Osteoarthritis and Cartilage 22 (2014) 71–75

Osteoarthritis and Cartilage

Brief report

Trabecular bone texture detected by plain radiography is associated with an increased risk of knee replacement in patients with osteoarthritis: a 6 year prospective follow up study

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ARTICLE INFO

Article history:
Received 10 January 2013
Accepted 29 October 2013

Keywords:
Trabecular bone
Radiography
Fractals
Knee replacement

SUMMARY

Objective: To examine the association between trabecular bone texture and knee joint replacement (KJR) measured using a variance orientation transform (VOT) method.
Methods: The association of trabecular bone texture and KJR was examined prospectively over 6 years in 123 subjects with symptomatic knee osteoarthritis (OA): data regarding KJR was available for 114 (93%). At baseline, weight-bearing anteroposterior tibio-femoral radiographs were acquired. Trabecular bone texture regions were selected from the medial and lateral subchondral tibia. The VOT method was applied to each region and five fractal bone texture parameters, i.e., mean fractal dimension (FD_{MEAN}), fractal dimensions in the horizontal (FD_H) and vertical (FD_V) directions, and along the roughest part of trabecular bone (FD_{Sta}), and texture aspect ratio (Str) were calculated. The association between groups with increasing baseline fractal parameters (defined using tertiles) with risk of JR was examined using logistic regression.
Results: 28 (25%) participants' study knees underwent KJR over 6 years. Participants with KJR had lower medial FD_{MEAN} and FD_H parameters ($P = 0.02$ for difference). With increasing FD_{MEAN}, adjusted for age, gender, body mass index (BMI), osteophyte grade, joint space narrowing (JSN) grade and WOMAC pain score, the odds of KJR was reduced ($P = 0.04$ for trend).
Conclusion: This study suggests that the texture of medial tibial trabecular bone measured from plain radiographs is related to the risk of KJR: with increasing FD_{MEAN} (the overall measure of bone texture roughness) the risk of KJR was reduced, independent of other clinical predictors of joint replacement. Tibial trabecular bone texture may be a useful marker of disease progression and a target of therapy in OA.

Introduction

Subchondral bone changes are a distinctive feature of knee osteoarthritis (OA). Bone changes are present from an early stage of OA[1]. Thus, there is a great interest in developing bone analysis techniques that are able to predict incident and progressive OA and clinically relevant outcomes such as knee joint replacement (KJR). One promising approach is the numerical analysis of trabecular bone texture detected by plain radiography. Trabecular bone texture has been quantified by fractal signature analysis (FSA)[2], directional fractal signatures[3], shape parameters[4] or dissimilarity measures[5]. Studies using these techniques have shown that bone texture differs between pre-radiographic OA knees with and without cartilage defects[6], between knees with and without radiographic OA[7] and predicts incident and progressive OA[4,5]. However, whether trabecular bone texture can be used to predict JR is unknown. Previous studies showed that OA changes occur in subchondral bone well before joint space width is present, which is a proxy for cartilage loss which is often present prior to KJR[8].

The current study aimed to test the hypothesis that the mean trabecular bone texture is associated with risk of KJR. We examined a cohort of subjects with symptomatic knee OA and related trabecular bone texture at baseline to the risk of JR over 6 years. Bone texture was quantified by fractal texture parameters calculated using a variance orientation transform (VOT)[3].

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1063-4584/$ – see front matter
http://dx.doi.org/10.1016/j.joca.2013.10.017

Methods

Subjects with symptomatic knee OA were recruited by advertising and in collaboration with musculoskeletal health care providers[9]. The study was approved by the ethics committee of the Alfred and Caulfield Hospitals in Melbourne, Australia. All subjects gave their informed written consent. Inclusion criteria were age over 40, knee symptoms (at least one pain dimension of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score above 20%) and at least grade 1 osteophytes[10] were present in the knee, thus meeting American College of Rheumatology clinical and radiographic criteria for knee OA[11]. Knees with grade 4 Kellgren Lawrence (K-L) were excluded. Where both knees were symptomatic, the knee with the least severe radiographic change was included. 123 subjects entered the study.

At baseline, weight was measured to the nearest 0.1 kg (shoes and bulky clothing removed), using a single pair of electronic scales. Height was measured to the nearest 0.1 cm (shoes removed) using a stadiometer. Body mass index (BMI) (weight (kg)/height^2 (m)) was calculated. Pain, stiffness and function were assessed by WOMAC (VAS, 100 mm per question).

Radiographs were obtained at baseline. Each subject had a weight-bearing anteroposterior tibio-femoral radiograph, taken in full extension, of their symptomatic knee. A film cassette (24 × 30 cm) that contained a sheet of Kodak T-Grain film and a single Kodak Lanex Fine Screen was used for all patients. The radiographic films obtained were digitized with a scan mode of 16-bit RGB and an optical resolution of 256 dpi. Digitized films were converted to 8-bit gray scale level images with a pixel resolution of 0.1 × 0.1 mm.

