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Can Anatomic Alignment Measured from a Knee Radiograph Substitute for Mechanical Alignment from Full Limb Films?

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Abstract

Objectives—To examine whether categories of anatomic alignment (varus, neutral,valgus) measured from knee x-rays agree with similar categories of mechanical alignment from the full limb film and whether varus anatomic malalignment predicts medial joint space loss on knee x-rays as well as varus mechanical alignment.

Methods—We used data from the OAI (full limb and flexed knee x-rays) to examine agreement of anatomic and mechanical alignment and data from BOKS to evaluate the association of full limb mechanical alignment vs. knee x-ray anatomic alignment with joint space loss. A four degree offset was used to correct for the more valgus angulation of the anatomic alignment.

Results—Of 143 subjects whose knee x-rays and full limb films were publicly released from the OAI, the agreement of varus, neutral and valgus alignment was only moderate (κ= 0.43, p<.001). In BOKS, varus mechanical and anatomic alignments measured from full limb and knee x-rays respectively both predicted a high risk of medial joint space loss vs. neutral alignment (for mechanical alignment, OR = 4.82 (95% CI 1.93, 12.00) and for anatomic alignment OR = 4.25 (95% CI 2.08,8.72).

Conclusions—While agreement of alignment from knee x-ray to full limb film was only moderate, varus malalignment measured from a flexed knee predicted the likelihood of progression well. Flexed knee alignment may be more relevant to knee OA risk than that of a fully extended knee, but a measurement of alignment from a short limb is an imperfect surrogate for full limb alignment.

Malalignment in the frontal or coronal plane is a potent risk factor for progression of knee osteoarthritis. High varus moments across the knee during gait markedly increase the risk of progression in diseased knees (1). A standing or static measure of alignment is the most widely used substitute for a gait lab-derived assessment with the gold standard version obtained from a full limb film. Using the full limb film, one can measure the mechanical axis of the femur consisting of a line from the middle of the femoral head through the middle of the distal femur in the knee and the mechanical axis of the tibia which extends from the center of the proximal tibia in the knee to the middle of the ankle joint. The femoral head is used as the origin of the femoral mechanical axis because muscles around the hip move the joint around its center in

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the middle of the femoral head. The angle subtended by these two axes describes the mechanical alignment (varus or bow-legged; valgus or knock-kneed). Mechanical alignment measured from full limb films, has also been found to be a potent risk factor for progressive knee OA (2)(3).

Full limb films are not widely available for clinical studies. They require a long cassette and substantial radiation exposure. Even when orthopedists are planning surgery, they rarely obtain a full limb film because of the challenges in obtaining these images. This may be to the patient's detriment if it compromises the ability of the surgeon to align the limbs optimally during surgery.

Other ways of evaluating alignment across the knee are available. Using the standard knee radiograph, one can measure anatomic alignment (as distinguished from mechanical alignment), the angle subtended by the line of the femoral shaft as it intersects in the knee with the line of the tibial shaft). There has been little work assessing whether the measurement of anatomic alignment obtained using the short limb knee x-ray provides an adequate approximation of mechanical alignment.

Among the few studies examining the relation of mechanical and anatomic alignment is one by Kraus et al (4) who reported that anatomic alignment correlated well ($r = 0.75$) with mechanical alignment. While this is reassuring, it leaves two important questions about the use of knee x-rays to assess alignment unanswered. First, studies examining the effects of alignment on knee OA have generally not examined continuous measurements of alignment as was done in the study by Kraus et al. They categorize alignment as varus, valgus and neutral (5) (6). It is possible that high correlations of continuous measures of alignment would yield less reassuring agreement with categories of alignment and that knees characterized as varus by mechanical alignment from a full limb film may be neutral or even valgus on a knee radiograph. (7)

Second, the work by Kraus and colleagues leaves unanswered the question of whether these correlations are sufficient to yield predictive validity. In other words, does anatomic alignment predict the likelihood of progression in knee osteoarthritis and is the relationship attenuated because anatomic alignment is an imperfect substitute for mechanical alignment? This latter question is critical especially since studies increasingly use anatomic alignment measured from the knee x-ray as a proxy for full limb assessment of mechanical alignment (5) (6).

