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Sensitivity of different measures of frontal plane alignment to medial and lateral joint space narrowing: From the osteoarthritis initiative

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ABSTRACT

Objectives: To explore cross-sectional relationships between a new radiographic measure of the femorotibial angle (FTA), the hip–knee–ankle angle (HKA), and the goniometry; to quantify sex differences between measures; and to evaluate the sensitivity of these measures to medial and lateral joint space narrowing (JSN).

Methods: Concurrent validity was evaluated in 2123 knees from the osteoarthritis (OA) initiative using Pearson correlation coefficients (r) and Bland–Altman plots (offsets). Diagnostic validity with respect to JSN was evaluated using areas under the receiver-operating characteristic curves (AUC) and standardized mean differences (SMD). Analyses were stratified by sex and JSN.

Results: JSN and sex contributed significantly to regression models predicting offsets between measures ($p < 0.001$), after controlling for age, BMI, and OA severity. There were weak correlations between FTA vs. goniometry (r: 0.16–0.22), and moderate correlations between FTA vs. HKA (r: 0.25–0.53) and HKA vs. goniometry (r: 0.40–0.67). The offset between the new FTA measure and HKA was larger in females than males ($p < 0.001$). Offsets between radiographic measures and goniometry also varied by sex and JSN (FTA: 2.9°–7.6°; HKA: 0.5°–2.4°). AUC (0.74–0.91) and SMD (0.53–3.80) between JSN strata were largest for FTA, whereas diagnostic validity was moderate for HKA (AUC: 0.69–0.80; SMD: 0.43–2.04) and weakest for handheld goniometry (AUC: 0.56–0.63; SMD: 0.07–0.90).

Conclusions: Compared to HKA, goniometry demonstrated poor diagnostic validity with respect to JSN. The new FTA measure, in contrast, represented a reasonable surrogate of radiographic disease severity (JSN). The new FTA measure was skewed in the varus direction when compared to HKA and more so in females. This requires cautious interpretation when measurements are related to previous studies.

Introduction

Lower limb malalignment and joint space narrowing (JSN) are potent risk factors for the structural progression of knee osteoarthritis (OA) and thus of great prognostic importance [1–4]. Establishing cost-effective and practical approaches for quantifying frontal plane alignment, with the potential to evaluate risk of progression, would be highly useful for clinicians [5]. Frontal plane alignment is commonly determined by weight-bearing radiography, either using standing full limb films to quantify mechanical alignment (hip–knee–ankle angle, HKA) or short knee films to quantify anatomical alignment (femorotibial angle, FTA). Although short knee films are more readily available across clinical settings and involve smaller radiation exposure, full limb films also capture the anatomical characteristics of the hip and ankle and therefore are considered the gold standard and most accurate method for evaluating alignment [5–9].

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Competing interests: R. Moyer has no competing interests to declare. W. Wirth is employed part-time at and is co-owner of Chondrometrics GmbH, a company providing MR image analysis services to researchers in academia and in the pharmaceutical industry. F. Eckstein is CEO and is co-owner of Chondrometrics GmbH, provides consulting services to Mariel Therapeutics, Snyarc, and Merck Serono, and provides educational sessions to Medtronic.

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The position of the femoral head influences the relationship between HKA and FTA, because FTA only incorporates the distal region of the femoral shaft. Consequently, an offset between these measurement methods [6,10,11] has previously been reported, with FTA being skewed in the valgus direction (i.e., FTA: 3°–5°) compared to knees with neutral HKA (i.e., HKA = 0°). Despite this systematic difference, correlations between HKA and FTA have been reported to be moderate to high (r: 0.46–0.93) but vastly inconsistent between studies [5–7,9–12]. The method proposed by Kraus et al. [6] originally defined FTA as the angle between the distal femur and proximal tibia, (i.e., the traditional method). However, a novel, highly automated method for measuring FTA was recently presented by Iranpour-Boroujeni et al. [12] and alignment data obtained with this method are now available for most of the osteoarthritis initiative (OAI) cohort. This method does not define FTA by the shaft but utilizes more local information around the joint space and femoral condyles [12–14]. The authors reported greater intra-rater and inter-rater reliability [12] for measuring FTA than the traditional method in participants with knee OA, and somewhat greater correlation with HKA (r = 0.75) than for the traditional FTA measurements (r = 0.68). However, the offset between the new FTA measurement methodology and HKA measures has not been studied. Further, whether the offset varies by sex and to what extent the new FTA measurement can differentiate categories of radiographic disease status (JSN), as a measure of diagnostic validity, is unclear.

Goniometry is the most easily accessible tool for measuring alignment, without need for radiographic equipment. However, prior studies have highlighted its inconsistent correlations with the gold standard and traditional FTA measures (r: 0.32–0.75) [5,6,8,9,15], likely because of the low precision and large random noise of the measurement. Evaluating the relationships between goniometry and radiographic measures of alignment categorized by different directions and magnitude of uni-compartmental JSN, however, may demonstrate whether or not clinicians can utilize non-radiographic measures of alignment to identify participants with compartment-specific knee OA and/or at risk for subsequent structural progression.

