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ORIGINAL RESEARCH

# Self-Reported Weather Sensitivity is Associated with Clinical Symptoms and Structural Abnormalities in Patients with Knee Osteoarthritis: A Cross-Sectional Study

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## ABSTRACT

*Introduction*: Patients with knee osteoarthritis (KOA) often complain about clinical symptoms affected by weather-related factors. The purpose of the present study was to use cross-sectional analysis to determine whether weather sensitivity was associated with clinical symptoms, as well as structure abnormalities, in KOA patients.
*Methods*: Data from 80 participants were obtained from the Feng Hans Shi Effects on OA (FHS) study, an OA cohort study initiated in

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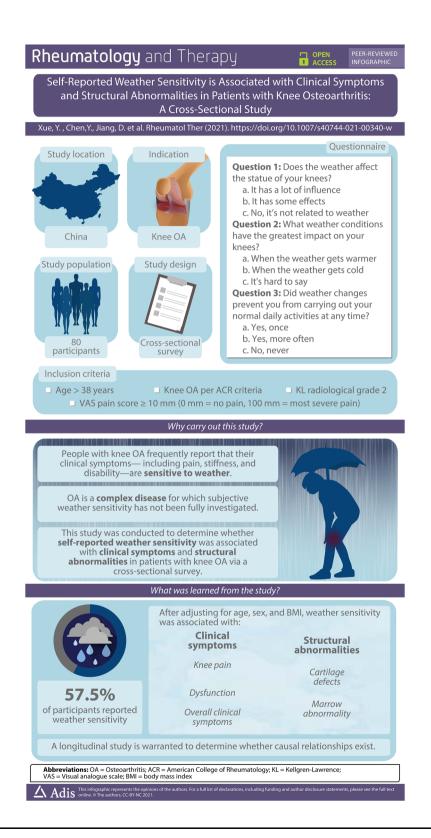e-mail: ningtcm@126.com

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China in 2015. The weather sensitivity of each participant was determined by a self-reported questionnaire. The following measurements were used to assess clinical outcomes: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for symptoms, and semi-quantitative Whole-Organ Magnetic Resonance Imaging Score (WORMS) for cartilage defects and marrow abnormalities of magnetic resonance imaging (MRI). Chi-square with Cochran–Armitage test for trend and regression analysis were used to evaluate the associations between weather sensitivity and WOMAC and WORMS of KOA patients.
*Results*: Most of the KOA participants (57.5%) perceived the weather as affecting their knee-joint clinical symptoms. After adjusting for age, gender, and body mass index (BMI), weather sensitivity was not only associated with knee pain [OR = 3.3 (95% CI 1.1, 9.9), $P = 0.032$], dysfunction [OR = 5.5 (95% CI 1.8, 16.8), $P = 0.003$], and overall clinical symptoms [OR = 3.3 (95% CI 1.1, 10.2), $P = 0.034$], but also associated with cartilage defect [OR = 3.1 (95% CI 1.1, 8.5), $P = 0.027$] and marrow abnormality [OR = 3.0 (95% CI 1.1, 8.1), $P = 0.029$].
*Conclusions*: In KOA patients, weather sensitivity was associated with clinical symptoms and structural abnormalities. Future longitudinal study is warranted for the causal relationship.

*Infographic*:

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## Self-Reported Weather Sensitivity is Associated with Clinical Symptoms and Structural Abnormalities in Patients with Knee Osteoarthritis: A Cross-Sectional Study

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**Study location**
China

**Indication**
Knee OA

**Study population**
80 participants

**Study design**
Cross-sectional survey

**Questionnaire**

**Question 1:** Does the weather affect the statue of your knees?
a. It has a lot of influence
b. It has some effects
c. No, it's not related to weather

**Question 2:** What weather conditions have the greatest impact on your knees?
a. When the weather gets warmer
b. When the weather gets cold
c. It's hard to say

**Question 3:** Did weather changes prevent you from carrying out your normal daily activities at any time?
a. Yes, once
b. Yes, more often
c. No, never

**Inclusion criteria**

☐ Age > 38 years   ☐ Knee OA per ACR criteria   ☐ KL radiological grade 2
☐ VAS pain score ≥ 10 mm (0 mm = no pain, 100 mm = most severe pain)

## Why carry out this study?

People with knee OA frequently report that their clinical symptoms— including pain, stiffness, and disability—are **sensitive to weather**.