With these unanswered questions in mind, we embarked on an examination of the agreement of mechanical vs. anatomic alignment and an evaluation of the predictive validity of both types of alignment in terms of predicting disease progression. We did so in an attempt to evaluate in an overall fashion whether a measure of anatomic alignment drawn from a standard knee radiograph was an adequate substitute for a full limb alignment measurement.

Methods

We used data from two different knee osteoarthritis studies, the Osteoarthritis Initiative, which provided full limb films and standard knee radiographs to evaluate the relations of anatomic and mechanical alignment and the Boston Osteoarthritis of the Knee Study (BOKS) which provided information on the predictive validity of mechanical vs. anatomic alignment. Patients with hip OA were not excluded from either study.

Data used in the preparation of this article were obtained from the Osteoarthritis Initiative (OAI) database, which is available for public access at http://www.oai.ucsf.edu/. Specifically, we used data from the 160 subjects in the progression cohort whose baseline and 12 month data and knee x-ray images have been publicly released. We used imaging datasets 0.B.1 and

1.B.1 and clinical dataset 0.1.1 As part of an ancillary study evaluating the effect of full limb alignment on knee osteoarthritis progression, we measured mechanical alignment on full limb films in the subset of these 160 subjects who had full limb films acquired. To obtain contemporaneous anatomic and mechanical alignments, we used the 12 month visit when most full limb films were acquired (none were obtained at baseline). In OAI, since full limb films were generally obtained at the twelve month visit and the image release used for this study included only baseline and twelve month visits, we could not, based on these data, look at full limb alignment as a predictor of later progression.

Our short limb alignments in OAI focused on the anatomic alignment using the PA knee x-ray done with the knee in fixed flexion using the Synaflexer frame (8). As in prior studies (4) (5) we included in our evaluation the ten centimeter shaft distance (10 cm up and 10 cm down from the knee). We also tested the full extent of the shaft visible on this film (which was often a bit longer than 10 cm) but results were not different than the 10 cm distance.

For both knee x-ray and full limb film, we used the femoral notch as the distal end of the femoral axis and the middle of the tibial spines (without osteophyte growth there) was the proximal end of the tibial axis.

In the analysis we evaluated the correlation with the mechanical alignment. We examined two different ways of assessing the relation of mechanical and anatomic alignment. First, like the values reported by Kraus et al., we calculated Pearson correlation coefficients. Second, we used previously definitions of varus and valgus mechanical alignment. Varus malalignment was defined as at least 2 degrees or more of varus angulation and valgus as at least 2 degrees of more of angulation in the valgus direction on the full limb film. (6)(9). Neutral was defined as the range of angulation extending from 1 degree varus to 1 degree valgus. Using these definitions and after adding an offset (see below) to the anatomic alignment to make it equivalent to mechanical alignment, we evaluated the agreement of the knee x-ray based anatomic alignment with categories of mechanical varus and valgus alignment. In terms of agreement of anatomic and mechanical alignment, we tried more extreme definitions of valgus and varus, and agreement was the same or worse as that presented here.

There is an offset from the anatomic axis to the mechanical axis because the shaft of the femur does not include the femoral neck which takes off medially from the femoral shaft. We tested different values of that offset. Among the different values we tried were ones recommended in the literature including four degrees (6) (10), five degrees (11) (12) (10)and the offset suggested by Kraus et al. which varied by gender. In total, we tested all gender neutral offsets from 0 to 6; for gender specific offsets, we used a 2 degree difference and tried all offsets from 0 to 6 also. We present here the gender specific one (2 in women, 4 in men and the gender neutral one (4 degrees) that had the highest kappa values (see below) in terms of agreement between mechanical and anatomic alignments.

