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Valgus Malalignment is a Risk Factor for Lateral Knee Osteoarthritis Incidence and Progression: Findings from MOST and the Osteoarthritis Initiative

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Abstract

Objective—We studied the effect of valgus malalignment on knee osteoarthritis (OA) incidence and progression.

Methods—We measured mechanical axis from long limb radiographs from the MOST Study and the Osteoarthritis Initiative (OAI) to define valgus limbs (>1° valgus) and examined the effect of valgus vs. neutral (neither varus nor valgus) on OA structural outcomes. Posteroanterior x-rays and knee MRIs were obtained in subjects at the time of the long limb x-ray and at follow-up examinations. Lateral progression was defined by an increase in joint space narrowing (on a semiquantitative scale) and incidence as new lateral narrowing in knees without x-ray OA. We defined lateral cartilage damage and progressive meniscal damage when WORMS (MOST) or BLOKS (OAI) scores for cartilage or meniscus increased at follow-up. We used logistic regression with adjustment for age, sex, BMI and Kellgren and Lawrence grade and used GEE to evaluate the effect of valgus vs. neutral alignment on disease outcomes.

Results—We studied 5046 knees (881 valgus) from MOST and 5953 knees (1235 valgus) from OAI. In both studies, all strata of valgus malalignment including 1.1 to 3° valgus were associated with an increased risk of lateral disease progression. In knees without radiographic OA, valgus alignment above 3° was associated with incidence (for example in MOST, adjOR = 2.7 (95% 1.1, 6.8)). Valgus 3° or more was also associated with cartilage damage on MRI in knees without OA (for example in OAI, adjOR = 5.9 (95% CI, 1.3, 30.3)). We found a strong relation of valgus with progressive lateral meniscal damage.

Conclusions—Valgus malalignment increases the risk of knee OA x-ray progression, incidence and of lateral cartilage damage. It may cause these effects, in part, by increasing the risk of meniscal damage.

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INTRODUCTION

Once knee osteoarthritis (OA) has developed, tibiofemoral malalignment has been shown to be an extremely potent risk factor for disease progression. Most malalignment in the frontal plane in patients with OA is varus, and knees with varus alignment when standing almost invariably have varus malalignment throughout the stance phase of gait.

The relation of valgus malalignment with tibiofemoral disease is not so clear cut. On the one hand, progression studies [1, 2] have suggested that, like varus malalignment, knees that already have OA and whose limbs show valgus malalignment are at increased risk of joint space loss and cartilage damage on the lateral side of the joint. However, among knees without any cartilage lesions or OA, Sharma and colleagues [3], recently noted that those from valgus limbs do not demonstrate a higher rate of cartilage damage than those from neutrally aligned limbs.

From a biomechanical perspective, valgus knees are not the same as varus knees. While in the static position the limb may appear valgus, during the stance phase of walking, the ground reaction force vector which extends from the center of pressure of the foot to the center of mass of the body passes medial to the knee in many valgus patients, and this generates a varus moment. In fact, many years ago Johnson and colleagues [4] reported that among persons with knee OA with valgus deformities, 71% (20/28) had predominantly medial loading. Only those with severe valgus deformities had predominant valgus moments. This would suggest that knees with mild or moderate valgus deformities would not be at risk of lateral knee OA or its progression.

The data from progression studies have not necessarily addressed the effect of mild to moderate valgus malalignment, since, in most of these studies, all levels of valgus malalignment are combined. Further, studies of disease incidence have reported no significant effect of valgus malalignment [5, 6], but these studies have used anatomic alignment from knee radiographs rather than the gold standard of long limb radiographs. The one study that used mechanical alignment to study incidence [7] also reported no association of incidence with valgus malalignment but studied overall incidence which predilects the medial knee compartment.

Since mild to moderate valgus does not necessarily load only the lateral compartment of the knee, other explanations for an effect of valgus malalignment need to be explored, such as effects of valgus malalignment on lateral meniscal damage. We are unaware of any studies examining effects of valgus malalignment on the meniscus.

