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

Yan Xue
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese University

Yan Chen
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Ding Jiang
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Lin Wang
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Xuezong Wang
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Ming Li
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Yuyun Wu
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Min Zhang
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Jian Pang
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Hongsheng Zhan
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Yuxin Zheng
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

Daofang Ding
Shanghai University of Traditional Chinese Medicine

Yuelong Cao (ningtcm@126.com)
Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine

https://orcid.org/0000-0001-5883-0347

Research article
Abstract

Background

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 China in 2015. The weather sensitivity of each participant was determined by a self-reported questionnaire. The following measurements were used to assess clinical and biological outcomes: a visual analog scale (VAS) for pain; Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC); and blood levels of tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and interleukin 1 (IL-1). Structural changes identified via magnetic resonance imaging (MRI) were also evaluated. Independent sample t-tests, chi-square tests, Fisher's exact tests, Cochran-Armitage tests for linear trends, and binary linear regression were used to evaluate the clinical characteristics, biomarkers, WOMAC, and Whole-Organ Magnetic Resonance Imaging Score (WORMS) of weather-sensitive KOA patients and non-weather-sensitive KOA patients.

Results

Most of the KOA participants (57.5%) perceived the weather as affecting their knee-joint clinical symptoms. Through logistic regression analysis, the presence of weather sensitivity was found to increase the risk of KOA participants reporting higher levels of WOMAC pain scores [OR = 3.3 (95% CI: 1.1, 9.9), P > 0.032], functional scores [OR = 5.5 (95% CI: 1.8, 16.8), P > 0.003], total scores [OR = 3.3 (95% CI: 1.1, 10.2), P = 0.034], WORMS cartilage scores [OR = 3.1 (95% CI: 1.1, 8.5), P < 0.027], and marrow abnormality scores [OR = 3.0 (95% CI: 1.1, 8.1), P > 0.029].

Conclusions

Weather-sensitive KOA patients were prone to show more serious clinical symptoms and structural abnormalities in their knee joints. Therefore, the existence of weather sensitivity may accelerate the progress of KOA.

Background

Knee osteoarthritis (KOA) is a degenerative 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. Therefore, 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 think that they are sensitive to the weather, such as via changes in temperature that affect their OA symptoms(8). Several studies have explored the influence of weather parameters on KOA. For example, research on the perceived association between weather change and OA has been conducted. Desirée et al. assessed the correlation between the surrounding weather conditions and clinical symptoms of patients with OA in the Netherlands(9). Timmermans et al. 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(7). Brennan et al. explored whether weather (in)stability has a greater impact on joint structures and pain perception in individuals from Southern Europe(10). 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 with clinical symptoms and structural abnormalities has not been fully investigated and, thus, remains unclear.

The purpose of the present study was to determine whether weather sensitivity from subjective feelings had an association with clinical symptoms and structural abnormalities assessed by magnetic resonance imaging (MRI) in KOA patients, as determined by cross-sectional analysis. Taken together, our findings suggest that weather sensitivity is likely a high-risk factor for severe KOA, which may provide valuable information for early intervention programs for KOA patients.

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 the three following clinical centers: Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine; Huadong Hospital Affiliated to Fudan University; and Zhongshan Hospital Affiliated to Guangzhou University of Traditional Chinese Medicine. In this study, 80 KOA patients were randomly selected from Shuguang Hospital affiliated to Shanghai University of traditional Chinese Medicine. 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; and (4) visual analogue scale (VAS) pain score ≥ 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) 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, participants were asked three questions concerning weather sensitivity, and there were three types of answers available for each question. These questions also referred to published questionnaires on temperature sensitivity (Table S1)(10).

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

**Clinical and biological outcomes**

The clinical characteristics included basic demographic data and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which measures knee pain (five items), knee stiffness (two items), and knee 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)(11).

Overnight-fasting venous blood samples were collected in anticoagulant tubes at baseline by a trained nurse. Blood was centrifuged at 3,500 g for 10 min to separate plasma, which was then aliquoted into collection tubes and stored at −80 °C. We used enzyme-linked immunosorbent assays (ELISAs) to analyze blood biomarkers of inflammation including tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and interleukin 1 (IL-1).