OA is a **complex disease** for which subjective weather sensitivity has not been fully investigated.

This study was conducted to determine whether **self-reported weather sensitivity** was associated with **clinical symptoms** and **structural abnormalities** in patients with knee OA via a cross-sectional survey.

## What was learned from the study?

After adjusting for age, sex, and BMI, weather sensitivity was associated with:

**57.5%**
of participants reported weather sensitivity

**Clinical symptoms**

*Knee pain*

*Dysfunction*

*Overall clinical symptoms*

**Structural abnormalities**

*Cartilage defects*

*Marrow abnormality*

A longitudinal study is warranted to determine whether causal relationships exist.

**Abbreviations:** OA = Osteoarthritis; ACR = American College of Rheumatology; KL = Kellgren-Lawrence; VAS = Visual analogue scale; BMI = body mass index

| Key Summary Points |
| --- |
| Knee osteoarthritis (KOA) is a multifactorially disease. |
| People with KOA frequently report that their clinical symptoms were sensitive to weather. |
| The purpose of the study was to determine the association between self-reported weather sensitivity and clinical symptoms as well as structural abnormalities in a cross-sectional design. |
| The results show that weather sensitivity present was independently associated with knee pain, cartilage defect, and marrow abnormality. |

## DIGITAL FEATURES

This article is published with digital features, including an infographic, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.15135216.

## INTRODUCTION

Knee osteoarthritis (KOA) is a very complicated pathophysiologic joint disease and one of the main causes of disability worldwide [1–3]. The main characteristics of KOA are knee cartilage wear, subchondral bone sclerosis, and deformation of the surrounding bone. KOA patients often experience joint pain and joint movement limitations, as well as other symptoms [4–6].

People with KOA frequently report weather conditions that affect the clinical symptoms of their knees, including pain, stiffness, and disability [7]. Furthermore, many patients with OA feel that they are sensitive to the weather, with changes in temperature affecting their symptoms [8]. Several studies have explored the influence of weather parameters on KOA. For example, research on the association between perceived weather change and OA has been conducted. Desirée et al. [9] assessed the correlation between the surrounding weather conditions and clinical symptoms of patients with OA in the Netherlands. Timmermans et al. [7] also investigated differences in perception of the effects of weather on joint pain among elderly people with OA in six European countries under different weather conditions. Brennan et al. [10] explored whether weather (in)stability has a greater impact on joint structures and pain perception in individuals from southern Europe. However, all of these studies emphasized objective and external weather parameters rather than subjective and internal feelings from patients. Given that OA is a multifactorial disease with a more individualized treatment approach, and subjective perception of temperature is often not consistent with actual changes in temperature, it is necessary to evaluate the influence of self-perceived weather sensitivity on KOA. Moreover, the relationship of weather sensitivity to clinical symptoms and structural abnormalities has not been fully investigated, and remains unclear.

Therefore, the purpose of this study was to determine whether weather sensitivity from subjective feelings had an association with clinical symptoms and structural abnormalities in KOA patients in a cross-sectional design.

## METHODS

### Design and Study Samples

Our study population comprised a subsample of participants of the Feng Hans Shi Effects on OA (FHS) study, which was a multicenter, prospective, cohort study focusing on KOA, from July 2015 to July 2017, at three clinical centers. In

this study, 80 KOA patients were randomly selected from one of the sub-centers. This study was registered at the Chinese Clinical Trial Registry (ChiCTR1800017777). All participants were interviewed and examined by trained researchers in hospital outpatient departments via related questionnaires and instruments.