The overall goal of this study was to evaluate the effects of valgus malalignment on knee joint damage. Since valgus malalignment and lateral OA are much less common than varus and medial disease, a robust evaluation of the relation of valgus malalignment with lateral disease requires large cohorts such as the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis Study (MOST). In part because it is infrequent, previous studies have categorized valgus malalignment as present or absent, preventing an examination of the relation of the degree of malalignment with disease incidence or progression. Lastly, valgus malalignment in osteoarthritic knees tends to be less severe than varus malalignment so that the failure to detect relations of valgus malalignment with OA outcomes may be due to the relative mildness of the malalignment if limbs are valgus.

There are four specific questions to be addressed. First, we will evaluate the risk of OA progression in mild to moderate valgus malalignment using MOST and OAI cohorts. Second, we will examine the risk of incident lateral OA in those with valgus malalignment.

Third, since x-ray worsening may not be due to cartilage damage, we will examine directly the relation of valgus malalignment with cartilage damage on MRI.

If valgus malalignment causes lateral knee OA, it might do so by increasing the risk of lateral meniscal tears, a major risk factor for lateral OA. The last of the four questions focuses on whether valgus malalignment affects the risk of lateral meniscal damage.

Addressing these issues will provide necessary guidance for biomechanical therapies for valgus deformity, such as braces or other strategies for realigning the knee.

METHODS

Data was drawn from two cohort studies, the Multicenter Osteoarthritis Study (MOST) and the Osteoarthritis Initiative (OAI).

MOST Study

The MOST cohort includes persons with or at high risk of knee OA recruited from the communities of Birmingham, Alabama and Iowa City, Iowa. The goal of the study was to evaluate risk factors for incidence and progression of knee OA. 3,026 subjects aged 50–79 at baseline were recruited and studied at baseline, 30 and 60 months. At each visit, weight and height were measured and PA and lateral weight bearing radiographs obtained. Long limb radiographs were acquired in all MOST subjects at the baseline visit as described elsewhere [7]. Mechanical alignment (also known as HKA) was measured to the nearest 0.1° on these x-rays with high inter-reader reproducibility (ICC = 0.98) by readers trained by Dr. Derek Cooke [9].

MRI's of the knee were acquired in MOST subjects at each visit using a 1.0 T magnet (OrthOne, ONI Inc., Wilmington, MA, USA) and circumferential extremity coil. The protocol included fat-suppressed (FS) fast spin-echo proton density-weighted (PDw) sequences in two planes, sagittal (TR = 4800 ms, TE = 35 ms, 3 mm slice thickness, 32 slices, 288 × 192 matrix, 2 excitations (NEX), 140 × 140 mm field of view (FOV), echo train length (ETL) = 8) and axial (TR = 4680 ms, TE = 13 ms, 3 mm slice thickness, 20 slices, 288 × 192 matrix, 2 NEX, 140 × 140 mm FOV, ETL = 8), and a short tau inversion-recovery (STIR) sequence in the coronal plane (TR = 6650 ms, TE = 15 ms, TI = 100 ms, 3 mm slice thickness, 28 slices, 256 × 192 matrix, 2 NEX, 140 mm^2 FOV, ETL = 8). MRI's were read by experienced MSK radiologists using the WORMS scale [10] using a random sample of the progression subcohort and several case control samples of the incidence subcohort (these two subcohorts were defined based on whether the subject had at least one knee with symptomatic OA at baseline). To evaluate change in cartilage damage, we excluded knees with maximal scores for cartilage damage on the baseline MRI in any weight bearing region (femur or tibia) and defined cartilage damage as present when scores in any region increased at follow-up. Meniscal damage in MOST was scored using the WORMS scale with meniscal extrusion also scored.