**MRI acquisition and assessment of structural changes**

A total of 96% of the participants (n = 77, three patients did not undergo examinations) underwent MRI of the knees using the same superconducting magnetic resonance scanners (1.5 T, Achieva, Philips, Netherlands) at baseline and follow-ups.

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 × 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 × 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 × 192 matrix, 2 NEX, 140-mm 2 FOV, 8 ETL).

All images were scored by two orthopedists with over 10 years of clinical experience who were blinded to each patient’s personal information. Cartilage and bone-marrow lesions were assessed using the semi-quantitative Whole-Organ Magnetic Resonance Imaging Score (WORMS) method(12) 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 (≥ 75% of the region) partial-thickness loss; 5 = multiple areas of full-thickness loss (grade 2.5) or a grade-2.5 lesion 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.

**Statistical analysis**

Differences in characteristics and biological markers 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. WOMAC and WORMS were converted into categorical variables with four levels for analyses via chi-square tests and logistic regression. We also categorized participants into quartiles for further analysis. When included in the regression analysis, originally discrete variables were converted into binary variables via the median.

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 of the weather-sensitive group and non-weather-sensitive group. Logistic regression analyses were then conducted on WOMAC and WORMS scores as the dependent variables. Binary logistic regression analysis was applied to estimate the odds ratio (OR) and 95% confidence interval (CI) for the association of weather sensitivity with WOMAC and WORMS scores. We also adjusted for covariates. The multivariable model included age, gender, and body mass index (BMI).

All statistical analyses were performed in IBM SPSS Statistics (version 17.0) and R (version 3.6.1). Two-tailed tests set at $P \leq 0.05$ were used to determine statistical significance.

**Results**
Participant characteristics

The characteristics of non-weather-sensitive and weather-sensitive participants are presented in Table 1. A total of 80 subjects (75% women) were recruited. Of these participants, 34 (42.5%) of them reported no weather sensitivity, whereas 46 (57.5%) of them did report having weather sensitivity. The average age was 61.5 years. The mean (± standard of the mean [SEM]) values for height, weight, BMI, KOA duration, and VAS pain were as follows: 162.1 (± 0.8) cm, 63.5 (± 1.0) kg, 24.1 (± 0.3) kg/m$^2$, 23.1 (± 0.9) months, and 28.3 (± 1.1) mm, respectively. No associations were found between weather sensitivity and TNF-α, IL-1, and IL-6 levels. There were no significant differences in demographic factors between the two groups, with the exception that there was a higher proportion of women in the weather-sensitive group.

Influence of weather sensitivity on WOMAC

The data revealed that the weather sensitivity of KOA participants was related to their WOMAC pain scores ($P = 0.014$), WOMAC function scores ($P = 0.001$), WOMAC stiffness scores ($P = 0.001$), and WOMAC total scores ($P = 0.004$) (Table 2). The Cochran-Armitage tests for linear trends suggested that higher WOMAC pain scores ($P < 0.001$), WOMAC stiffness scores ($P = 0.003$), WOMAC function scores ($P < 0.001$), and WOMAC total scores ($P < 0.001$) were all associated with weather sensitivity (Table 2).

Influence of weather sensitivity on WORMS

There were significant differences in the WORMS cartilage scores ($P = 0.047$) and WORMS marrow abnormality scores ($P = 0.014$) between non-weather-sensitive and weather-sensitive groups (Table 3). The WORMS cartilage scores ($P = 0.026$) and WORMS marrow abnormality scores ($P = 0.006$) of the weather-sensitive group were higher than those of the non-weather-sensitive group (Fig. 1). Furthermore, tests for trends indicated that WORMS cartilage scores ($P = 0.015$) and WORMS marrow abnormality scores ($P = 0.009$) were associated with weather sensitivity (Table 3).

