Are Joint Structure and Function Related to Medial Knee OA Pain?

A Pilot Study

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Abstract

Background Although the severity of knee osteoarthritis (OA) usually is assessed using different measures of joint structure, function, and pain, the relationships between these measures are unclear.

Purpose Therefore, we: (1) examined the relationships between the measures of knee structure (flexion-extension range of motion, radiographic tibiofemoral angle, and medial joint space), function (Knee Osteoarthritis Outcome Scores [KOOS], peak adduction angle, and moment), and pain (visual analog scale [VAS]); and (2) identified variables that best predicted knee pain.

Methods We assessed 15 patients with medial knee OA using VAS pain, KOOS questionnaire, 3-D gait analysis,

and radiographic examination. Parameter relationships were assessed using Pearson correlation, and variables most predictive of knee pain were determined using a stepwise multiple regression.

Results Subjective measurements correlated ($|r| \geq 0.54$) with one another, as did most of the objective measurements ($|r| \geq 0.56$) except for adduction moment which did not correlate with any variable. All variables correlated ($|r| > 0.54$) with VAS knee pain except peak adduction moment. Medial joint space and peak adduction angle best predicted knee pain, accounting for approximately three-quarters of the model variance ($r^2 = 0.73$).

Conclusions Medial joint space and peak adduction angle may be useful for predicting knee pain in patients with medial knee OA. Therapies that target these structural and functional variables may reduce knee pain in this population.

Clinical Relevance Increasing the medial joint space and limiting the peak knee adduction angle may be critical in achieving effective pain relief in patients with varus knee OA.

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Each author certifies that his or her institution approved or waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

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Introduction

Knee OA is a debilitating disease that affects millions and impairs their capacity to work and to perform activities of daily living (ADLs) [76]. With various surgical and nonsurgical modalities of treatment being available, the course of treatment of a patient with knee OA largely depends on the disease severity. Several subjective and objective measurements of knee structure, function, and pain can be used for clinical assessment [25]. However, patient’s self-reported knee pain and functional impairment, despite subjectivity, often are considered the primary indicators of disease severity. Numerous scales

have been developed for quantifying patient-reported measures in knee OA, with different validity and reliability values [72]. Efforts are underway by organizations such as OARSI and OMERACT to determine the appropriate outcome measures for use in clinical trials, and for treatment decision-making [25].

Knee pain often is quantified on a VAS, which is a validated method for assessing pain immediately after a functional task [20]; however, it is still a subjective measurement. Knee structure may be assessed clinically, in terms of flexion-extension range of motion (Flex-Ext ROM), malalignment, and other structural abnormalities using simple tools such as a goniometer [39]. Radiographically, the knee structure is assessed based on medial joint space (JS), tibiofemoral (TF) angle, and Kellgren-Lawrence (K-L) grade [41]; these are considered mechanical indicators of progression of knee OA [33, 54, 65, 67, 68]. Knee function may be assessed subjectively using validated questionnaires such as the KOOS [60] and objectively, using 3-D gait analysis that yields several kinematic and kinetic variables of dynamic knee function [26, 49, 56]. In medial knee OA with a varus malalignment, which is the most common presentation, the knee adduction angle and (externally referenced) adduction moment during gait are considered important [6, 11, 21, 29]. The knee adduction moment is considered a surrogate of medial compartment load [1], and has been correlated with pain in medial knee OA [71], disease severity [66], and rate of disease progression [50]. However, gait analysis is not a part of routine clinical examinations of patients with knee OA. Likewise, MRI, which is an excellent tool for examining joint cartilage, menisci, and other soft tissues, is expensive and not routinely performed for knee OA. In contrast, plain radiographs, which are a part of the routine examination of a patient with knee OA, reveal only limited information, and the findings may not always correlate with the severity of knee pain [7, 18, 27]. Better diagnostic tools that can predict the progression of knee OA are warranted. It is known that an aberrant structure predisposes an individual to abnormal function; however, the relationships between measures of knee structure, function, and pain have not been clearly established. It also is unclear which structural and functional measurements best predict knee damage. Investigation of these issues would be helpful to better understand the pathomechanics of primary knee OA.