The inclusion criteria were as follows: (1) older than 38 years; (2) diagnosis of primary KOA according to the American College of Rheumatology criteria (ACR)[9]; (3) Kellgren–Lawrence (KL) radiological grade 2[11]; and (4) visual analogue scale (VAS) pain score $\geq$ 10 mm (0 mm = no pain, 100 mm = most severe pain). Participants were excluded from the study if they met any of the following exclusion criteria at the beginning of, or during, the study: (1) rheumatoid arthritis; (2) serious cardiovascular or kidney diseases; (3) severe KOA and recently proposed to take knee-joint replacement surgery; (4) magnetic resonance imaging (MRI) contraindications such as the installation of pacemakers, artificial metal valves, or cornea/artery retention.

## Self-Perceived Weather Sensitivity

To assess self-perceived weather sensitivity, participates were asked to answer a questionnaire concerning weather sensitivity, which included three questions, each with three types of answers. These questions were also referred to published questionnaire concerning weather sensitivity (Table S1) [10].

Patients who chose option A or B for any of the three questions were classified as weather-sensitive patients, while those who chose option C for all three questions were classified as non-weather-sensitive patients.

## Assessment of Osteoarthritis Symptoms

The clinical characteristics included basic demographic data and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which measures knee pain (five items), stiffness (two items), and function (17 items) over the past 48 h. The traditional 24-item WOMAC is scored using a VAS ranging

from "none" to "most severe" (the total range is from 0 to 240; higher scores indicate worse KOA symptoms) [12]. The VAS was used to assess knee pain for initial participant screening.

## MRI Acquisition and Assessment of Knee Structure

Participants underwent MRI of the knees using the same superconducting magnetic resonance scanners (1.5 Tesla, Achieva, Philips, The Netherlands). Imaging sequences included the following: sagittal proton density (PD)-weighted fast spin-echo (FSE) (TR 4800 ms, TE 35 ms, 3-mm slice thickness, 0-mm interslice gap, 32 slices, $288 \times 192$ matrix, 2 NEX, 140-mm 2 FOV, 8 ETL); axial T2-weighted (TR 4680 ms, TE 13 ms, 3-mm slice thickness, 0-mm interslice gap, 20 slices, $288 \times 192$ matrix, 2 NEX, 140-mm 2 FOV, 8 ETL); and coronal PD-FSE (TR 6650 ms, TE 15 ms, TI 100 ms, 3-mm slice thickness, 0-mm interslice gap, 28 slices, $256 \times 192$ matrix, 2 NEX, 140-mm 2 FOV, 8 ETL).

Cartilage and bone marrow lesions were assessed using the semi-quantitative Whole-Organ Magnetic Resonance Imaging Score (WORMS) method [13] for KOA. The assessment of cartilage defects was based on 14 regions, which were made up of the medial and lateral compartments of the tibia (anterior, central, and posterior), femur (anterior, central, and posterior), and patella. Bone marrow lesions were graded in the 14 regions mentioned above, as well as in the region of the tibia beneath the tibial spine.

Cartilage signal and morphology were scored with an eight-point scale, as follows: 0 = normal thickness and signal; 1 = normal thickness but increased signal on T2-weighted images; 2.0 = partial-thickness focal defect < 1 cm in greatest width; 2.5 = full-thickness focal defect < 1 cm in greatest width; 3 = multiple areas of partial-thickness (Grade 2.0) defects intermixed with areas of normal thickness, or a Grade 2.0 defect wider than 1 cm but < 75% of the region; 4 = diffuse ($\geq$ 75% of the region) partial-thickness loss; 5 = multiple areas of full-thickness loss (grade 2.5) or a grade-2.5 lesion

