Osteoarthritis and Cartilage 21 (2013) 1185–1190

Osteoarthritis and Cartilage

Radiographic joint space width is correlated with 4-year clinical outcomes in patients with knee osteoarthritis: data from the osteoarthritis initiative

S.R. Oak †*, A. Ghodadra †, C.S. Winalski ‡, A. Miniaci §, M.H. Jones §

† Cleveland Clinic Lerner College of Medicine, 9500 Euclid Ave, NA-21, Cleveland, OH 44195, USA
‡ Imaging Institute and Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, USA
§ Orthopaedic and Rheumatologic Institute and Sports Health Center, Cleveland Clinic, USA

ARTICLE INFO

Article history:
Received 15 January 2013
Accepted 25 June 2013

Keywords:
Knee osteoarthritis
Clinical progression
Joint space width
X-ray

SUMMARY

Objective: To evaluate if quantitative joint space width (JSW) measurements from radiographs correlate with 4-year Knee injury and Osteoarthritis Outcome Scores (KOOS) and clinical performance measures.
Method: The study group consisted of 942 patients with symptomatic knee osteoarthritis (OA). 4-year outcomes for six measures (KOOS Pain, Symptom, Quality of Life, and Function scores, 20-m walk pace, and chair stand time) were used to create six multiple linear regression models. Primary predictors were baseline minimum JSW and 4-year change in JSW measured from fixed flexion radiographs. Age, gender, body mass index (BMI), race, knee alignment, and baseline measures of the outcomes of interest were covariates.
Results: Lower baseline minimum JSW and a greater decrease in 4-year JSW significantly correlated with worse 4-year KOOS Pain, Symptom, and Quality of Life. With all other factors constant, a 4.1, 4.8, and 5.6 mm lower baseline JSW correlated with a clinically significant eight-point drop in 4-year KOOS Pain, Symptom, and Quality of Life scores respectively. Additionally, a 3.5, 3.1, and 4.0 mm loss of JSW over 4 years correlated with a clinically significant eight-point drop in 4-year KOOS Pain, Symptom, and Quality of Life scores respectively.
Conclusions: Our results indicate quantitative radiographic JSW measurements correlate with 4-year clinical outcomes. Since patients with narrower JSW at the onset of study had lower KOOS scores at 4 years even after controlling for 4-year change in JSW and baseline KOOS scores, clinical outcomes in knee OA may be predetermined once the disease process begins. These findings suggest early treatment with disease modifying therapies may be necessary to influence outcomes.

Introduction

Osteoarthritis (OA) is one of the most common causes of disability in the United States and presents a large burden on individuals and the healthcare system. The knee is one of the most common joints affected by OA with an estimated prevalence in adults over 45 of 19.2% and 27.8% in the Framingham Study and Johnson County Osteoarthritis Project, respectively[1]. The prevalence is expected to grow in the coming years as a result of an aging population. Furthermore, the lifetime risk of having symptomatic knee OA is estimated to be 45% for the general population and 61% among obese individuals[2]. In terms of healthcare utilization, patients with knee OA have been shown to have significantly more doctor's visits and hospitalizations than patients without knee OA[3]. In 2009, one study estimated over 600,000 hospital discharges in the US as a result of knee OA costing $28.5 billion[4].

The pathogenesis of knee OA involves articular cartilage degradation, inflammation of synovial tissues, and changes in subchondral bone[5]. As a standard measure of anatomical disease progression, joint space width (JSW) is the distance measured between the femoral condyle and tibial plateau on radiographs obtained in a standardized fashion. Articular cartilage loss is indirectly inferred based on loss of JSW and referred to as joint space narrowing (JSN)[6]. Magnetic resonance imaging (MRI) has proved to be a very sensitive technique to evaluate the status of most knee

* Address correspondence and reprint requests to: S.R. Oak, Cleveland Clinic Lerner College of Medicine, 9500 Euclid Ave, NA-21, Cleveland, OH 44195, USA.
E-mail addresses: oaks@ccf.org (S.R. Oak), ghodada@ccf.org (A. Ghodadra), winalsc@ccf.org (C.S. Winalski), miniaca@ccf.org (A. Miniaci), jonesm7@ccf.org (M.H. Jones).

1063-4584/$ – see front matter
http://dx.doi.org/10.1016/j.joca.2013.06.024

structures including cartilage, meniscus, bone, and ligaments. However, despite the advances in MRI and quantitative image analysis techniques, radiographic JSN is currently the biomarker accepted by the United States Food and Drug Administration (FDA) and European Agency for the Evaluation of Medicinal Products (EMEA) as an end point in clinical trials for measurement of OA progression[6].

JSN measurements are appropriate to estimate structural disease progression, but they do not directly evaluate the impact of knee OA on patients' lives. The Knee injury and Osteoarthritis Outcome Score (KOOS) is a validated and reliable patient-reported outcome measure evaluating pain, symptoms, function, and quality of life[7]. Other objective performance tests, including 20-m walk pace and time to perform five chair stands, can also be used to measure patients' abilities[8]. These clinical measurements are suitable to evaluate the progression of knee OA as experienced by the patient.