We therefore: (1) examined the relationships between the measures of knee structure (Flex-Ext ROM, radiographic TF angle, and medial JS), function (KOOS values, peak adduction angle, and moment), and pain (Table 1); and (2) identified the variables that best predicted knee pain.

Table 1. Categorization schemes for the variables of interest

Scheme 1	Variables	Scheme 2
Subjective	<div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle;">{</div> <div style="display: inline-block; vertical-align: middle;"> VAS pain KOOS – pain KOOS – symptoms KOOS – ADLs KOOS – sport/rec KOOS – QOL </div> </div>	<div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle;">}</div> <div style="display: inline-block; vertical-align: middle;"> Pain Function </div> </div>
Objective	<div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle;">{</div> <div style="display: inline-block; vertical-align: middle;"> Peak adduction angle Peak adductor moment Flexion-extension ROM Radiographic TF angle Medial joint space </div> </div>	<div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle;">}</div> <div style="display: inline-block; vertical-align: middle;"> Structure </div> </div>

VAS = visual analog scale; KOOS = Knee Osteoarthritis Outcome Score; ADLs = activities of daily living; QOL = quality of life; ROM = range of motion; TF = tibiofemoral.

Patients and Methods

We recruited 15 patients with unilateral primary OA of the medial knee compartment from advertisements in local newspapers. Patients with no history of a major knee injury (eg, meniscus tear or cruciate ligament injury) or knee surgery were selected. Each respondent participated in a formal screening process, and was enrolled after providing informed consent. Seven participants were men and eight were women, with an average age of 67.8 ± 8.3 years, height of 1.7 ± 0.1 m, and mass of 79.6 ± 8.4 kg. All participants had unilaterally symptomatic medial knee compartment OA with K-L grades ranging from 1 to 4 [41]. Specifically, 10 patients had Grade 4 OA, one had Grade 3, one had Grade 2, and three had Grade 1 OA.

During clinical assessment, the knee Flex-Ext ROM was recorded by an experienced physical therapist using a 1°-resolution goniometer. The reliability of such goniometric measurements reportedly is high (ICC = 0.98–0.99) [24, 74]. The participants recorded their knee pain on a 100-mm VAS after a 5-minute brisk walk, and completed the KOOS questionnaire for assessment of knee function during the preceding week. This survey consists of questions arranged in five separate categories (or subscales): pain, symptoms, function during ADLs, function in sport and recreation, and knee-related quality of life. Larger KOOS values of all subscales (including pain) indicate better knee performance [59, 60]. The reliability of VAS pain (ICC = 0.92 [31]) and KOOS values (ICC = 0.75–0.93 [59, 60]) has been documented.

Reflective markers were fixed on bony landmarks of the pelvis and lower limbs (Fig. 1). The participants were asked to walk at a self-selected comfortable speed along an

8-m long walkway, which was instrumented with force plates (AMTI; Watertown, MA; Bertec; Columbus, OH, USA). The analog data were collected at a sampling frequency of 1000 Hz. Marker trajectories were recorded at 100 Hz in a precalibrated 4 m × 2 m × 2 m field-of-view directly over the force plates using a 12-camera 3-D motion capture system (Motion Analysis Corp; Santa Rosa, CA, USA). Typical residual errors for marker position were less than 0.5 mm, with a standard deviation less than 0.25 mm. The data of five acceptable walking trials of each participant were processed using Visual3D® (C-Motion Inc; Rockville, MD, USA). A seven-segment (pelvis, two thighs, two shanks, and two feet) rigid body model was created based on 50 skin-mounted markers. The center of the hip joint was determined using a functional method based on the relative motion between the thigh and the pelvis [64]. The center of the knee joint was determined as the midpoint between the medial and lateral femoral condyles, and the ankle joint center was determined as the midpoint between the medial and lateral malleoli. Euler decomposition methods were used to calculate knee angles (shank motion with respect to the femur) in the sagittal, frontal, and transverse planes, in that order. Knee moments were calculated using six degree-of-freedom inverse dynamics solutions. The peak knee adduction angle and adduction moment during the stance phase of gait were the kinematic and kinetic variables of interest respectively.