**Table 1** Characteristics of the KOA participants according to weather sensitivity

| Characteristic | Non-weather-sensitive group ($n = 34$) | Weather-sensitive group ($n = 46$) | P value |
|---|---|---|---|
| Age (years) | 61.1 (1.1) | 61.8 (0.9) | 0.638 |
| Gender (% female) | 21 (35) | 39 (65) | **0.019**[a] |
| Height (cm) | 162.7 (1.3) | 161.7 (1.0) | 0.538 |
| Weight (kg) | 63.3 (1.8) | 63.6 (1.2) | 0.883 |
| BMI (kg/m$^2$) | 23.8 (0.5) | 24.4 (0.5) | 0.427 |
| KOA duration (months) | 24.2 (1.3) | 22.2 (1.1) | 0.264 |
| VAS pain (0-100 mm) | 26.1 (1.4) | 30.0 (1.5) | 0.085 |

Bold value indicate the $P < 0.05$

Results displayed as mean (SEM) unless otherwise indicated, $P$ values for independent $t$ tests unless otherwise indicated

*BMI* body mass index, *KOA* knee osteoarthritis, *VAS* visual analogue scale/score

[a] Pearson Chi-squared test

wider than 1 cm but < 75% of the region; 6 = diffuse (≥ 75% of the region) full-thickness loss.

Subarticular bone marrow abnormality was defined as poorly marginated areas of increased signal intensity in the normally fatty epiphyseal marrow on PD-weighted FSE images. The following four-point grading scale was used: 0 = none; 1 = less than 25% of the region; 2 = 25–50% of the region; 3 = greater than 50% of the region.

All images were scored by two orthopedists with over 10 years of clinical experience who were blinded to each patient's personal information. WORMS of 30 randomly selected subjects were then scored independently by them to determine intra- and inter-rater reproducibility. Intraclass correlation coefficients (ICCs) for intra- and inter-reader agreement of the WORMS cartilage scores were 0.973 (95% CI 0.944, 0.987) and 0.986 (95% CI 0.971, 0.993), respectively. For WORMS marrow abnormality scores, intra-reader ICC was 0.972 (95% CI 0.942, 0.986) and inter-reader ICC was 0.986 (95% CI 0.970, 0.993).

### Statistical Analysis

Differences in characteristics between weather-sensitive and non-weather-sensitive KOA participants were examined with independent sample $t$-tests for continuous data (except WOMAC and WORMS) and Chi-square tests for categorical data.

According to the quartile of all participants in the cross-sectional analysis, WOMAC and WORMS were converted into four levels of categorical variables by interquartile range for further analysis. The differences in WOMAC and WORMS between weather-sensitive and non-weather-sensitive participants were first tested using Pearson's Chi-square tests and Fisher's exact tests. Cochran–Armitage tests for linear trends were also conducted for variables that showed statistically significant relationships following Chi-square tests. In addition, a Mann–Whitney test was used to compare the WORMS between the weather-sensitive group and non-weather-sensitive group.

Binary logistic regression analysis was applied to estimate the association of weather sensitivity with WOMAC and WORMS scores. When included in the regression analysis, originally discrete variables of them were converted into binary dependent factors via the median, while the presence or absence of weather sensitivity was used as an independent factor. All models were adjusted for age, gender, and body mass index (BMI).

All statistical analyses were performed in IBM SPSS Statistics (version 17.0) and R (version