Osteoarthritis Initiative (OAI)

The OAI is a longitudinal cohort study of risk factors for incidence and progression of OA. Subjects with or at high risk of knee OA were recruited from four sites, Columbus, Ohio, Providence, Rhode Island, Baltimore, Maryland and Pittsburgh, Pennsylvania. Eligibility for OAI was similar to that of MOST with a few exceptions: in OAI, the risk factors permitting eligibility to the study were broader and the age range extended to as young as age 45. Assessments were similar to those in MOST except that they were done annually. The other relevant difference between OAI and MOST is that in OAI, long limb radiographs using the same protocol as in MOST, were acquired at the 12 month visit in most subjects, but if time

did not permit, these x-rays were acquired for some but not all subjects at later visits. In OAI, knee radiographs were read and adjudicated by the same team as in MOST using the same protocol. The same rule for designating the presence of radiographic OA was used. Also, long limb x-rays were measured using the same protocols and personnel as in MOST.

MR images were acquired at four OAI clinical centers using dedicated Siemens Trio 3T scanners in all subjects. Details of the acquisition protocols have been published [11]. The coronal intermediate weighted (IW) 2D turbo spin-echo (TSE), the sagittal 3D dual echo at steady state (DESS) sequence, coronal and axial multiplanar reformations of the 3D DESS and a sagittal IW fat suppressed TSE sequence were used for semiquantitative assessment and were read by the same experienced MSK radiologists as read MRI's in MOST using a BLOKS scale that was modified so that smaller WORMS regions were read [10, 12, 13]. As part of a study to evaluate effects of alignment on disease worsening, we selected a subset of OAI MRI's to read as those knees that had no radiographic OA at baseline (KL 0 or 1) and developed radiographic incidence (KL grade at least 2) and controls matched to cases on baseline KL grade that did not develop incidence. To evaluate change in cartilage damage, we excluded knees with maximal scores for cartilage damage on the baseline MRI in any weight bearing region (femur or tibia) and defined cartilage damage as present when scores on either area or depth of cartilage lesions in any region increased at follow-up.

Definition of Variables

For examination of both MOST and OAI data, we defined valgus malalignment as mechanical axis of 1.1° or more valgus on a long limb x-ray. Mechanical alignment was characterized as neutral when values fell between 1.0° valgus and 1.0° varus. We studied strata of valgus malalignment to examine the effects of different degrees of valgus. For knees with OA, valgus malalignment of at least 5° was more prevalent than in knees without OA and for the latter, there were not enough limbs with valgus malalignment >5° to study. Therefore for OA progression (knees with OA, we studied strata up to 5.1 or greater valgus and for OA incidence (and for cartilage damage in knees with OA), we studied valgus strata up to 3.1° or greater valgus.

In MOST and OAI, subjects obtained posteroanterior weight bearing knee radiographs using a Synaflexer frame to create a fixed standardized and reproducible knee position. This protocol has been shown to provide reproducible estimates of joint space and to provide consistency in terms of the image of the knee over time [10, 14]. X-ray readings for both studies were carried out centrally at Boston University by a team of three readers. For each subject, all x-rays were read paired. Each of two readers read all x-rays from all subjects. If there was a disagreement as to whether the knee at any time point had radiographic OA (Kellgren & Lawrence Grade 2 or greater) or if between time points, there was disagreement as to whether there was a worsening of disease (defined either as an increase in Kellgren and Lawrence grade or as an increase in joint space narrowing grade), the reading was adjudicated by a panel of three experienced readers including the two who read the films and one other (DTF). A consensus reading was arrived at when at least two of three readers agreed. Because of the large change required in a joint space width to progress a whole integer in score (e.g. from grade 0–1, 1–2 or 2–3), we created a partial grade narrowing scoring system that allowed us to characterize change in joint space width when that change was clearcut but did not reach an integer change threshold (for details, see [8]). For example, if a baseline knee had a medial joint space score of 1 and medial narrowing had clearly progressed in a subsequent image but the subsequent narrowing did not reach the threshold for grade 2 narrowing according to the OARSI Atlas [15], then we gave that subsequent knee a partial grade (e.g., 1.5) between 1 and 2. In previous work [8] we have validated these partial grades by showing that they corresponded to other measures of worsening such as malalignment, cartilage damage and others. We defined lateral progression on the x-ray