Association of weather sensitivity with WOMAC and WORMS

Binary logistic regression analysis revealed that weather-sensitivity was independently associated with WOMAC pain scores [OR = 3.6 (95% CI: 1.4, 9.1), $P = 0.008$], WOMAC function scores [OR = 5.7 (95% CI: 2.2, 15.3), $P < 0.001$], and WOMAC total scores [OR = 3.6 (95% CI: 1.4, 9.1), $P = 0.008$] (Table 4). After adjusting for baseline age, gender, and body mass index, we found that weather-sensitive participants were more likely to have significantly higher WOMAC pain scores [OR = 3.3 (95% CI: 1.1, 9.9), $P = 0.032$], WOMAC function scores [OR = 5.5 (95% CI: 1.8, 16.8), P = 0.003], and WOMAC total scores [OR = 3.3 (95% CI: 1.1, 10.2), P = 0.034] (Table 4). For all variables entering regression analysis (not shown), the variance inflation factor (VIF) for quantifying the severity of multiple collinearities was between 1.013 and 1.104, indicating that there was no statistical caveat caused by the strong correlation between explanatory variables.
Binary logistic regression analysis revealed that weather sensitivity was independently related to WORMS cartilage scores [OR = 3.7 (95% CI: 1.4, 9.5), P = 0.008] and WORMS marrow abnormality scores [OR = 3.3 (95% CI: 1.3, 8.6), P = 0.014] (Table 4). After adjusting for baseline age, gender, and body mass index entered into the regression analysis, the weather-sensitive participants tended to have higher WORMS cartilage scores [OR = 3.1 (95% CI: 1.1, 8.5), P = 0.027] and WORMS marrow abnormality scores [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 VIF values were between 1.018 and 1.117, indicating that there was no statistical caveat caused by the strong correlation between the explanatory variables.

Discussion

The purpose of the present study was to investigate the relationship of weather sensitivity with clinical symptoms and structural abnormalities (via MRI of knee joints) in KOA patients. There were significant differences in WOMAC scores between the weather-sensitive and non-weather-sensitive groups. With the increase of the classification grade of WOMAC, the proportion of KOA patients in the non-weather-sensitive group was decreased, while the ratio of KOA patients in the weather-sensitive group was increased. As a result, KOA patients in the weather-sensitive group were more likely to have higher WOMAC scores compared with those in the non-weather-sensitive group. After the correction of baseline characteristics, weather sensitivity was found to be an independent risk factor for more severe knee pain, dysfunction, and overall clinical symptoms. This suggests that the presence of weather sensitivity increases the risk of severe knee pain, dysfunction, and overall clinical symptoms in KOA patients.

We found that there was a strong correlation between weather sensitivity factors and knee-joint pain and dysfunction in KOA patients. This result may have been due to weather-sensitive patients being more vulnerable to external climate change, thus aggravating the symptoms associated with KOA. Although a previous study reported that weather was not associated with pain(13), some studies have confirmed that weather factors are inextricably linked to knee joint pain(7, 8, 14 – 17). For example, in a randomized placebo-controlled trial of glucosamine, weather conditions were found to influence pain in OA patients(8). A two-week clinical study of European KOA also showed that weather-sensitive individuals suffered more joint pain than did non-weather-sensitive individuals with KOA(7). Another study has reported that weather can affect OA symptoms (pain and disability)(18).

In our present study, there were significant differences in the scores of cartilage and marrow abnormalities between the weather-sensitive and non-weather-sensitive groups. As the classifications of cartilage and marrow abnormalities increased, the proportion of KOA patients in the weather-sensitive group increased, while that in the non-weather-sensitive group decreased. Hence, compared with that in the non-weather-sensitive group, the weather-sensitive group was more likely to have higher scores of cartilage and marrow abnormalities. By correcting the baseline characteristics, weather sensitivity was also found to be an independent risk factor for more severe knee cartilage defects and bone marrow abnormalities. This suggests that weather sensitivity can lead to an increased risk of severe knee cartilage defects and bone marrow abnormalities.
In a study of Russian clinical samples, climatic factors were found to affect the radiological severity of OA patients (19). It is possible that weather-sensitive patients are more likely to be affected by climatic factors than are non-weather-sensitive patients, which may contribute to the physiological mechanism of joint degeneration (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 the relationship between self-perceived weather sensitivity and pain (7, 8, 15). 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 correlates of interindividual differences in subjective experiences of pain, we also obtained objective evaluations of the relationship of self-perceived weather sensitivity with cartilage defects and bone marrow abnormalities in KOA patients. Our current study also included assessment of MRI scans of joint structure in weather-sensitive and weather-insensitive KOA patients. Our findings suggest that early treatment to weather-sensitive KOA patients may help in delaying their progression of knee joint degeneration.

