Association between climate conditions and osteoarthritis: protocol for a systematic review and meta-analysis

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Abstract

Background

Osteoarthritis (OA) is the most common form of arthritis, causing by multiple factors. It has long been a belief that arthritis pain is influenced by the weather. However, scientific studies have documented inconsistent results. To date, neither systematic review nor meta-analysis of existing findings has comprehensively considered their relations. The present study will critically appraise and synthesize the existing evidence from observational studies that examined the relationship between certain climate conditions and OA.

Methods and design:

This protocol will be conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines. There are no restrictions on the study date or publication status for searches in the Cochrane Library, EMBASE, Web of Science, PubMed, and other relative databases. All eligible observational studies will be included, with weather conditions as effect factors and OA symptom or imaging abnormality as outcomes. Two reviewers will be responsible for data extraction and analysis. Risk of bias and quality appraisal will be performed for the included studies using Newcastle-Ottawa Scale (NOS). Meta-analysis will be conducted using Rev Man V.5.3 with the associations between weather conditions and OA presented by odds ratios (ORs), relative risks (RRs), hazard ratios (HRs) and the 95% confidence intervals (CIs).

Results

This systematic review and meta-analysis will present the overall association between weather conditions and OA. The association of climate factors influencing OA incidence or progression would be further illustrated in subgroup analysis depending on whether that has been extensively described in the literature.

Discussion

This study will provide the analysis evidence on the effect of meteorological factors on OA. In an approach of dealing with weather conditions, the results will benefit the daily management of OA.

Background

Osteoarthritis (OA) is a chronic disease with a highly worldwide incidence that poses a high risk of disability and results in a huge burden on many aspects of life(1, 2). Almost 303 million people were affected in 2017 across the world(3).

The disease is caused by multiple factors that gradually leads to articular cartilage degradation and synovial inflammation. The general factors include age, obesity, strenuous joint movements and injury(4, 5). Many osteoarthritis patients often reported that the joint stiffness and pain was influenced by precipitation and temperature(6). More than half (62 percent) OA patients felt they were sensitive to weather. Temperature and precipitation resulted in more terrible clinical symptom(7). Some previous studies showed that weather changes influenced OA progression(8, 9). Cold and damp weather conditions could increase severity of joint pain(10). A

prospective study reported that low temperature and high humidity aggravate pain severity of OA patients(11). Several researchers have indeed found the relationship between weather and rheumatic disorders(12, 13). Assessment of inflammatory joint activity in rheumatoid arthritis and changes in atmospheric conditions(14). So the weather conditions may be another major pathogenic factor. But the results of published literature are hardly comparable because of the small sample, different meteorological variable, disparate diagnoses and measuring pain(14, 15). A systematic review focus on the relationship of joint pain and weather found no consensus on this issue(16). At present, a consistent relationship between osteoarthritis and climate conditions is still strikingly difficult to prove.

Collectively, low temperature, decrease in barometric pressure, and high relative humidity are seem to be the main weather conditions influencing OA symptoms and joints movement (7, 11, 14, 17–19). Nevertheless, as no comprehensive and reliable study has been concluded to date, taken the partial evidence of the single study into consideration, it is necessary to verify the relationship between climate and OA through a systematic review and meta-analysis.

Objectives

Our study will synthesize observational evidence regarding the relationship between weather conditions and osteoarthritis. We will answer the following question: “For osteoarthritis patient, is climate conditions associated with osteoarthritis based on current evidence?”

Methods/design

We will undertake a systematic review of observational evidence. When the research data are sufficient and available, a meta-analysis will be performed. This study has been registered to the International Prospective Register of Systematic Reviews(PROSPERO). This protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines(20, 21). The final review will be reported following the PRISMA format.

Criteria for considering studies for this review

Type of studies

We will include all retrospective and prospective studies (ie, cross-sectional, case-control or cohort study) instead of theraputic research of Randomized Controlled Trials (RCTs), focusing on the relationships between different weather conditions described below and OA. There is no limitation on the date of publication and language. When the reported studies are not enough, relevant descriptive articles will be considered for inclusion.

Type of participants

The participants of these studies have been clearly diagnosed with OA of any joints. All research investigate the relationship between joint pain, function, incidence or progression of OA and weather condition. There is no limitation in age of participants or their geographic regions.

Types of exposure(s)

All the weather conditions examined will be included, for example wind, temperature, relative humidity, barometric pressure.

Outcomes

The main outcomes include pain intensity and functional capacity of joint. The research data may be measured by different instruments, such as Visual Analogue Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The odds ratios (ORs), relative risks (RRs), hazard ratios (HRs), and 95% confidence intervals (CIs) will be considered. The secondary outcomes are visible radiologic changes in joint, bone, and periarticular tissue in OA patients, measured by X ray and Magnetic Resonance Imaging (MRI).