Fig. 1 A six degree-of-freedom marker set was applied to the lower body to track knee angles and moments.

The reliability of the kinematic and kinetic gait measurements was calculated by comparing the mean values of the peak knee adduction angle and moment during the first and second trials with the respective mean values of the third and fourth trials across all 15 participants. These measurements were reliable across trials (ICC [2.2] = 0.99 and 0.91 respectively).

Radiographic assessment was performed by a board-certified radiologist (EB) using a calibrated Picture Archiving and Communication System (PACS; Carestream Health, Rochester, NY, USA). Medial JS was measured on postero-anterior flexed knee radiographs with each subject in a standardized position (approximately 20° knee flexion and 10° foot abduction), which was achieved using a SynaFlexer® frame (CCBR-Synarc; Portland, OR, USA) (Fig. 2) [14]. The TF angle was measured on AP radiographs in full extension [44]. The reliability of the radiographic measurements of the TF angle (ICC ≥ 0.93 [38, 44]) and medial knee JS (ICC = 0.94 [43]) have been documented in the past.

We used two categorization schemes: (1) subjective or objective and (2) pain, structure, or function (Table 1). Statistical analyses were conducted using SPSS 19.0 software (SPSS Inc; Chicago, IL, USA). Pearson's correlation coefficients (pairwise two-tailed test) were calculated between all variables of interest. Stepwise multiple regression was performed with VAS knee pain as the dependent variable. The independent variables were comprised of structural (TF angle, medial JS, and Flex-Ext ROM) and functional (peak knee adduction angle and moment) parameters. A variable was accepted in the

Fig. 2 Fixed knee flexion radiographs were taken as participants stood in a SynaFlexer® frame.

stepwise model if p was < 0.05 , and was eliminated if p was > 0.1 .

Results

Examination of the relationships between knee structure, function, and pain revealed several correlations (Table 2). All subjective variables (VAS knee pain and five KOOS subscale values [Table 3]) were correlated to one another. With the exception of peak knee adduction moment, the objective variables (TF angle, medial JS, Flex-Ext ROM, and peak knee adduction angle [Table 3]) also were correlated to each other. The mean ($\pm$ SD) knee adduction angle and moment during the stance phase of gait showed classic patterns (Fig. 3). Among the objective and subjective variables, the medial JS was correlated with VAS pain and all KOOS subscales (Table 3), as was radiographic TF angle (except for KOOS sport). Knee Flex-Ext ROM was correlated to VAS pain, KOOS symptoms, KOOS ADLs, and KOOS quality of life. Peak knee

adduction angle during gait was correlated with VAS pain and KOOS quality of life. Peak knee adduction moment did not correlate with any variable. However, with the exception of peak knee adduction moment, all experimental variables correlated with VAS knee pain. Greater knee pain levels correlated to worse (lower) KOOS values, decreased knee Flex-Ext ROM, increased TF angles, decreased medial JS, and increased peak knee adduction angles.

A stepwise regression analysis revealed that radiographic medial JS and peak knee adduction angle during gait were the best predictors of knee pain. The regression model with only the medial JS had an adjusted $r^2 = 0.61$; while the model consisting of both the medial JS and peak knee adduction angle had an adjusted $r^2 = 0.73$.