Although a relationship between radiographic and clinical knee OA progression would be anticipated, evidence to date has not established a strong correlation. A systematic search of the literature by Bedson and Croft in 2008 concluded that radiographic changes in knee OA were an imprecise marker of knee pain[9]. They concluded the discordance was caused by variations in X-ray views, X-ray grading, pain definition, and study population. A systematic review conducted in 2011 supported the discordance and found only 10% of reviewed studies associated radiographic and clinical OA features[10].

The Osteoarthritis Initiative (OAI) is a longitudinal, multicenter, prospective, observational cohort study of knee OA. A publically available database has been established containing yearly clinical assessments, biospecimens, MRI, X-ray, and outcome data from patients with symptomatic OA or at elevated risk of OA[11]. Over 4,700 patients ages 45–79 were enrolled between February 2004 and May 2006. This database provides a valuable opportunity to follow a large, nationwide patient group. In this study, we evaluate the association of radiographic disease state and clinical outcome measures in a cohort of OAI patients. We hypothesize that JSN over 4 years would be associated with worsening clinical outcomes after adjusting for demographic factors, baseline JSW, and baseline clinical scores.

Methods

Study population

Data used in the preparation of this article were obtained from the OAI database, which is available for public access at http://www.oai.ucsf.edu/. Specific datasets used were AllClinical 0.2.2 and 6.2.1 and kXR quantJSW 0.5 and 6.2. Patients for the current study were derived from the progression subcohort. Inclusion into this subcohort was based on having both of following criteria in at least one knee at enrollment: "pain, aching, or stiffness in or around the knee on most days" for at least 1 month in the past 12 and definite tibiofemoral osteophytes (Osteoarthritis Research Society International atlas grades 1–3 or Kellgren and Lawrence grade $\geq$2) on the fixed flexion radiograph. With these criteria, we identified 1,278 patients of which 942 had complete data for all variables of interest and were included in our analyses. The patient's right knee was chosen as the unit of analysis to avoid duplication of nonbilateral data.

Predictor variables

Minimum and fixed location JSW measurements for the medial compartment and fixed location JSW measurements for the lateral compartment from radiographs that were obtained under the standardized fixed flexion acquisition protocol (http://oai.epi-ucsf.org/datarelease/operationsManuals/RadiographicManual.pdf) were colle cted from the OAI database. Minimum quantitative JSW and fixed location JSW were measured for the OAI using an automated software method[12,13]. Minimum JSW from the OAI was defined as the minimum distance between the femur and tibia in the medial tibiofemoral compartment. In fixed location JSW measurements, the distance between the femur and tibia was measured at fixed intervals in the medial and lateral compartments. In the current study, the variable quantitative minimum JSW represented the lowest fixed interval measurement made from the medial or lateral compartment. The predictor variables of primary interest were baseline quantitative minimum JSW and 4-year change in minimum JSW (JSN). The 4-year JSN was calculated by subtracting the baseline minimum JSW from the minimum JSW at 4 years after enrollment. This analysis was repeated for the most responsive JSW at $x = 0.275$. To control for potential confounding, several covariates were included in the analyses based on previous literature[14,15]. These included age, gender, body mass index (BMI), race, knee alignment, and baseline measures of the 4-year outcome of interest. OAI variable names for the predictor variables used were V00AGE, P02SEX, P01BMI, P02RACE, V00rkdefcv, V00RKALNMT, V00KOOSKPR, V00KOOSYMR, V00KOOSQOL, V00KOOSFSR, V00CSTIME1, and V0020MPACE.

Outcome measures

Six clinical outcome measures were selected from the OAI database and were categorized as either patient-reported outcomes or performance measures. The patient-reported outcomes were KOOS Pain, Symptom, Quality of Life, and Function, Sports, and Recreation scores measured 4 years after enrollment. KOOS scores range from 0 to 100. A score of 0 represents extreme knee problems, 100 represents no knee problems, and a score change of eight represents the minimum perceptible clinical improvement[7]. The performance measures were 20-m walk pace and time to perform five chair stands measured 4 years after enrollment. OAI variable names for the outcome variables used were V06KOOSKPR, V06KOOSYMR, V06KOOSFSR, V06KOOSQOL, V06CSTIME1, and V0620MPACE.

Statistical analysis

To test for significant differences between all patients and patients included in the analysis, two-tailed two-sample student's t tests with equal variances or two-proportion z tests were performed. To estimate the effect of multiple predictors on outcomes, multiple linear regression modeling was performed using the statistical software package JMP 9 (SAS Institute, Cary, NC). Each model consisted of one outcome measure, nine predictor variables, and two interaction product terms. The nine predictor variables consisted of four demographic variables, two alignment variables, one baseline measure of the outcome of interest, and two JSW variables. Two cross product terms to account for potential interaction were 4-year JSN multiplied by baseline JSW and 4-year JSN multiplied by alignment. The assumptions of normality and constant variance of residuals and independence between observations were met. Effect tests using the f-ratio were used to test for statistical significance of each variable in the models. An α level of 0.05 was used in evaluating significance in Table I. An α level of 0.01 was used to evaluate statistical significance in the multiple linear regression model. A significance level of 0.01 was chosen to reduce the risk of a Type 1 error as a result of performing six regressions.

Results

Patient characteristics

Descriptive statistics for each predictor can be found in Table I. Hypothesis testing was performed comparing means between all patients (n = 1,278) and patients included in analysis (n = 942).