Our present study also had some potential limitations. We only included cross-sectional analyses. The relatively small sample size of our study may also represent a limiting factor. Participants were defined as weather-sensitive individuals if they indicated that they experienced changes in knee joint pain or daily activities as a result of weather changes. If subjects noted that knee joint symptoms were not affected by weather changes, they were considered to be insensitive to the weather. However, our questionnaire on weather changes only considered temperature changes, whereas other weather factors were not considered, such as precipitation, atmospheric pressure, relative humidity, and wind speed (20). Therefore, clinical symptoms and changes in MRI features of the knee joint structures may be affected by these factors. Furthermore, a longitudinal study is needed to further clarify the relationship between weather sensitivity and KOA.

**Conclusions**

In conclusion, our present study showed that weather-sensitive KOA patients were more likely to exhibit more severe clinical symptoms (such as knee pain and dysfunction) and knee structural abnormalities (such as cartilage defects and marrow abnormalities) than those of non-weather-sensitive KOA patients. The current results emphasize the importance of weather sensitivity in the daily lives of KOA patients. As such, weather-sensitive KOA patients may require earlier treatment interventions compared with those of non-weather-sensitive KOA patients in order to delay the progression of KOA.

**List Of Abbreviations**
Declarations

Authors' contributions

YX, YC and YLC have contributed to the design of the study and the analysis of data. DJ, LW, XZW and ML have contributed to the recruitment of research subjects and data acquisition. YYW, MZ, JP, HSZ, YXZ and DDF have contributed to the revision of the manuscript. All the authors read and approved the final version of the manuscript.

Funding

This study was supported by the National Natural Science Foundation of China (81973874; 81373665), the Summit Plateau Team Project in Traumatology of Shanghai University of TCM, Shanghai chronic
musculoskeletal disease clinical medical research center (20mc1920600).

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

This study, registered at the Chinese Clinical Trial Registry (ChiCTR1800017777), was approved by the research ethics committee of Shuguang Hospital affiliated with Shanghai University of Traditional Chinese Medicine (approval number: 2013-296-65-01). Informed consent was obtained from each participant included in the present study.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

**Acknowledgements**

Not applicable.

**References**

1. Arden N, Nevitt MC. Osteoarthritis: epidemiology. Best Pract Res Clin Rheumatol. 2006;20(1):3-25.
2. Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. Lancet. 2011;377(9783):2115-26.
3. Yang M, Jiang L, Wang Q, Chen H, Xu G. Traditional Chinese medicine for knee osteoarthritis: An overview of systematic review. PLoS One. 2017;12(12):e0189884.
4. Farr li J, Miller LE, Block JE. Quality of life in patients with knee osteoarthritis: a commentary on nonsurgical and surgical treatments. Open Orthop J. 2013;7:619-23.
5. de Rooij M, van der Leeden M, Heymans MW, Holla JF, Hakkinen A, Lems WF, et al. Prognosis of Pain and Physical Functioning in Patients With Knee Osteoarthritis: A Systematic Review and Meta-Analysis. Arthritis Care Res (Hoboken). 2016;68(4):481-92.
6. Muraki S, Akune T, Oka H, En-yo Y, Yoshida M, Saika A, et al. Association of radiographic and symptomatic knee osteoarthritis with health-related quality of life in a population-based cohort study in Japan: the ROAD study. Osteoarthritis Cartilage. 2010;18(9):1227-34.
7. Timmermans EJ, van der Pas S, Schaap LA, Sanchez-Martinez M, Zambon S, Peter R, et al. Self-perceived weather sensitivity and joint pain in older people with osteoarthritis in six European countries: results from the European Project on OSteoArthritis (EPOSA). BMC Musculoskelet Disord. 2014;15:66.

8. McAlindon T, Formica M, Schmid CH, Fletcher J. Changes in barometric pressure and ambient temperature influence osteoarthritis pain. Am J Med. 2007;120(5):429-34.

9. Altman RD. Classification of disease: osteoarthritis. Semin Arthritis Rheum. 1991;20(6 Suppl 2):40-7.

10. von Mackensen S, Hoepppe P, Maarouf A, Tourigny P, Nowak D. Prevalence of weather sensitivity in Germany and Canada. Int J Biometeorol. 2005;49(3):156-66.

11. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988;15(12):1833-40.