Discussion

The severity of knee OA usually is assessed using different measures of specific and often limited aspects of joint structure, function, and pain. However, the relationships

Table 2. Mean and standard deviation values for each variable of interest

Variable	VAS pain (%)	KOOS pain (%)	KOOS symptoms (%)	KOOS ADLs (%)	KOOS sport (%)	KOOS QOL (%)	Adduction angle (degrees)	Adduction moment (N-m/kg)	Flex-Ext ROM (degrees)	TF angle (degrees)	Medial JS (mm)
Mean	51.5	56.2	65.0	59.9	43.2	42.5	4.7	-0.5	123.5	2.7	1.5
SD	29.1	18.3	18.8	19.5	28.4	19.7	3.5	0.1	13.6	3.7	2.2

SD = standard deviation; VAS = visual analog scale; KOOS = Knee Osteoarthritis Outcome Score; ADLs = activities of daily living; QOL = quality of life; Flex-Ext ROM = flexion-extension range of motion; TF angle = tibio-femoral angle; JS = joint space.

Table 3. Pearson correlation coefficients

Variable	Subjective						Objective				
	VAS pain	KOOS pain	KOOS symptoms	KOOS ADLs	KOOS sport/recreation	KOOS QOL	Adduction angle	Adduction moment	Flex-Ext ROM	TF angle	Medial JS
Subjective											
VAS pain	1										
KOOS pain	-0.83**	1									
KOOS symptoms	-0.64**	+0.73**	1								
KOOS ADL	-0.79**	+0.91**	+0.81**	1							
KOOS sport/recreation	-0.54*	+0.69**	+0.74**	+0.77**	1						
KOOS QOL	-0.73**	+0.71**	+0.69**	+0.73**	+0.74**	1					
Objective											
Adduction angle	+0.78**	-0.48	-0.47	-0.44	-0.37	-0.65*	1				
Adduction moment	0.00	-0.22	-0.28	-0.30	-0.23	0.00	-0.38	1			
Flex-Ext ROM	-0.61*	+0.49	+0.68**	+0.53*	+0.47	+0.55*	-0.57*	+0.12	1		
TF angle	+0.73**	-0.79**	-0.67**	-0.66*	-0.46	-0.68**	+0.63*	-0.09	-0.56*	1	
Medial JS	-0.80**	+0.69**	+0.53*	+0.69**	+0.64*	+0.72**	-0.62*	+0.00	+0.66**	-0.58*	1

VAS = visual analog scale; KOOS = Knee Osteoarthritis Outcome Score; ADLs = activities of daily living; QOL = quality of life; Flex-Ext ROM = flexion-extension range of motion; TF = tibiofemoral; JS = joint space; * = $p < 0.05$; ** = $p < 0.01$.

Fig. 3A–B Mean stance-phase knee adduction (A) angles and (B) moments from five walking trials across all participants ($n = 15$) are shown.

between these measures are unclear. Our goals were to: (1) examine the relationships between knee structure (Flex-Ext ROM, radiographic TF angle, and medial JS), function (KOOS values, peak adduction angle, and moment), and pain; and (2) identify the variables that best predict knee pain. The rationale was that such information would be helpful to better understand the pathomechanics of primary knee OA.

This was a preliminary study with several limitations. First, we used a small sample size ($n = 15$), recruited through advertisements in the New York City area; and therefore, future studies should be conducted on larger samples from the general population. However, we consider these initial results important because the data suggest a link between structure, function, and pain in the patient with primary knee OA. Second, our study was limited to evaluating the macromechanical characteristics and knee pain in patients with primary medial knee OA. Other painful knee conditions such as meniscus and cruciate ligament injuries were beyond the scope of our study. Also, the degenerative changes in knee OA, including subarticular bone attrition, bone marrow lesions, synovitis, and effusion, have been associated with knee pain [34]; however, evaluating these relationships was not the focus of our study. Third, our findings are limited to assessment at one instant in time, whereas the relationships between variables might vary during the natural course of the disease.