The purpose of the current study was therefore to explore the cross-sectional relationship of the new FTA measurement, HKA, and handheld goniometry in participants with medial, lateral, or no JSN; to quantify sex differences in the offsets between these measurements; and to evaluate which measure of alignment best differentiates JSN grades (1–3). We hypothesized that the new FTA measure would perform as good as the gold standard (HKA) in differentiating JSN grades, with good to excellent concurrent and diagnostic validity. We further hypothesized that goniometry would be less reliable in differentiating important, prognostic JSN grades, and have only poor validity.

Methods

Participants with or at high risk for developing knee OA were selected from the osteoarthritis initiative (OAI, http://www.oai.ucsf.edu), an ongoing, prospective, multi-center study with publicly accessible data [16,17]. The OAI includes 4796 participants aged 45–79 years, with clinical, radiographic, and other data collected at baseline and at annual follow-up visits up to 4 years. The specific OAI inclusion/exclusion criteria have been published [17]. OAI participants were excluded from the current study if they were part of the healthy reference cohort (no radiographic knee OA or risk factors for incident knee OA), had bi-compartmental (medial and lateral) JSN or did not have one or more alignment measures (HKA, FTA, and/or goniometry) completed at any visit.

The primary outcome measures of interest included frontal plane lower limb alignment and uni-compartmental JSN, in either the medial or the lateral compartment. Figure 1 illustrates a simplified version of the OAI timeline and at what visit alignment measures were obtained. Whereas fixed flexion radiographs and goniometric measurements were obtained at baseline and each annual follow-up time point throughout the OAI, bilateral, standing hip-to-ankle (full limb) postero-anterior radiographs were added to the OAI protocol after the baseline visits had been completed. These were generally acquired at 12- or 24-month follow-up but were repeated at 24-, 36-, or 48-month follow-up (Fig. 1) if they were missing or of poor quality (Version 1.2, Version 3.1, Version 5.1, and Version 6.1 from the OAI database, respectively). The gold standard HKA alignment measure was determined according to Cooke et al. [18] (Fig. 2). HKA was defined as the inclusion angle formed between a line drawn from the center of the femoral head to the center of the knee (distal femoral notch), and a line drawn from the center of the ankle to the center of the knee (tibial spines). Negative values indicated varus alignment.

Baseline fixed flexion radiographs were used to quantify the new FTA measurement (Version 0.1) [12] and currently, FTA measures are available for the baseline visit only (Fig. 1). Participants were positioned in a fixed knee flexion, plexiglass positioning frame (Synaflexor TM) with the knees positioned in 20°–30° of flexion [19]. The FTA measurement was defined using a coordinate system to identify the distal aspect of the femoral condyles based on anatomical landmarks for establishing a location-specific joint space width measurement (Fig. 2) [13,14]. Using the largest prominence of the medial and lateral femoral condyles, two lines were identified perpendicular to a tangent at the distal aspect of the condyles. The femoral axis was centered between the outer aspects of the femur and perpendicular to the tangent. The tibial axis was centered along the shaft of the tibia between medially and laterally placed points at 1 and 10 cm distal to the tibial plateau. FTA was defined as the inclusion angle between these axes. Negative values indicated varus alignment.

Using the same fixed flexion radiographs, semi-quantitative measures of medial and lateral JSN were categorized a priori using the OARSI atlas in accordance with the OAI protocol (0 = no JSN; 1 = mild JSN; 2 = moderate JSN and; 3 = severe JSN) [20], and knee OA severity was quantified using the Kellgren–Lawrence grading (KLG) system. JSN and KLGs were obtained using the central readings from Boston University (Version 0.6) [21].

Handheld goniometry was determined at baseline (Version 0.2.2) and all annual follow-up time points (Version 1.2.1, Version 3.2.1, and Version 5.2.1). Goniometric measurements were obtained manually with the participant in full knee extension

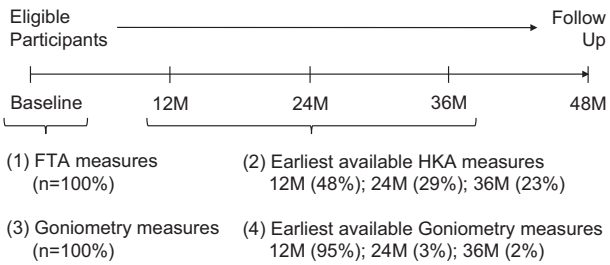

Fig. 1. A simplified representation of the osteoarthritis initiative (OAI) data collection timeline. Alignment measures using FTA (1) were obtained only at baseline. Earliest available alignment measures using HKA (2) were obtained at 12 months (48% of knees), 24 months (29% of knees), or 36 months (23% of knees). Alignment measures using goniometry were obtained at baseline (3) or the earliest available time point (4) from 12 months (95% of knees), 24 months (3% of knees), or 36 months (2% of knees). Comparisons were made between: (1) and (3), (2) and (4), and (1) and (2).