**Table 2** Comparison of KOA participants with and without weather sensitivity in WOMAC

| WOMAC | | Non-weather-sensitive group ($n = 34$) | Weather-sensitive group ($n = 46$) | Total participants ($n = 80$) | $\chi 2$ | P for independence (Pearson's Chi-square test) | P for trend (Cochran–Armitage trend tests) |
|---|---|---|---|---|---|---|---|
| Pain score (0–50) | ≤ 5.5 | 14 (41.2%) | 6 (13%) | 20 (25%) | 10.539 | **0.014** | **< 0.001** |
| | 5.5–10.6 | 9 (26.5%) | 11 (23.9%) | 20 (25%) | | | |
| | 10.6–19.5 | 7 (20.6%) | 14 (30.4%) | 21 (26.3%) | | | |
| | > 19.5 | 4 (11.8%) | 15 (32.6%) | 19 (23.8%) | | | |
| Stiffness score (0–20) | ≤ 0.9 | 15 (44.1%) | 5 (10.9%) | 20 (25%) | 17.401 | **0.001** | **0.003** |
| | 0.9–4.5 | 5 (14.7%) | 16 (34.8%) | 21 (26.3%) | | | |
| | 4.5–9.0 | 11 (32.4%) | 10 (21.7%) | 21 (26.3%) | | | |
| | > 9.0 | 3 (8.8%) | 15 (32.6%) | 18 (22.5%) | | | |
| Function score (0–170) | ≤ 16.9 | 15 (44.1%) | 5 (10.9%) | 20 (25%) | 15.754 | **0.001** | **< 0.001** |
| | 16.9–31.1 | 10 (29.4%) | 10 (21.7%) | 20 (25%) | | | |
| | 31.1–61.5 | 5 (14.7%) | 15 (32.6%) | 20 (25%) | | | |
| | > 61.5 | 4 (11.8%) | 16 (34.8%) | 20 (25%) | | | |
| Total score (0–240) | ≤ 26.9 | 15 (44.1%) | 5 (10.9%) | 20 (25%) | 13.299 | **0.004** | **< 0.001** |
| | 26.9–51.7 | 8 (23.5%) | 12 (26.1%) | 20 (25%) | | | |
| | 51.7–87.0 | 7 (20.6%) | 13 (28.3%) | 20 (25%) | | | |
| | > 87.0 | 4 (11.8%) | 16 (34.8%) | 20 (25%) | | | |

Bold value indicates the $P < 0.05$
*WOMAC* Western Ontario and McMaster University Osteoarthritis Index

**Table 3** Comparison of KOA participants with and without weather sensitivity in WORMS

| WORMS | | Non-weather-sensitive group ($n = 33$) | Weather-sensitive group ($n = 44$) | Total participants ($n = 77$) | $\chi 2$ | P for independence (Pearson's Chi-square test) | P for trend (Cochran–Armitage trend tests) |
|---|---|---|---|---|---|---|---|
| Cartilage score (0–84) | $\leq 10.5$ | 12 (36.4%) | 8 (18.2%) | 20 (26%) | 7.959 | **0.047** | **0.015** |
| | 10.5–15.0 | 11 (33.3%) | 9 (20.5%) | 20 (26%) | | | |
| | 15.0–20.0 | 4 (12.1%) | 15 (34.1%) | 19 (24.7%) | | | |
| | > 20.0 | 6 (18.2%) | 12 (27.3%) | 18 (23.4%) | | | |
| Marrow abnormality score (0–45) | 0.0 | 22 (66.7%) | 14 (31.8%) | 36 (46.8%) | 10.256 | **0.014**[a] | **0.009** |
| | 1.0 | 1 (3.0%) | 4 (9.1%) | 5 (6.5%) | | | |
| | 1.0–5.0 | 5 (15.2%) | 18 (40.9%) | 23 (29.9%) | | | |
| | > 5.0 | 5 (15.2%) | 8 (18.2%) | 13 (16.9%) | | | |

Bold value indicates the $P < 0.05$
*WORMS* Whole-Organ Magnetic Resonance Imaging Score
[a] Fisher's exact test

3.6.1). Two-tailed tests set at $P < 0.05$ were used to determine statistical significance.

# RESULTS

## Participant Characteristics

A total of 80 subjects (75% women) were recruited. Of those, 34 (42.5%) reported no weather sensitivity, whereas 46 (57.5%) did report having weather sensitivity. A total of 96% of the participants ($n = 77$, three patients did not undergo examinations) acquired MRI of the knees. The average age was 61.5 years. The mean ($\pm$ standard of the mean [SEM]) values for height, weight, BMI, KOA duration, and VAS pain were as follows: 162.1 ($\pm$ 0.8) cm, 63.5 ($\pm$ 1.0) kg, 24.1 ($\pm$ 0.3) kg/m$^2$, 23.1 ($\pm$ 0.9) months, and 28.3 ($\pm$ 1.1) mm, respectively. The characteristics of non-weather-sensitive and weather-sensitive participants are presented in Table 1. There were no significant differences in demographic factors between the two groups, with the exception that there was a higher proportion of women (65%) in the weather-sensitive group.