There are inconsistent reports regarding relationships between variables of knee structure, function, and pain. For example, medial JS has been correlated with changes in cartilage volume on MRI [9], bone mineral density [46], body mass [52, 55], and severity of knee OA symptoms [15, 23], and it has been used routinely in clinical practice to assess the status and progression of medial knee OA [8, 41]. However, substantial discordance also has been observed between the severity of patient's symptoms, and radiographic evidence of degenerative changes in knee OA (including JS narrowing). [7, 19, 27, 62] Likewise, peak knee adduction moment during gait has been correlated with medial knee OA pain [36, 63], varus alignment [17], mechanical axis [52], load distribution [5, 36], compartmental bone mineral content [37], and radiographic evidence of disease progression [4, 50, 66]. However, conflicting reports exist related to knee adduction moment. Heiden et al. reported that larger adduction moment was correlated with lower self-perceived knee pain and other OA symptoms [29], whereas Maly et al. observed no correlation between knee adduction moment and knee OA pain [47]. Also, a lack of correlation between knee adduction moment and limb varus/valgus alignment has been reported [57, 73, 75]. McNicholas et al. observed in patients who had a total meniscectomy, that knee adduction moment did not correlate with either limb alignment or radiographic severity of OA [48].

The means and standard deviations for all variables of interest in this study (Table 2) were comparable to those in several studies [3, 69], as were the mean knee adduction angle and moment curves during gait (Fig. 3) [53]. All subjective measurements were correlated ($|r| \geq 0.54$) with one another (Table 3), as were most of the objective measurements ($|r| \geq 0.56$) except for the peak knee adduction moment which did not correlate with any variable. The lack of correlation of the peak adduction moment to VAS knee pain and other variables was puzzling as it was contrary to the expected outcomes based on several previous reports [29, 30, 36, 37]. However, other researchers also have observed a lack of correlation of knee adduction moment with knee pain, and other variables pertinent in knee OA. This may be attributable to differences in research methods.

Numerous variables have been studied regarding their usefulness for predicting the progression of knee OA (Table 4) [13, 15, 23, 35, 47]; however, amid conflicting reports, few predictive variables have strong supporting evidence [51]. We found that the radiographic medial knee JS and the peak knee adduction angle were the best predictors of knee pain in our study; and that these variables accounted for approximately three-quarters of the model variance ($r^2 = 0.73$). Our analysis included a combination of a static measurement (medial JS) indicative of knee structure, and a dynamic measurement (peak knee adduction angle) indicative of knee function. The peak knee

Table 4. Structural and functional predictors of pain in medial knee OA

Study	Knee adduction angle	Knee adduction moment	Flex-Ext ROM	Radiographic TF angle	Radiographic medial JS	r ² value
Cooper et al. [15]					×	Not provided
Fukui et al. [23]					×	Not provided
Maly et al. [47]			×		×	0.17
Hurwitz et al. [35]		×				0.06
Chang et al. [13]				×		
Current study	×				×	0.73

Flex-Ext ROM = flexion-extension range of motion, TF = tibiofemoral; JS = joint space.

adduction angle during gait corresponds to the ‘varus thrust’, sudden lateral bowing of the knee during the diagonal weight shift in patients with medial knee OA [12]. The peak knee adduction angle is not used routinely in clinical practice, although it has been recommended as an important clinical index for knee OA [45]; our data support this recommendation.

The treatment goal in varus knee OA, by means of surgical (eg, high tibial osteotomy) [16, 22, 61] and non-surgical methods (eg, wedging foot orthoses, unloading knee braces) [10, 42, 58], is to reduce deviation of the mechanical axis of the lower extremity from the knee joint center. However, the ‘mechanical axis’ is a static 2-D radiographic measurement that varies with foot position [32] and weightbearing status (eg, single versus double-limb support) [70], and it might not always correlate with complex 3-D loading or dynamic function of the knee [2, 28, 40]. Based on our preliminary results, we believe that a combination of static measurement (eg, medial JS) and dynamic (or functional) measurement might be more predictive of the patient’s perceived knee pain than any one type of variable, and that such a mixed model might be useful for monitoring progression of knee OA and for assessing treatment outcomes.

We determined the relationships among several measurements of knee structure, function, and pain. Among the examined variables, radiographic medial knee JS (a structural variable) and peak knee adduction angle (a functional variable) were most predictive of patient-perceived knee pain. Therefore, the value of the peak knee adduction angle as a tool for assessing knee OA severity and treatment efficacy warrants further investigation.

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