To examine the predictive validity of mechanical and anatomic alignment, we turned to the BOKS study where long limb films were acquired at the second longitudinal visit and subjects were followed to the third visit, fifteen months later. Knee x-rays consisted of fluoroscopy positioned PA views which like the fixed flexion views in OAI, were obtained with the knee flexed although unlike fixed flexion views, the amount of knee flexion was determined by what level of flexion optimized imaging of the medial joint (3). As noted previously (3), these were read for progression on the knee radiograph using semi-quantitative scales and we scored progression based on joint space loss on a scale of 0 to 3 (0 being normal and 3 being bone on bone) and we used 0.5 increments on this scale. Any increase of 0.5 or more was considered progression, an approach we recently reported and validated (13). Most of the progressing knees showed medial and not lateral joint space loss. There were too few with lateral progression to robustly evaluate the different relation of anatomic and mechanical axis to progression and therefore we focused on medial progression. The anatomic alignment in this study was assessed using the fluoroscopy-positioned knee films at the second longitudinal visit, the same time point at which mechanical alignment was evaluated (3) and for this analysis, we evaluate progression from the second to the third visits. We examined the relation of categories of varus and valgus malalignment using the full limb to the risk of medial progression characterized by joint space loss. Then using the offset to identify a similar degree of malalignment on the anatomic axis, we created categories of varus neutral and valgus malalignment using the short limb film and tested whether it yielded the same risk of prediction as the long limb film. We used logistic regression with a generalized estimating equation correction for the correlation between two knees to evaluate odds ratio and 95% confidence intervals for this risk using the neutrally aligned knees as the referent category.

We used the following agreement statistics: the intraclass correlation coefficient (ICC) was used to measure the reproducibility of alignment measurement (not the agreement of different types of alignment measures). We also used a weighted kappa to evaluate agreement between ordinal categories of offset corrected anatomic alignment and mechanical alignment (we assumed that with the offset correction, mechanical and anatomic alignment would provide equal values). The agreement statistics provided include both knees. To obtain p values, we selected one knee (rather than 2 correlated knees per person) and computed the p value for one knee

Results

Subjects studied in OAI and BOKS were of similar age (see table 1), but 51% of OAI subjects were female, whereas among BOKS subjects, who were mostly Veterans, 57% were male. Both studies focused on persons with symptomatic radiographic knee OA; Mechanical alignment in both studies was slightly varus suggesting that medial knee OA predominated over lateral disease. Reading of mechanical alignment was associated with a high agreement (for both studies, the intraclass correlation coefficient (ICC= .97). Agreement was also high for the measurement of anatomic axis both for fixed flexion films from the OAI (ICC = 0.97) and for fluoroscopically positioned films from BOKS (ICC = 0.93).

In OAI, only 143/160 subjects in the progression cohort had long limb films acquired at the 12 month visit. In these 143, the correlation of anatomic alignment from fixed flexion films with mechanical alignment was $r = .66$ ($p<.001$)

We examined the agreement between full limb and OAI knee x-ray films in characterizing knee angle as varus, neutral or valgus (see table 2). For fixed flexion views, the weighted kappa for agreement was moderate with weighted $\kappa = 0.43$ ($p<.001$).35, 0.51) at the optimal gender neutral offset, 4 degrees. While most knees showed agreement within at least one alignment category (varus mechanical alignment usually connoted varus or neutral anatomic alignment), there were a few cases of ‘extreme disagreement’, specifically 12 (approximately 5% of knees) where valgus mechanical was accompanied by varus anatomic alignment or vice versa (see table 3). When we used a gender specific offset (the one with the best overall kappa was 2 degrees in women, 4 degrees in men), the agreement of full limb and knee x-ray based alignment was a bit better ($\kappa = 0.50$, $p<.001$) (table 2), but even so, extreme disagreement of alignments occurred (13 knees, approximately 5%) (varus anatomic alignment with valgus mechanical alignment or vice versa). Other gender neutral offsets such as 5 degrees showed slightly worse agreement ($\kappa = 0.41$, $p <.001$).

We then turned to the predictive validity of anatomc alignment using data from the BOKS study (see table 4). We excluded knees with grade 3 joint space narrowing (bone on bone) at the 2^{nd} visit because these knees had no opportunity for progression. The agreement of full limb mechanical alignment with anatomic alignment measured from the knee radiograph in BOKS was r = .68 (p<.001). If the full limb was used to classify varus malalignment, the risk of medial progression was OR = 4.82. If, on the other hand, we used anatomic alignment to define varus malalignment using a four degree offset, the risk of medial progression in varus knees was OR = 4.25. If we used a gender specific offset correction for anatomic alignment, the risk of medial progression in varus knees dropped to an OR = 3.00 (table 4). In all cases the increased risk was highly significantly increased. We had few cases of valgus knees with medial progression, limiting analyses of this relationship.