## Relation of Weather Sensitivity and WOMAC

The data showed significant differences in WOMAC pain scores [$\chi^2$ (3, $n = 80$) = 10.539; $P = 0.014$], stiffness scores [$\chi^2$ (3, $n = 80$) = 17.401; $P = 0.001$], function scores [$\chi^2$ (3, $n = 80$) = 15.754; $P = 0.001$], and total scores [$\chi^2$ (3, $n = 80$) = 13.299; $P = 0.004$] in the ratio of quartile distribution between non-weather-sensitive and weather-sensitive participants (Table 2). The Cochran-Armitage tests for linear trends suggested that higher WOMAC pain ($P < 0.001$), stiffness ($P = 0.003$), function ($P < 0.001$), and total scores ($P < 0.001$) were all associated with weather sensitivity (Table 2).
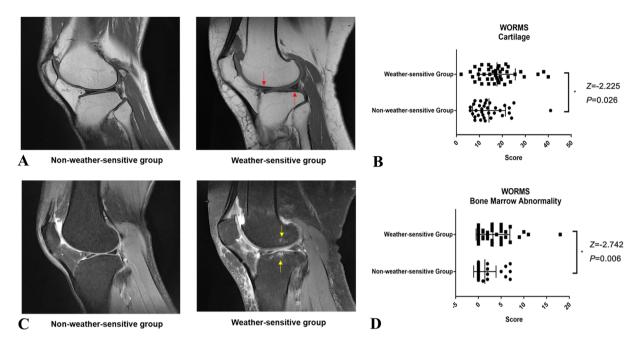
**Fig. 1** Comparison of KOA participants with and without weather sensitivity in Cartilage and Marrow abnormality. **A** Magnetic resonance images (SAG T1-weighted FSE) of two groups. *Red arrowheads* show cartilage loss of the lateral tibia and femur. **B** The cartilage defects were obviously increased in weather-sensitive group ($^*P < 0.05$). **C** Magnetic resonance images (SAG PD FSE) of two groups. *Yellow arrowheads* showed bone marrow abnormality of the medial tibia and femur. **D** The marrow abnormalities were obviously increased in weather-sensitive group ($^*P < 0.05$)

## Relation of Weather Sensitivity and WORMS

With regard to the comparison of non-weather-sensitive and weather-sensitive group, significant differences were tested for the ratio of quartile distribution of WORMS cartilage [$\chi^2$ (3, $n = 77$) = 7.959; $P = 0.047$] and marrow abnormality scores [$\chi^2$ (3, $n = 77$) = 10.256; $P = 0.014$] (Table 3). In overall value, WORMS cartilage ($Z = -2.225$, $P = 0.026$) and marrow abnormality scores ($Z = -2.742$, $P = 0.006$) of the weather-sensitive group were higher than those of the non-weather-sensitive group (Fig. 1). Furthermore, analysis for trends indicated that WORMS cartilage ($P = 0.015$) and marrow abnormality scores ($P = 0.009$) were both associated with weather sensitivity (Table 3).

## Association of Weather Sensitivity with WOMAC and WORMS

Binary logistic regression analysis revealed that weather sensitivity present was independently associated with severe knee pain [OR = 3.6 (95% CI 1.4, 9.1), $P = 0.008$], severe knee dysfunction [OR = 5.7 (95% CI 2.2, 15.3), $P < 0.001$], and severe overall clinical symptoms of knee [OR = 3.6 (95% CI 1.4, 9.1), $P = 0.008$) (Table 4). After adjusting for age, gender, and BMI, we found that weather-sensitive participants were more likely to have severe knee pain [OR = 3.3 (95% CI 1.1, 9.9), $P = 0.032$], severe knee dysfunction [OR = 5.5 (95% CI 1.8, 16.8), $P = 0.003$], and severe overall clinical symptoms of knee [OR = 3.3 (95% CI 1.1, 10.2), $P = 0.034$] (Table 4).