12. Peterfy CG, Guermazi A, Zaim S, Tirman PF, Miaux Y, White D, et al. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage. 2004;12(3):177-90.

13. Wilder FV, Hall BJ, Barrett JP. Osteoarthritis pain and weather. Rheumatology (Oxford). 2003;42(8):955-8.

14. Timmermans EJ, Schaap LA, Herbolsheimer F, Dennison EM, Maggi S, Pedersen NL, et al. The Influence of Weather Conditions on Joint Pain in Older People with Osteoarthritis: Results from the European Project on OSteoArthritis. J Rheumatol. 2015;42(10):1885-92.

15. Ferreira ML, Zhang Y, Metcalf B, Makovey J, Bennell KL, March L, et al. The influence of weather on the risk of pain exacerbation in patients with knee osteoarthritis - a case-crossover study. Osteoarthritis Cartilage. 2016;24(12):2042-7.

16. Peultier L, Lion A, Chary-Valckenaere I, Loeuille D, Zhang Z, Rat AC, et al. Influence of meteorological elements on balance control and pain in patients with symptomatic knee osteoarthritis. Int J Biometeorol. 2017;61(5):903-10.

17. Brennan SA, Harney T, Queally JM, O’Connor McGoona J, Gormley IC, Shannon FJ. Influence of weather variables on pain severity in end-stage osteoarthritis. Int Orthop. 2012;36(3):643-6.

18. Dorleijn DM, Luijsterburg PA, Burdorf A, Rozendaal RM, Verhaar JA, Bos PK, et al. Associations between weather conditions and clinical symptoms in patients with hip osteoarthritis: a 2-year cohort study. Pain. 2014;155(4):808-13.

19. Kalichman L, Korosteshevsky M, Batsevich V, Kobyliansky E. Climate is associated with prevalence and severity of radiographic hand osteoarthritis. Homo. 2011;62(4):280-7.

20. Timmermans EJ, van der Pas S, Dennison EM, Maggi S, Peter R, Castell MV, et al. The Influence of Weather Conditions on Outdoor Physical Activity Among Older People With and Without Osteoarthritis in 6 European Countries. J Phys Act Health. 2016;13(12):1385-95.
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 |
|------------------------------|-------------------------------------|---------------------------------|---------|
| Demographic and clinical     |                                     |                                 |         |
| Age(years)                   | 61.1(1.1)                           | 61.8(0.9)                       | 0.638   |
| Gender(%female)              | 21(35)                              | 39(65)                          | 0.019†  |
| 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/m²)                  | 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   |
| Inflammatory biomarkers      |                                     |                                 |         |
| TNF-α, pg/ml                 | 11.4(1.0)                           | 13.6(1.3)                       | 0.189   |
| IL-1, pg/ml                  | 31.5(0.8)                           | 30.6(0.7)                       | 0.366   |
| IL-6, pg/ml                  | 7.6(1.3)                            | 12.7(3.5)                       | 0.220   |

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

† Pearson Chi-squared test

BMI, body mass index; KOA, knee osteoarthritis; VAS, visual analogue scale/score
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) | P for independence (Pearson's chi-square test) | P for trend (Cochran-Armitage trend tests) |
|----------------------|-------------------------------------|---------------------------------|----------------------------|-----------------------------------------------|------------------------------------------|
| Pain score (0–50)    | ≤ 5.5                                | 14(70%)                         | 6(30%)                     | 20(100%)                                      | 0.014                                    |
|                      | 5.5–10.6                             | 9(45%)                          | 11(55%)                    | 20(100%)                                      | < 0.001                                  |
|                      | 10.6–19.5                            | 7(33%)                          | 14(67%)                    | 21(100%)                                      |                                         |
|                      | > 19.5                               | 4(21%)                          | 15(79%)                    | 19(100%)                                      |                                         |
| Stiffness score (0–20)| ≤ 0.9                                | 15(75%)                         | 5(25%)                     | 20(100%)                                      | 0.001                                    |
|                      | 0.9–4.5                              | 5(24%)                          | 16(76%)                    | 21(100%)                                      | 0.003                                    |
|                      | 4.5–9.0                              | 11(52%)                         | 10(48%)                    | 21(100%)                                      |                                         |
|                      | > 9.0                                | 3(17%)                          | 15(83%)                    | 18(100%)                                      |                                         |
| Function score (0–170)| ≤ 16.9                              | 15(75%)                         | 5(25%)                     | 20(100%)                                      | 0.001                                    |
|                      | 16.9–31.1                            | 10(50%)                         | 10(50%)                    | 20(100%)                                      | < 0.001                                  |
|                      | 31.1–61.5                            | 5(25%)                          | 15(75%)                    | 20(100%)                                      |                                         |
|                      | > 61.5                               | 4(20%)                          | 16(80%)                    | 20(100%)                                      |                                         |
| Total score (0–240)  | ≤ 26.9                               | 15(75%)                         | 5(25%)                     | 20(100%)                                      | 0.004                                    |
|                      | 26.9–51.7                            | 8(40%)                          | 12(60%)                    | 20(100%)                                      | < 0.001                                  |
|                      | 51.7–87.0                            | 7(35%)                          | 13(65%)                    | 20(100%)                                      |                                         |

