Injury 11 (5.6%)	No Prior Knee Injury 186 (94.4%)	Prior Knee Injury 22 (16.3%)	No Prior Knee Injury 116 (83.7%)
Knee rOA, n (%)	9 (81.8)	20 (29.9)	3 (27.3)	43 (23.1)	6 (27.3)	32 (27.6)
aOR† (95% CI)	11.02 (4.03–30.1)		0.81 (0.19–3.42)		1.89 (0.54–6.63)	
Beighton < 4	**N=2,263**		**N=1,675**		**N=1,849**	
	Prior Knee Injury 238 (10.5%)	No Prior Knee Injury 2,025 (89.4%)	Prior Knee Injury 181 (10.8%)	No Prior Knee Injury 1,494 (89.2%)	Prior Knee Injury 301 (16.3%)	No Prior Knee Injury 1,548 (83.7%)
Knee rOA, n (%)	151 (63.4)	808 (39.9)	98 (54.1)	446 (29.9)	136 (45.2)	592 (38.2)
aOR† (95% CI)	2.67 (1.99–3.58)		2.91 (2.09–4.06)		1.83 (1.38–2.45)	
p-value for interaction §	0.009		0.090		0.866	

OA=osteoarthritis, rOA=radiographic osteoarthritis, aOR=adjusted odds ratio, CI=confidence interval

†Adjusted for age, gender, and body mass index; additional adjustment for race in the Johnston County OA Project and for family membership in the Genetics of Generalized OA study

§Interaction between prior knee injury and joint hypermobility in relation to knee rOA

Table 4.

Association between knee injury and knee symptomatic OA, overall and by joint hypermobility status.

	Genetics of Generalized OA (GOGO)		Genetics of OA (GO)		Johnston County OA Project (JoCoOA)	
Total Sample	**N=2,341**		**N=1,872**		**N=1,987**	
	Prior Knee Injury 249 (10.6%)	No Prior Knee Injury 2,092 (89.4%)	Prior Knee Injury 192 (10.3%)	No Prior Knee Injury 1,680 (89.7%)	Prior Knee Injury 323 (16.3%)	No Prior Knee Injury 1,664 (83.7%)
Knee sxOA, n (%)	144 (57.8)	619 (29.6)	54 (28.1)	197 (11.7)	116 (35.9)	344 (20.7)
aOR[†] (95% CI)	3.41 (2.54–4.58)		2.59 (1.73–3.86)		2.76 (2.05–3.71)	
By Joint Hypermobility Status						
Beighton ≥ 4	**N=78**		**N=197**		**N=138**	
	Prior Knee Injury 11 (14.1%)	No Prior Knee Injury 67 (85.9%)	Prior Knee Injury 11 (5.6%)	No Prior Knee Injury 186 (94.4%)	Prior Knee Injury 22 (16.3%)	No Prior Knee Injury 116 (83.7%)
Knee sxOA, n (%)	8 (72.7)	14 (20.9)	1 (9.1)	17 (9.1)	6 (27.3)	15 (12.9)
aOR[†] (95% CI)	9.16 (3.46–24.3)		0.73 (0.09–6.25)		3.41 (0.96–12.1)	
Beighton < 4	**N=2,263**		**N=1,675**		**N=1,849**	
	Prior Knee Injury 238 (10.5%)	No Prior Knee Injury 2,025 (89.4%)	Prior Knee Injury 181 (10.8%)	No Prior Knee Injury 1,494 (89.2%)	Prior Knee Injury 301 (16.3%)	No Prior Knee Injury 1,548 (83.7%)
Knee sxOA, n (%)	136 (57.1)	605 (29.9)	53 (29.3)	180 (12.0)	110 (36.5)	329 (21.3)
aOR[†] (95% CI)	3.25 (2.40–4.41)		3.00 (2.07–4.35)		2.72 (2.00–3.69)	
p-value for interaction [§]	0.032		0.203		0.545	

OA=osteoarthritis, sxOA=symptomatic osteoarthritis, aOR=adjusted odds ratio, CI=confidence interval

[†]Adjusted for age, gender, and body mass index; additional adjustment for race in the Johnston County OA Project and for family membership in the Genetics of Generalized OA study

[§]Interaction between prior knee injury and joint hypermobility in relation to knee sxOA