Univariably, weather sensitivity was independently related to cartilage defect [OR = 3.7 (95% CI 1.4, 9.5), $P = 0.008$] and marrow abnormality [OR = 3.3 (95% CI 1.3, 8.6), $P = 0.014$] (Table 4). After adjusting for age,

**Table 4** Associations of weather sensitivity present with WOMAC and WORMS

| Variables | Weather sensitivity present | | | | | |
|---|---|---|---|---|---|---|
| | Unadjusted | | | Adjusted[a] | | |
| | OR | 95% CI | P value | OR | 95% CI | P value |
| WOMAC | | | | | | |
| Degree of knee pain | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 3.6 | (1.4–9.1) | **0.008** | 3.3 | (1.1–9.9) | **0.032** |
| Degree of knee stiffness | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 1.7 | (0.7–4.2) | 0.245 | 1.1 | (0.4–3.0) | 0.900 |
| Degree of knee dysfunction | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 5.7 | (2.2–15.3) | **< 0.001** | 5.5 | (1.8–16.8) | **0.003** |
| Degree of overall clinical symptoms of knee | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 3.6 | (1.4–9.1) | **0.008** | 3.3 | (1.1–10.2) | **0.034** |
| WORMS | | | | | | |
| Degree of the cartilage defect | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 3.7 | (1.4–9.5) | **0.008** | 3.1 | (1.1–8.5) | **0.027** |
| Degree of marrow abnormality | | | | | | |
| Mild | 1.0 [Reference] | | | 1.0 [Reference] | | |
| Severe | 3.3 | (1.3–8.6) | **0.014** | 3.0 | (1.1–8.1) | **0.029** |

Bold value indicates the $P < 0.05$
Independent variable: weather sensitivity present; Dependent variable: degree of knee clinical symptoms and structural abnormalities (dichotomized by the median). Mild: the value is less than the median; Severe: the value is more than the median
*CI* confidence interval, *OR* odds ratio
[a] Adjusted for age, gender, BMI

gender, and BMI, the weather-sensitive participants tended to have severe cartilage defect [OR = 3.1 (95% CI 1.1, 8.5), $P = 0.027$] and severe marrow abnormality [OR = 3.0 (95% CI 1.1, 8.1), $P = 0.029$] (Table 4).

For all the variables that entered the regression analysis (not shown), the variance inflation factor (VIF) for quantifying the severity of multiple collinearities was between 1.013 and 1.104 (WOMAC formulation) and 1.018 and 1.117 (WORMS formulation), indicating that there was no statistical caveat caused by the strong correlation between the explanatory variables.

# DISCUSSION

To our knowledge, the current study was the first to investigate the association between self-reported weather sensitivity and clinical symptoms and structural abnormalities assessed using MRI in KOA patients.

KOA is a chronic disease with high heterogeneity, and patients' clinical symptoms often fluctuate and recur. As a small sample study, the current study needed to avoid as much bias as possible in order to ensure the reliability of the results. Therefore, the cases included in the study were all symptomatic KOA patients (VAS pain score $\geq 10$ mm) with generally mild radiographic features (KL grade = 2).

There were significant composition ratio differences in WOMAC scores between the participants with or without weather-sensitivity, and the Cochrane–Armitage test indicated a trend across different WOMAC levels. Collectively, KOA patients in the weather-sensitive group were more likely to have higher WOMAC scores. After the correction of confunders, weather sensitivity was found to have an independent association with knee pain, dysfunction, and overall clinical symptoms. In our results, there was a significant difference in WOMAC pain scores between the weather-sensitive and weather-insensitive groups, however, difference in VAS scores was not significant. The possible reason is that VAS method is relatively more concise, whereas the WOMAC pain score with five items refining specific evaluation components may reflect patients' conditions more accurately and reliably [12, 14].