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) | P for independence (Pearson’s chi-square test) | P for trend (Cochran-Armitage trend tests) |
|------------------------|-------------------------------------|---------------------------------|-----------------------------|------------------------------------------------|------------------------------------------|
| Cartilage score (0–84) | ≤ 10.5                               | 12(60%)                         | 8(40%)                      | 20(100%)                                       | 0.047                                    | 0.015                                    |
|                        | 10.5–15.0                            | 11(55%)                         | 9(45%)                      | 20(100%)                                       |                                          |                                         |
|                        | 15.0–20.0                            | 4(21%)                          | 15(79%)                     | 19(100%)                                       |                                          |                                         |
|                        | > 20.0                               | 6(33%)                          | 12(67%)                     | 18(100%)                                       |                                          |                                         |
| Marrow abnormality score (0–45) | 0.0                          | 22(61%)                         | 14(39%)                     | 36(100%)                                       | 0.014$                                  | 0.009                                   |
|                        | 1.0                                  | 1(20%)                          | 4(80%)                      | 5(100%)                                        |                                          |                                         |
|                        | 1.0–5.0                              | 5(22%)                          | 18(78%)                     | 23(100%)                                       |                                          |                                         |
|                        | > 5.0                                | 5(39%)                          | 8(61%)                      | 13(100%)                                       |                                          |                                         |

WORMS, Whole-Organ Magnetic Resonance Imaging Score.

$Fisher’s exact test
Table 4

Associations of weather sensitivity present with WOMAC and WORMS.

| Variables                  | Unadjusted          | Adjusted*          |
|----------------------------|---------------------|--------------------|
|                            | OR      | 95% CI | P value | OR      | 95% CI | P value |
| WOMAC                      |         |        |         |         |        |         |
| Higher pain score          |         |        |         |         |        |         |
| Weather sensitivity        | 3.6     | (1.4 to 9.1) | 0.008   | 3.3     | (1.1 to 9.9) | 0.032   |
| Higher stiffness score     |         |        |         |         |        |         |
| Weather sensitivity        | 1.7     | (0.7 to 4.2) | 0.245   | 1.1     | (0.4 to 3.0) | 0.900   |
| Higher function score      |         |        |         |         |        |         |
| Weather sensitivity        | 5.7     | (2.2 to 15.3) | < 0.001 | 5.5     | (1.8 to 16.8) | 0.003   |
| Higher total score         |         |        |         |         |        |         |
| Weather sensitivity        | 3.6     | (1.4 to 9.1) | 0.008   | 3.3     | (1.1 to 10.2) | 0.034   |
| WORMS                      |         |        |         |         |        |         |
| Higher cartilage score     |         |        |         |         |        |         |
| Weather sensitivity        | 3.7     | (1.4 to 9.5) | 0.008   | 3.1     | (1.1 to 8.5) | 0.027   |
| Higher marrow abnormality score |       |        |         |         |        |         |
| Weather sensitivity        | 3.3     | (1.3 to 8.6) | 0.014   | 3.0     | (1.1 to 8.1) | 0.029   |

Independent variable: the state of weather sensitivity; Dependent variable: WOMAC or WORMS.

CI: confidence interval; OR: odds ratio.

* Adjusted for baseline age, gender, body mass index.

Figures
Figure 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 showed cartilage loss of the medial 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).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TableS1.docx