Search strategy

A comprehensive electronic literature search will be conducted to identify relevant literature among the main electronic database (the Cochrane Library, EMBASE, PubMed, Web of Science). The search strategy will be constructed using Medical Subject Headings (MeSH) and free text words in relation to keyword "osteoarthritis", and "climate", "weather". There will be no restrictions on the study date or publication status. The subject terms will be used for separate retrievals, connected by the Boolean operators "OR" and "AND".

More than that, we will hand search the unpublished and ongoing studies in the Chinese clinical registry (ChiC TR), the American clinical trials registry website (Clinical Trials. gov), the Congress abstract of Osteoarthritis Research Society International (OARSI), the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR).

Selection of studies

All the searched literature will be imported and managed using the Endnote X9 software. Two reviewers will independently screen titles and abstracts of all articles identified to select potentially eligible studies as the predefined inclusion. Full text version of all potentially eligible studies will be reviewed. If the consensus cannot be reached between the two reviewers, a senior investigator shall be present to resolve it by discussion. A Meta-analysis of Observational Studies in Epidemiology (MOOSE)(22) flowchart will be generated to reveal the study selection process, the number of records in each selection phase, and the reasons for the exclusion of full-text articles.

Data extraction and management

Two authors will independently extract the following data from the observational studies using a standardized form:

1. Study characteristics: design, setting, publication year, and authors;
2. Population: sample size, sex, age, and percentage of people with OA in the sample;
3. Exposure: all weather conditions like wind, temperature, relative humidity, air pressure;
4. Statistical analyses methods;

5. Outcomes and follow-up: pain intensity, functional capacity of joints, radiologic changes in joint, bone, and periarticular tissue, ORs, RRs, HRs, respective 95% CIs, the total observation duration and follow-up. Two reviewers' extraction results will be unified after checking each other. Where necessary, missing or incomplete information shall be supplemented by contacting the study's author. If we are unable to reach the author within one month of the request, we will define the data as unobtainable and the study will be excluded.

Assessment of quality and risk of bias in included studies

To ensure a high quality assessment of the included studies, two experienced reviewers applied the Newcastle-Ottawa Scale (NOS)(23). The scale, with a total score of 9, is divided into two parts and each part has three columns. Studies scored ≥ 5 will be considered as having high methodological quality and ≤ 5 scores will be defined as the low methodological quality research. A third reviewer will be consulted if there is disagreement regarding the any of the elements of NOS scores.

Data synthesis

A meta-analysis of the data will be conducted using RevMan5.3(24). We will pool the associations between weather conditions and OA presented by OR, RR, and HR with the upper and lower limits of the 95% confidence intervals (CI) of all comparisons. When possible, we will convert different outcome effect size measures into compatible values to complete the meta-analysis(25, 26). The fixed-effect model (FEM) or random-effects model (REM) combination methods will be chosen based on the methodological similarities of the included studies, by estimating the forest plots, c^2 and I^2 tests statistical heterogeneity. The high heterogeneity is defined as the standard c^2 value with a significance level of $P < 0.10$, $I^2 > 50\%$ (27). When comparisons are statistically heterogeneous, a random-effects model will be applied, and when studies are statistically homogeneous, we will use a fixed-effect model(23). If there is a high heterogeneity among studies, we will then delete each of the trials one-by-one to observe the changes in the I^2 results and P-value, and then determine the specific study causing the heterogeneity and explore the reasons for this. In addition, if the comparisons are deemed to have a high risk of bias, we will perform sensitivity analyses to assess the reliability of the overall studies by deleting the studies determined to have a high risk of bias. We will then analyze the studies we deem to have a low risk of bias again and compare them to the overall results. Summary tables and narrative text will be prepared to present the characteristics of included studies. If the collected data on the effect of one specific weather condition on OA provides insufficient or equivocal answers to our specific aim, or we are unable to compare the index statistics among studies for meta-analysis, we will make a qualitative summary in the form of chart description.

Subgroup analysis

If we are able to pool adequate data, subgroup analyses will be conducted to more deeply explore the relationships between weather conditions and OA as following: 1) the pain intensity; 2) the functional capacity of; 3) incidence; 4) progression; 5) radiologic changes in joint, bone, and periarticular tissue.

Assessment of publication bias

In meta-analysis, if we include numerous available studies over 10, we will perform publication bias by visual funnel plots. While if not, publication biases will be assessed depended on the characteristics of the included studies.