Discussion

Our results suggest that the anatomic alignment assessed from the knee radiograph is not exactly the same as a mechanical alignment measurement from the full limb. Pearson correlations of the two measures were moderate to high but the categorical agreement of varus and valgus malalignment between the knee x-ray and the full limb film was only moderate (highest kappas ranged from 0.43 – 0.50) and there were even knees that were valgus on the knee x-ray that were varus on full limb film and vice versa.

Even so, anatomic alignment measured from the knee x-ray effectively predicted the risk of joint space loss. In the BOKS study, varus mechanical and anatomic malalignment yielded almost exactly the same risk of progression. There was a slight attenuation of the odds ratios derived from the fluoroscopically position knee x-ray but probably not enough to warrant the added cost and challenge of acquiring full limb films in a large number of persons.

We were surprised by the high level of predictive validity of the anatomic alignment measured from a fluoroscopically positioned knee radiograph, especially given the frequent misclassification of malalignment when alignment from the knee x-ray was compared with the gold standard mechanical alignment from the full limb film. Usually, such misclassification introduces large biases often attenuating odds ratios substantially (14).That our odds ratios were not so biased suggests that flexed films may provide useful and valid information regarding relevant malalignment . Specifically, the flexed position of the knee more closely reflects the loading position of relevance to injury and osteoarthritis. After all, the knee is generally flexed when walking, running or climbing, and x-rays of flexed knees are more likely to show disease than those obtained in full extension. The flexed knee may better represent the position that poses a risk to the knee during activity than the fully extended film, which is taken during standing.

Thus, there are pro's and cons in using a knee radiograph to measure anatomic alignnment. On the one hand, this approach does not provide a terribly accurate surrogate for mechanical alignment especially if the knee radiograph is acquired in knee flexion. This may be due in part to the effect of measuring anatomic alignment from a flexed view of the knee and mechanical alignment with the knee fully extended. Further, the beam of the x-ray in the fixed-flexion knee view does not necessarily come from the same vertical plane as it does in a full limb film, introducing additional possible bias. On the other hand, the flexed knee may be a position more relevant to knee injury and dynamic loading than the fully extended one. Some have suggested that the ideal measure would be of the mechanical alignment during knee flexion (15). Offsets between knee and long limb films could be affected by the severity of knee pain experienced during acquisition of the x-ray which could affect the comfort of knee flexion.

While for the predictive validity component of this analysis, we used fluoroscopically positioned views which permit the knee to flex physiologically; in the fixed flexion view used in OAI and other large studies, the foot and ankle are forced into a small degree of external rotation that may, in turn, obligate knee varus or valgus angles that may not be physiologic. Thus, the high predictive validity we found using the fluoroscopic view may not generalize to the fixed flexion view. The predictive validity of anatomic alignment obtained with a fixed flexion view needs to be tested.

One limitation of our study is the relatively small size of the BOKS sample with few neutral knees showing medial joint space progression. The confidence bounds around our odds ratios were wide. Thus, our results comparing the full limb and knee radiographs in BOKS are consistent with anatomic alignment from the knee radiograph having either comparable or somewhat inferior predictive validity vs. the full limb film. Large longitudinal samples, to be available soon, may help make more precise the tradeoff of knee x-ray vs. full limb films to measure alignment.

Also, the BOKS study is one of patients with moderate to severe osteoarthritis and the predictive validity of alignment may be different at an earlier stage of disease when the issue may be more salient to prevention of disease progression.

Our study also provides evidence not hitherto published on the appropriate offset to make anatomic and mechanical alignments comparable. We used 4 degrees (more valgus in anatomic alignment). Based on preliminary work with the central images from full limbs with the knee imaged in full extension, we suggest that the appropriate offset depends on whether the knee is flexed or extended when it is imaged. In full extension, the appropriate offset is close to 5 degrees, whereas it is less (the knee is more varus) when the knee is flexed.