as present when there was at least a partial grade change in lateral joint space from the knee x-ray acquired at the time of the long limb x-ray to the later knee x-ray. Agreement was high when the same knee films were sent repeatedly by the coordinating center (for Kellgren and Lawrence grade, weighted kappa = 0.75, p<.0001 and for lateral JS grade, weighted kappa = 0.86, p <.0001).

For knees without OA (KL 0 or 1) at the time of the long limb x-ray, we used the same approach as for progression, looking for lateral joint space narrowing as the outcome [16]. This is not the same as the conventional definition of incidence (new onset KL 2) which samples mostly those developing medial compartment disease; it was our goal to examine whether valgus limbs increased the risk of lateral disease.

For MRI readings, we characterized cartilage damage as occurring when there was an increase in WORMS score for cartilage morphology in any weight bearing region of the lateral knee (central and posterior lateral femur; all lateral subregions of tibia) (MOST Study). For OAI, we used BLOKS scoring and defined cartilage worsening as present when either area or depth of cartilage lesion changed in these same knee regions. For MRI analyses, we excluded from eligibility knees that already showed maximal grade of cartilage damage in any of these regions in the MRI acquired at the time of the long limb film.

For meniscal changes, we used any change in meniscal damage score or in extrusion in the lateral compartment either in the WORMS scale (MOST) or BLOKS scale (OAI). We note that WORMS and BLOKS have been shown for both cartilage and meniscus to provide remarkably similar estimates of damage [17]. We have previously published data on the reliability of MRI readings using WORMS and BLOKS in OAI and MOST MRI's and these have been high [3, 17, 18].

Analysis

For both studies, we excluded knees that underwent knee replacement at follow-up. All subjects who had radiographic follow-up at 30 months (MOST) and radiographic follow-up at either 12 or 24 months after the long limb x-ray in OAI were included in this analysis.

Logistic regression was used to evaluate the odds of OA outcomes (lateral progression of OA, incident lateral OA, cartilage damage in the lateral compartment and meniscal deterioration) according to valgus malalignment. We used generalized estimating equations to adjust for the correlation between knees within subjects in both MOST and OAI and adjusted for age, sex, BMI and Kellgren and Lawrence grade all at the time of the long limb x-ray. For analyses of meniscal damage, we additionally controlled for a self reported history of meniscal surgery.

RESULTS

In both MOST and OAI cohorts (see Table 1), mean age of subjects was in the 60's at the time of the long limb x-ray. The preponderance of subjects were women and on average, BMI was in the overweight or obese range as is typical of persons with knee OA or at risk of disease. Also, consistent with the selection criteria for these cohorts, many subjects had evidence of pain in one or both knees. Only 1.7% of the knees in these cohorts combined had any evidence of medial joint space narrowing at the time of the long limb film (narrowing score ≥ 1). Compared with knees in the neutral group, knee injury history was more common in knees in the most valgus group only (5.1 degrees of above) but not in the other valgus groups (for MOST, 22.1% of neutral vs. 32.5% of most valgus knees had history of injury (comparison p =.009); for OAI, the prevalence was 26.0% vs. 43.8% (comparison p < .001)).

We first examined whether valgus malalignment increased the odds of disease progression in knees which at the time of the long limb x-ray were affected by radiographic OA (see Table 2). We found (see Table 2) that mild degrees of valgus malalignment (1.1 to 3° valgus) were associated with a substantial increased odds of subsequent radiographic progression (adjusted odds ratio = 2.2, 95% CI, 1.5, 3.1). In the OAI there was also an increased odds of disease progression with increasing valgus deformity, and the risk of progression was increased even among limbs that were only mildly valgus (1.1–3° valgus). When valgus malalignment was slightly greater (e.g. 3.1 to 5° valgus), the risk was substantially higher (for MOST, there was a 3.9 fold increased adjusted odds ratio and for OAI, the odds ratio was increased 5.9-fold).