As a multifactorial disease, the clinical symptoms of KOA may be altered by external factors, such as environmental and climatic factors [15–17]. We found that there was a strong correlation between weather sensitivity and knee pain and dysfunction. This result may have been due to weather-sensitive patients being more vulnerable to external climate change, thus aggravating the symptoms associated with KOA. Despite a previous study that reported weather was not associated with pain [18], a number of studies have confirmed that weather factors are inextricably linked to knee pain [7, 8, 17, 19–21]. In a randomized placebo-controlled trial of glucosamine, weather conditions were found to influence pain in OA patients [8]. A 2-week clinical study in European KOA participants also showed that weather-sensitive individuals suffered more joint pain than did non-weather-sensitive individuals [7]. Another study has also reported that weather can affect OA symptoms of pain and disability [22].

In a study of Russian clinical samples, climatic factors were found to affect the radiological severity of OA patients [23]. Due to the limitations of radiography, MRI has been identified by the Osteoarthritis Research Society International (OARSI) as the most appropriate imaging modality to assess joint status in OA research studies [24]. We thus used WORMS scores to evaluate and reflect joint structure. In our present study, weather sensitivity was related to the cartilage and marrow abnormalities, with a proportion of patients in the weather-sensitive group coinciding with the increased scores of WORMS. By adjusting the covariance, weather sensitivity was also independently associated with knee cartilage defects and bone marrow abnormalities. Related studies have found that the weather may affect the contraction of different tissues in the affected joint and lower temperatures may lead to increased viscosity of synovial fluid in the joint cavity, which may cause joint pain and stiffness [15, 16]. In addition, weather changes can also lead to early changes in bones and joints [25]. It is possible that weather-sensitive patients are more likely to be affected by weather factors than are non-weather-sensitive patients, implying a potential physiological mechanism for joint degeneration in OA [7].

Previous studies performed in the United States, Australia, and Europe have primarily focused on objective weather parameters rather than individual perceptions of weather, such as barometric pressure, ambient temperature and relative humidity [8, 20]. With the increasing importance of patient subjective feeling in clinical practice, patient-reported outcome had been appeared more importantly, and had been approved by OARSI as one of clinical trials recommendations [26]. Since the influence of

weather on the human body varies across individuals, we focused on analyzing subjective self-perception of weather in KOA patients in our present study. Furthermore, by targeting weather reflection of interindividual differences in subjective experiences of pain, using quantitive joint structural assessment, we also obtained objective evaluations of the relationship of self-perceived weather sensitivity with cartilage defects and bone marrow abnormalities in KOA patients.

Our present study also had some potential limitations. Firstly, we only included cross-sectional analyses. The relatively small sample size of our study is also a limiting factor. Secondly, our questionnaire on weather conditions only referred to temperature changes, whereas other weather factors, such as precipitation, atmospheric pressure, humidity, and wind speed, were not considered [27]. Therefore, association between weather sensitivity and symptomatic or structural features of the knee joint may be biased by those factors above. Thirdly, as few studies examined the correlation between weather sensitivity and osteoarthritis clinical symptoms, the reliability and validity examination of the conducted instrument were lack. Pain, as a subjective experience, is usually influenced by complex interactions of biological, psychological, and social factors [28]. It is partly possible that the associations detected between the questions posed to determine the sensitivity to changes in temperature with OA damage are spuriously due to the global component of pain. Indeed, future studies testing the performance of the instrument using to detect changes in the pain by the weather would further enhance validity of the scale. Most importantly, more longitudinal studies are warranted to further clarify the causal relationship between weather sensitivity and KOA.

## CONCLUSIONS

The current results imply the associations of weather sensitivity and clinical symptoms and structural degradations in KOA patients. Weather-sensitive individuals may be more likely to exhibit severe knee pain, dysfunction,

as well as cartilage defects and marrow abnormalities, however, the causal relationship between weather sensitivity and OA is still unclear.

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Traditional Chinese Medicine (approval number: 2013-296-65-01) and performed in accordance with the Helsinki Declaration of 1964, and its later amendments. Informed consent was obtained from each participant included in the present study.

*Data Availability.* The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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