In summary, while anatomic alignment measured using a knee x-ray has only modest agreement with mechanical alignment assessed using a full limb film, both measures of alignment have strong and comparable predictive validity, at least in our studies. Discrepancies between the results in agreement and predictive validity may be due, in part to the technique of the knee films, which is one study were done using fixed flexion radiographs and in the other were obtained with fluoroscopic positioning. Given this discrepancy between our agreement statistics and the predictive validity of anatomic alignment, we suggest that further research is needed in this area.

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Table 1

Description of OAI and BOKS cohorts used for the analysis of anatomic vs. mechanical alignment

	OAI Cohort (n=143*)	BOKS Cohort (n=183)
Age, years (mean ± s.d.) (range)	60.5 ± 9.7 (45, 79)	65.9 ± 9.3 (47, 93)
BMI, kg/m2 (mean ± s.d.) (range)	30.2 ± 4.5 (20.9, 43.0)	30.4 ± 4.9 (21.5, 45.0)
%women	51.1	43.2
Mechanical Alignment (mean ± s.d.) (range)	-1.3 ± 4.0 (-12.6, 8.8)	-2.3 ± 4.3 (-11, 16)
Anatomic Alignment (mean ± s.d.) (range)	2.4 ± 3.9 (-7, 17)	3.0 ± 4.2 (-22, 10)
% of knees by KL grade		
0	10.3	13.0
1	18.2	23.4
2	34.2	27.6
3	31.0	32.8
4	0	3.2

* for OAI, this is the 160 subjects (minus those without full limb films) in the progression cohort whose data have been publicly released. For BOKS, this is the group obtaining long limb films who had follow-up at the third examination

Table 2

Kappa for agreement between OFFSET + anatomic alignment vs. mechanical alignment (HKA) by neutral/varus/valgus group

	Gender Neutral Offsets	Gender Specific Offset (each the offset in the left column is for women; add 2 to offset for men)
offset =0	0.2912	0.3765
offset =1	0.3708	0.4364
offset =2	0.4002	0.4967
offset =3	0.4091	0.4478
offset =4	0.4316	0.4264
offset =5	0.3599	0.3765
offset =6	0.2912	0.4364

Table 3

Categories of Alignment and their agreement in Full limb vs. fixed flexion knee x-rays from OAI†: Uses 4 degree gender neutral offset based on findings from table 2.

Mechanical Alignment category on Full limb film	**Anatomic Axis using 10 cm of Tibial and Femoral shaft from Fixed Flexion knee x-ray**			
Frequency Percent	**2^0 or less (varus)**	**between 2^0 and 6^0 (neutral)**	**6^0 or above (valgus)**	**Total**
-2^0 or less (varus)	91*	24	6	125 43.1%
between -2^0 and 2^0 (neutral)	32	45	22	103 35.2%
2^0 or above (valgus)	6	29	26	61 21.7%
Total	129 45.9%	98 34.9%	54 19.2%	281 100.0

*number of knees

†Results shown here are for 4 degree offset. Results for gender specific offset (2 degrees in women, 4 in men) showed 13 with extreme disagreement (valgus knee radiograph with varus long limb or vice versa).

Table 4

Alignment groups and Medial JSN progression: BOKS Study

Alignment Groups		N of knees	N(%) with medial JSN progression	OR (95% CI)	p-value
Mechanical Alignment	Valgus (>=2)	60	1 (1.7)	0.33 (0.05, 2.24)	0.2553
	Neutral (-1 to 1)	69	3 (4.4)	1.0	
	Varus (<= -2)	174	44 (25.3)	4.82 (1.93, 12.00)	0.0007
Anatomic Alignment using 4 degree offset (gender neutral)	Valgus (>= 6)	71	3 (4.2)	0.86 (0.30, 2.41)	0.7689
	Neutral (5 to 3)	99	7 (7.1)	1.0	
	Varus (<=2)	133	38 (28.6)	4.25 (2.08, 8.72)	<.0001
Anatomic Alignment (gender specific offset)	Valgus (>= 6 in men, >= 4 in women)	105	4 (3.8)	0.48 (0.16, 1.40)	0.1791
	Neutral (5 to 3 in men 3 to 1 in women)	95	13 (13.7)	1.0	
	Varus (<=2 in men <=0 in women)	103	31 (30.1)	3.00 (1.48, 6.09)	0.0002