We then turned to knees without evidence of radiographic OA at the time of the long limb radiograph (Table 3). There were fewer knees with valgus malalignment, especially of a severe degree, in limbs whose knees did not have OA, but even so, we detected an association of valgus malalignment with an increased risk of incident lateral disease. For example, among 148 knees in the 3.1° or greater valgus stratum in MOST where the knees had no radiographic OA at baseline, 8 (5.4%) developed OA over the first 30 months, conferring an adjusted odds ratio of OA of 2.5 (95% CI 1.0–5.9). There were fewer numbers in the OAI, but results pointed in the same direction (see Table 3).

Focusing on knees without evidence of radiographic disease at baseline, we then examined worsening of cartilage morphology scores on MRI between the time of the long limb assessment and a later evaluation. Among those limbs with valgus malalignment in MOST (see Table 4), there was an increased risk of cartilage damage in the lateral compartment. This result, although based on small numbers, reached significance for those limbs where there was a valgus deformity of 5.1° or greater and was also elevated, although not significantly so, in limbs that showed valgus deformities of 3.1–5°. In the OAI where MRIs were also acquired and assessed between the time of the HKA assessment and 24 months thereafter, there was also an increase in risk of lateral cartilage damage for those limbs that had valgus malalignment of 3.1° or more (see Table 4).

We examined the relation of valgus malalignment with meniscal damage in MOST and OAI. There were insufficient numbers of MRI's in knees with lateral meniscal damage in OAI to examine this issue (a total of only 6 knees with MRI readings had increasing lateral meniscal damage or extrusion). Even so, we found a clear relation of valgus malalignment with worsening meniscal tear or extrusion in MOST (Table 5), an association that appeared stronger among knees which showed no radiographic evidence of OA (Kellgren and Lawrence grade 0 or 1) than knees with radiographic OA. For example, 8 of 53 knees with valgus malalignment of at least 3.1° in MOST and no x-ray OA had progressive lateral meniscal damage or extrusion, conferring an increased odds ratio of 4.3 (95% CI 1.9, 9.7).

DISCUSSION

Our results suggest that valgus malalignment increases the risk of OA worsening in the lateral knee compartment. It appears to increase the risk of early disease development and when disease is present, it also increases the risk of disease progression defined as lateral cartilage or joint space loss on the radiograph. Further, the effect of valgus alignment is not limited to limbs where the malalignment is severe. The increased risk is present even when there is a mild to moderate degree of malalignment.

These results run counter to what might be expected given the biomechanics of the knee and the repeated demonstration that many and perhaps most knees with mild valgus deformities have a predominant varus moment during the stance phase of gait. What could explain these

findings? First, it should be noted that while the medial compartment receives the brunt of force across the knee during walking, it is designed to do so. It has a concave surface in the tibial plateau that effectively distributes the weight-bearing load across a large surface area, especially if the meniscus is intact. The contact area for the medial compartment during weight bearing is usually substantially greater than that for the lateral compartment [19]. The contact stress, the force per unit contact area, may or may not be greater in the medial compartment. It is likely that the knee developed in such a way that any increase in the contract stress in any local region would increase the risk of local damage. This might occur with mild valgus malalignment.