Discussion

This work is focused to integrate valid data from observational studies to explore the overall associations between climate conditions and OA, then with possible subgroup analysis of the relation of incidence or progression of OA and specific weather conditions, such as temperature, barometric pressure, and humidity. OA is a multiple etiologies-related disease, and meteorological factors may have an influence on the joint. In clinical practice, individuals with OA often complain that the severity of their symptom is affected by the weather conditions (such as temperature, humidity, and barometric pressure), but there is no consensus for this issue. In order to distinguish the traditional beliefs from science, several studies performed and showed that the increasing of patients' pain intensity and the limited joints movement are caused by the high humidity and low barometric pressure conditions(18, 28, 29). Tim and co-workers performed a longitudinal analysis, within 200 knee osteoarthritis patients, showed that the pressure change and ambient temperature were the main factors-raised WOMAC score(19). Up to now, there have been a number of observational studies proved the positive relation as mentioned above(30–33). But due to the characteristics of observational research, most of them just performed in a single region with a limited race and meteorological factor. Moreover, the outcome like VAS or WOMAC of each study belongs to a subjective and individual tool which researchers cannot standardize patients' cognition of functional ability and pain intensity or stiffness to a unified level(34). The conclusions of these surveys may have been relatively one-sided, with low credibility to explain the substantial relationship between OA and weather condition. Meanwhile, the mechanism of weather-derived OA has been also reported. Several studies has reported that the air pressure has an important role in stabilizing synovial fluid(30), while the change of air pressure may stimulate the sensitized mechanoreceptors in joints, or destroy the equilibrium of intra and extra articular pressure leading to joints pain(35, 36). About ambient temperature change inducing joints pain or stiffness, Ng J(37) explored that the cold may decrease the lubrication and flow function of synovial fluid, leading to joint stiffness and pain increase. With respect to high humidity, it aggravates the patient's pain by increasing joints inflammation. In general, the lacking of evidence credibility from both pragmatism and observational research could be better interpreted through a substantial and systematic conclusions.

Meta-analysis is a scientific and rigorous statistical method, which we can use to pool the single study's OR and %95 CI together to calculate the overall effects size of climates-related OA. The pooled effects will be more comprehensive and precise compared to the initial evidence(38, 39). Moreover, depending on the study outcomes and weather variables, if sufficient literature are included, we will also conduct subgroup analysis to further distinguish those special weathers affecting incidence or progression of OA. At the same time, we would plan to rank the degree of different climate factors to distinguish which one have the most or the least impact on OA.

The results of the meta can be regarded as a qualitative conclusion. Assuming the climate condition acting as a risk factor for OA, the estimated effect size of subgroup analysis and ranking results can not only provide the accurate reference to clinicians, but also lay the groundwork to further mechanism research. More importantly, it may educate OA patients to be aware of the ambient weather effecting on their joints as the daily management approach.

Abbreviations

OA: Osteoarthritis; PRISMA-P: the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols; NOS: Newcastle-Ottawa Scale; ORs: odds ratio; RRs: relative risks; HRs: hazard ratios; CIs: the upper and lower limits of the 95% confidence intervals; VAS: Visual Analogue Scale; WOMAC: Western Ontario and McMaster

Universities Osteoarthritis Index; PROSPERO: International Prospective Register of Systematic Reviews; MRI: Magnetic Resonance Imaging; MeSH: Medical Subject Headings; MOOSE: Meta-analysis of Observational Studies in Epidemiology; FEM: fixed-effect model; REM: random-effects model. RCT; Randomized Controlled Trial; ChiC TR: Chinese clinical registry; Clinical Trials. Gov: the American clinical trials registry website; OARSI: Osteoarthritis Research Society International; ACR: the American College of Rheumatology; EULAR: European League Against Rheumatism.

Declarations

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Authors' contributors

YL Cao, L Wang and QG Xu conceived the review topic. L Wang and QG Xu undertook background exploratory searches and drafted the initial search strategy. YL Cao, L Wang and QG Xu co-wrote the initial protocol. YL Cao, QG Xu, Y Chen and XZ Wang provided critical appraisal and senior oversight of the protocol. For the systematic review, Y Xue, YY Wu, D Jiang will undertake the searches, data extraction and analysis. L Wang and QG Xu will perform oversight of the searches, data analysis and extraction and provide statistical input for data analysis. YL Cao and YX Zheng will complete critical appraisal and senior oversight of the final manuscript.

Ethics approval and consent to participate

Not applicable as the study will be a systematic review.

Competing interests

None declared.

Consent for publication

Not applicable.

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Appendix: Search Strategy

The example of MEDLINE search strategy for PubMed: <https://www.ncbi.nlm.nih.gov/PubMed/>) as follows:

```
("Osteoarthritis"[Mesh]) OR (((((((Osteoarthritis) OR (Osteoarthrosis[Title/Abstract])) OR
(Osteoarthroses[Title/Abstract])) OR (Arthritis Degenerative[Title/Abstract])) OR (Arthritides
Degenerative[Title/Abstract])) OR (Degenerative Arthritides[Title/Abstract])) OR (Degenerative
Arthritis[Title/Abstract])) OR (ArthrosisArthroses[Title/Abstract])) OR (Osteoarthrosis Deformans[Title/Abstract]))
AND (((("Climate"[Mesh]) OR (climates[Title/Abstract])) OR ("Weather"[Mesh]) OR ((Fog[Title/Abstract]) OR
(Fogs[Title/Abstract]))))
```

Supplementary Files

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