The knees were individually scored by two trained observers who classify disease in the medial and lateral tibio-femoral joint according to OARSI atlas[10]. Intraobserver and interobserver reproducibilities (k statistic) were 0.93 and 0.86 for osteophytes (grade 0,1 v 2,3) and 0.93 and 0.85 for joint space narrowing (JSN) (grade 0,1 v 2,3).

In each X-ray image, 128 × 128 pixel trabecular bone texture regions of interest (ROIs) were selected on the subchondral bone immediately under the medial and lateral cortical plates of the tibia using an automated method[12]. The ROI covers a bone area of 12.8 × 12.8 mm.

Each medial and lateral trabecular bone ROI was quantified by the means of five fractal texture parameters:

- Mean (FD_{MEAN}), horizontal (FD_H) and vertical (FD_V) fractal dimensions: These FDs are a measure of the overall (FD_{MEAN}), and then specifically the vertical (FD_H) and horizontal (FD_H) direction roughness of trabecular bone texture, respectively.
- Minor axis fractal dimension (FD_{Sta}): This provides a measure of texture roughness in the direction of the roughest part of trabecular bone. The part contains the shortest bone length components.
- Texture aspect ratio (Str): This measures a degree of the bone anisotropy, taking values between 0 and 1. A higher anisotropy corresponds to a lower value of the aspect ratio.

FD_{MEAN}, FD_{Sta}, FD_H, FD_V and Str were calculated as the mean of fractal signatures FS_{MEAN}, FS_{Sta}, FS_H, FS_V, and aspect ratio signature StrS, respectively. The signature parameters were FDs calculated at individual scales obtained using a VOT method[3,6]. The averaging was performed over trabecular image sizes ranging from 0.6 to 1.4 mm with steps of 0.1 mm.

Subjects were contacted at year 6 to determine whether they had JR.

Statistics

Baseline characteristics of the subjects were tabulated. Unpaired Student's t tests, Mann–Whitney U tests and Chi-square tests, where appropriate, were used to compare baseline characteristics between subjects who did and those who did not undergo a JR. The relationship between texture parameters and the incidence of JR was studied by means of logistic regression. As the fractal parameters were not normally distributed, subjects were categorized into groups, using tertiles, of each fractal parameter. The first group has the lowest values of parameters. Odds ratios (ORs) were calculated for the two groups with the higher parameters in comparison with the first group (reference). Results were adjusted for baseline age, sex, BMI, WOMAC score and grade of osteophyte and JSN for the respective compartment. $P < 0.05$ was considered as significant. Analyses were performed using IBM SPSS statistical software (version 20.0; SPSS, Cary, NC).

Results

Of the 123 subjects in the original study, complete data was available for 114 participants (93%). The reasons for non-participation were that in seven cases, radiographs were not available for digitisation and in two cases, the quality of digitised radiographs was inadequate for fractal analysis. Whilst those lost to follow up were younger than those who completed the study (mean age 57.4 vs 63.9 years old) there were no other significant differences between them. The baseline characteristics of those who underwent KJR were compared to those who did not (Table I). In those who underwent KJR all WOMAC scores were higher and the severity of medial tibiofemoral osteophyte was worse at baseline. Whilst baseline FD_{MEAN} and FD_H was significantly lower in those who underwent JR, there were no differences in other texture parameters.

We examined whether the groups with increased fractal texture parameters were predictive of KJR. In the medial compartment, with increasing medial FD_{MEAN}, there was a reduction in risk of KJR ($P = 0.02$), after adjustment for age, sex, BMI and grade of medial tibiofemoral osteophytes and JSN (Table II). The only other significant predictor of KJR was the grade of medial tibiofemoral osteophyte (OR = 2.0, 95% CI [1.27, 3.13], $P = 0.003$). For other texture parameters the adjusted odd ratios were not significant.

To better understand the relationship between KJR and increasing medial FD_{MEAN}, we examined the relationship of the parameter and the severity of medial JSN and osteophytes. Whilst increasing grade of JSN was related to increased FD_{MEAN} (Chi-square, $P = 0.96$), there was no relationship between FD_{MEAN} and the grade of medial tibiofemoral osteophyte (Chi-square, $P = 0.01$). This suggests that FD_{MEAN} is an independent predictor of KJR.

We performed the same analysis in the lateral compartment. We found that with increasing lateral fractal parameters results were similar to those obtained in the medial compartment, although they did not reach statistical significance.

Discussion

In this prospective study of 123 subjects with mild to moderate OA we found that knees with lower trabecular bone texture mean fractal dimension (FD_{MEAN}) at baseline had an increased risk of KJR over 6 years. This association was linear and independent of age, gender, BMI, grade of osteophyte and JSN. This is the first report relating trabecular bone texture to risk of KJR, and showing that fractal measures may contribute to the identification of people with OA at higher risk of KJR.