One explanation for the deleterious effect of valgus malalignment is that it increases the risk of lateral meniscal damage which in turn is a major risk factor for OA. Previous studies (for instance [3]) have shown that varus malalignment increases the risk of medial meniscal tears. However, we are unaware of any study which has reported on the risk for lateral meniscal damage in limbs with valgus malalignment. According to data from MOST (Table 5A), the risk is high. It is possible that the lateral meniscus is as or more vulnerable to malalignment than is the medial meniscus (in the recent study by Englund [3], varus malalignment conferred only a 2 fold increased risk of medial meniscal damage). The lateral meniscus has more anteroposterior motion during flexion and is far more mobile than the medial meniscus [19]. This mobility is not only in the anteroposterior direction but includes rotational mobility with external and internal rotation being critically important in flexion and extension. [19]. While in a neutrally aligned joint, the mobility of the lateral meniscus may serve to protect it from injury and damage, this may not be the case when the knee becomes increasingly valgus malaligned. Such malalignment may combine increasing compressive stress that inhibits the normal motion of a structure that moves back and forth during weight bearing flexion and extension. The effect of malalignment on lateral meniscal tears suggests one explanation for the deleterious effect of valgus malalignment on knee incidence and progression. In addition, the lateral tibia is flat or even slightly convex, in contrast to the concave shape of the medial compartment. This may put increased stress on the lateral vs. the medial meniscus during weight bearing.

In the current study, we used a compartment specific definition of incidence in line with our recent recommendation [16] that incidence should be defined based on the development of joint space narrowing on the x-ray. When we did this, we could isolate early lateral compartment disease and found a relation with valgus. We could have alternatively labeled this as a study of lateral joint space narrowing and could have labeled incidence as ‘early disease development.’ However, as we have suggested elsewhere [16], this definitional approach to incidence allows one better to compare risk factors for incidence and progression as the latter is defined based on compartment specific narrowing.

There are a number of limitations to our study. First, we did not evaluate the dynamic alignment status of our subjects. It is conceivable that valgus static malalignment in many subjects corresponded to valgus dynamic malalignment and that entirely explains our findings. Second, at least in OAI not enough MRIs have yet been read to more definitively evaluate effects of valgus malalignment on cartilage damage and other joint structures. Fortunately, this is not necessarily the case for the MOST study. Another potentially important limitation is that we selected MRI’s from nested case control samples where the cases were defined based on radiographic incident disease. Ideally, the case control sample should be selected from those with MRI, not x-ray, incidence and the effect of this biased selection is unclear. Lastly, while collider bias has been noted by our group [20] as a problem for studies of risk factors for disease progression (Table 2 for example), this issue is not of as much concern when risk factor status changes with disease development as occurs

with malalignment (note the higher prevalence of 5+° of valgus malalignment in knees with prevalent (Table 2) vs. nonprevalent (Table 3) disease.

In conclusion, notwithstanding biomechanical considerations that would suggest that mild to moderate valgus malalignment is not injurious to knees, our data suggest that valgus malalignment is a potent cause of lateral compartment OA incidence and progression as well as cartilage damage and lateral meniscal damage.

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Table 1

Characteristics of Subjects and Knees in those with Long Limb Films and follow-up from MOST and OAI

	MOST Study (5046 knees from 2617 subjects)	OAI (5953 knees from 3034 subjects)
Age in years, mean (SD)	62.4 (8.0)	63.2 (9.2)
BMI, kg/m^2, mean (SD)	30.4 (5.6)	28.7 (4.8)
Female, N (%)	1555 (59.4)	1720 (56.7)
Knee pain on most of the past 30 days, N (%)	1873 (37.1)	1643 (27.7)
WOMAC knee pain subscale (0–20), mean (SD)	2.6 (3.3)	2.1 (3.0)
Kellgren & Lawrence grade, N (%)		
0	2355 (46.6)	2029 (34.1)
1	882 (17.4)	1026 (17.2)
2	725 (14.4)	1671 (28.1)
3	809 (16.0)	936 (15.7)
4	282 (5.6)	291 (4.9)

Table 2

Valgus and lateral JSN progression in 30 months on PA view radiograph in the knees with Radiographic OA at the time of the long limb film

MOST STUDY					
HKA	**N of knees**	**N (%) of lateral cartilage progression**	**Crude OR (95% CI)**	**Adjusted OR* (95% CI)**	**p-value**
−1.1 or below-- varus	1084	24 (2.2)	0.2 (0.1, 0.3)	0.1 (0.1,0.2)	<.0001
ref: −1 to 1	376	46 (12.2)	1.0	1.0	
1.1 to 3 (valgus)	158	39 (24.7)	2.0 (1.4, 3.0)	2.2 (1.5,3.1)	<.0001
3.1 to 5 (valgus)	69	35 (50.7)	4.1 (2.9, 6.0)	3.9 (2.7,5.5)	<.0001
5.1 or above – (valgus)	64	34 (53.1)	4.3 (3.0, 6.2)	3.7 (2.6,5.4)	<.0001
OAI					
HKA	N of knees	N (%) of lateral JSN progression	Crude OR (95% CI)	Adjusted OR (95% CI) **	p-value
−1.1 or below--varus	1583	16 (1.0)	0.4 (0.2,0.7)	0.3 (0.1,0.6)	0.0005
ref: −1 to 1	579	16 (2.8)	1.0	1.0	
1.1 to 3 valgus	368	34 (9.2)	3.3 (1.9,6.0)	3.5 (2.0,6.3)	<.0001
3.1 to 5 valgus	183	33 (18.0)	6.5 (3.6,11.9)	5.9 (3.2,10.6)	<.0001
5.1 or above -- valgus	94	22 (23.4)	8.5 (4.5,15.9)	5.8 (3.1,10.7)	<.0001

*Adjusting age, sex, BMI, and Kellgren & Lawrence grade at baseline

**Adjusting age, sex, BMI, and Kellgren & Lawrence grade at the visit when alignment was measured

Table 3

Valgus and lateral JSN progression in 30 months on PA view radiograph in knees without radiographic OA at the time of the long limb film

MOST STUDY					
HKA	**N of knees**	**N (%) of lateral cartilage progression**	**Crude OR (95% CI)**	**Adjusted OR (95% CI) ***	**p-value**
−1.1 or below-- varus	1314	6 (0.5)	0.2 (0.1, 0.6)	0.2 (0.1,0.6)	0.0019
ref: −1 to 1	1333	25 (1.9)	1.0	1.0	
1.1 to 3 valgus	442	14 (3.2)	1.7 (0.9, 3.3)	1.5 (0.8,3.0)	0.2262
3.1 or above --valgus	148	8 (5.4)	2.9 (1.2, 6.7)	2.5 (1.0,5.9)	0.0406
OAI					
HKA	N of knees	N (%) of lateral JSN progression	Crude OR (95% CI)	Adjusted OR (95% CI) **	p-value
−1.1 or below--varus	1454	3 (0.2)	0.5 (0.1,2.7)	0.5 (0.1,2.6)	0.3844
ref: −1 to 1	888	4 (0.5)	1.0	1.0	
1.1 to 3 valgus	531	3 (0.6)	1.3 (0.3,5.6)	1.3 (0.3,5.7)	0.7641
3.1 or above --valgus	182	3 (1.7)	3.7 (0.8,16.3)	3.6 (0.9,14.8)	0.0822

*Adjusting age, sex, BMI, and Kellgren & Lawrence grade at baseline

**Adjusting age, sex, BMI, and Kellgren & Lawrence grade at the visit when alignment was measured

Table 4

Valgus and lateral cartilage progression in 30 months on MRI films among knees with baseline KL 0–1

MOST STUDY					
	N of knees	**N (%) of lateral cartilage progression**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)** *	**p-value**
−1.1 or below-- varus	490	46 (9.4)	0.6 (0.5,0.9)	0.6 (0.4,0.9)	0.0138
ref: −1 to 1	463	67 (14.5)	1.0	1.0	
1.1 to 3 valgus	169	27 (16.0)	1.1 (0.7,1.7)	1.1 (0.7,1.7)	0.6286
3.1 or above --valgus	53	14 (26.4)	1.8 (1.1,3.0)	1.8 (1.1,3.0)	0.0198
OAI					
HKA	N of knees	N (%) of **lateral** cartilage progression	Crude OR (95% CI)	Adjusted OR (95% CI) *	p-value
−1.1 or below-- varus	59	7 (11.9)	2.0 (0.4,9.1)	1.5 (0.3,6.6)	0.5842
ref: −1 to 1	34	2 (5.9)	1.0	1.0	
1.1 to 3 valgus	20	2 (10.0)	1.7 (0.3,11.2)	1.5 (0.3,9.3)	0.6353
3.1 or above --valgus	11	3 (27.3)	4.6 (0.9,24.3)	5.9 (1.1,30.3)	0.0343

*Adjusting age, sex, BMI, and Kellgren & Lawrence grade at baseline

**Adjusting age, sex, BMI, and Kellgren & Lawrence grade at the visit when alignment was measured

Table 5

Valgus and lateral meniscal progression in 30 months on MRI films in the MOST Study

Progression of either lateral meniscal tear or lateral meniscal extrusion							
	N of knees	**N (%) of lateral cartilage progression**	**Crude RR (95% CI)**	**Adjusted RR (95% CI) ***	**p-value**	**Adjusted RR (95% CI) ****	**p-value**
All knees							
−1.1 or below -- varus	933	25 (2.7)	0.7 (0.4,1.2)	0.5 (0.3,1.0)	0.0341	0.5 (0.3,0.9)	0.0245
ref: −1 to 1	637	25 (3.9)	1.0	1.0		1.0	
1.1 to 3 valgus	249	19 (7.6)	1.9 (1.1,3.6)	1.8 (1.0,3.2)	0.0719	1.7 (0.9,3.1)	0.0905
3.1 to 5 valgus	74	7 (9.5)	2.4 (1.1,5.3)	2.1 (0.9,4.6)	0.0694	2.1 (0.9,4.6)	0.0771
5.1 or above -- valgus	41	11 (26.8)	6.8 (3.7,12.8)	3.7 (1.7,8.2)	0.0013	3.4 (1.6,7.5)	0.0022
Knees with baseline KL 0-1							
−1.1 or below --varus	486	9 (1.9)	0.6 (0.3,1.3)	0.6 (0.3,1.3)	0.1683	0.6 (0.3,1.3)	0.1775
ref: −1 to 1	465	15 (3.2)	1.0	1.0		1.0	
1.1 to 3 valgus	171	9 (5.3)	1.6 (0.7,3.9)	1.5 (0.6,3.7)	0.3426	1.5 (0.6,3.6)	0.3452
3.1 or above -- valgus	53	8 (15.1)	4.7 (2.1,10.4)	4.3 (1.9,9.7)	0.0004	4.3 (1.9,9.7)	0.0004
Knees with baseline KL 2+							
−1.1 or below -- varus	447	16 (3.6)	0.6 (0.3,1.3)	0.5 (0.2,1.0)	0.0493	0.4 (0.2,0.9)	0.0245
ref: −1 to 1	172	10 (5.8)	1.0	1.0		1.0	
1.1 to 3 valgus	78	10 (12.8)	2.2 (0.9,5.3)	2.0 (0.8,4.7)	0.1344	1.7 (0.7,4.2)	0.2365
3.1 to 5 valgus	28	2 (7.1)	1.2 (0.3,5.3)	1.1 (0.2,4.8)	0.9076	1.1 (0.2,4.8)	0.9458
5.1 or above -- valgus	34	8 (23.5)	4.0 (1.7,9.4)	2.4 (0.9,6.2)	0.0762	2.0 (0.8,5.1)	0.1436

* Adjusting age, sex, BMI, and Kellgren & Lawrence grade at baseline

** Adjusting age, sex, BMI, Kellgren & Lawrence grade at baseline, and history of meniscal surgery