Influence of ambient temperature and humidity on joint pain and swelling in rheumatoid arthritis and spondyloarthritis. What should our patients expect as climate change progresses?

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ABSTRACT

Objective. *To demonstrate the influence of temperature and humidity on swelling (SJC) and tenderness (TJC) of finger joints in patients with rheumatoid arthritis (RA) and patients with spondyloarthritis (SpA).*

Methods. *TJC and SJC of our RA and SpA cohorts, CRP and Disease Activity Score (DAS) were modelled using regional weather data on average temperature and humidity on the day of the study and 5 days before examination.*

Results. *2,116 patients with 17,256 visits were documented over 18 years. The mean temperature was 11°C (-10°C to 31°C) and the mean humidity was 76% (33%-99%). The RA cohort showed a temperature-dependent linear increase in SJC by a factor of 1.05 per 10°C for the range -10°C to +30°C, but no tendency for TJC, CRP or DAS to be influenced by temperature. Regarding humidity, we saw a linear decrease in SJC and TJC. This tendency is also seen when the average values of the 5 days before to the examination are chosen as predictors. In the SpA cohort, we found no tendency for SJC and CRP to be influenced by temperature. A slight increase in the number of swollen joints was observed at higher relative humidity.*

Conclusion. *The outpatient cohort of well-treated, controlled RA showed a linear increase in SJC with increasing ambient temperature and decreasing relative humidity. The SpA cohort showed an opposite trend. An impending rise in temperature and prolonged periods of drought indicate an increase in RA disease activity. Large cohorts are required to make valid predictions.*

Introduction

Rheumatic musculoskeletal diseases (RMDs) are a burden for patients, their relatives, friends, and their social and professional environment. In many cases, rheumatic diseases lead to reduced quality of life and health, frequent physician visits, medication use, disability, and early retirement. RMDs are very heterogeneous, with functional and degenerative diseases being very common and inflammatory systemic diseases being particularly severe.

Climate forecasts assume that the global average temperature will rise by at least 1.5°C in the coming years due to the greenhouse effect. If no immediate measures are taken to reduce CO_2 emissions, the predicted temperature increase will be significantly higher.

Everyday clinical practice provides many examples of how temperature and other climatic factors can affect the well-being of patients with RMD.

For example, heat relaxes muscles and promotes potentially regenerative metabolism. Many patients report an improvement in their musculoskeletal symptoms in dry, warm summer weather, and heat is also used as part of various therapeutic approaches for chronic pain. In addition, humid weather and weather changes can increase musculoskeletal pain and disease-related disability (1-10) and (therefore) lead to increased use of health services (11, 12). On the other hand, patients with peripheral joint inflammation in particular benefit from cold applications. Local and systemic cold application reduce blood flow in the area of inflammation and can therefore have a positive effect on inflammatory processes in peripheral joints. Cold chambers are

an established therapeutic device in many speciality clinics.

However, systematic studies on the influence of climate and weather factors on disease activity in patients with RMD and in particular inflammatory joint diseases are rare.

The Lower Rhine and especially the greater Düsseldorf area, where we provide rheumatologic care, have typical Central European westerly weather. Low pressure weather with humid air masses move into the region from the Atlantic, while stable high pressure weather with dry air are rare. Winters are mild and our summers are not as hot as in the continental climate.

Weather data for our region have been available since 1880, and climate forecasts are calculated on the basis of this data. The long-term annual average temperature has already increased by 1.6°C from 9.1°C to 10.7°C, especially in spring and winter (by 1.8°C). Without drastic climate change protection measures, a further increase of 3°C is expected in the next few years (13). Over the course of records, precipitation has decreased slightly in summer and increased by more than 25% in winter.

The examination of the hands is particularly well standardized for pain and swelling, and joint swelling is easily detected by palpation of the joint space. In addition, the fingers are less affected by heat-related general tissue swelling, as would be expected in the feet, for example. We have developed and trained standards for this examination (14). Rheumatoid arthritis (RA) and the spondyloarthritis (SpA) group (psoriatic arthritis, inflammatory bowel disease (IBD)-associated arthritis, ankylosing and non-radiographic spondyloarthritis) are the most common inflammatory rheumatic diseases that frequently affect the finger joints. Therefore, we selected patients with these diseases for analysis.

The aim of our study is to demonstrate the influence of temperature and humidity on swelling and tenderness of finger joints in well-treated patients with RA or SpA in Western Central Europe and to use the data to project possible effects of climate change.

Patients and methods

As a secondary and tertiary care provider, we treat and follow adult patients with arthritis and inflammatory systemic diseases in our outpatient clinic. The documented 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD10) codes were used for patient stratification. Patients with a confirmed ICD10 of M05.- and M06.0- were grouped as RA patients, and patients with an ICD10 of M07.-, M45.-, and M46.- were grouped as SpA patients. Patients with juvenile-onset disease were excluded from the analysis.

All our patients with a confirmed diagnosis of RA and SPA are treated according to the current guidelines, with the aim of achieving remission or at least low disease activity. They are automatically recalled and re-examined every 3 to 6 months, preferably by the same rheumatologist. In this context, tenderness and swelling of knees, shoulders, elbows, wrists, metacarpophalangeal joints (MCP I-V), proximal interphalangeal joints (PiP I-V), and interphalangeal joints of the thumbs (IP I) of both hands are assessed. C-reactive protein (CRP) is measured, patient's assessment of their general health is documented on a visual analogue scale, and the disease activity score DAS28 is calculated. The MCP I-V, PiP II-V and IP I joints of the patients in our RA and SpA cohorts have been examined and documented at each visit by specialists for more than 20 years. We use the IT platform DocuMed.rh for structured documentation of joint swelling and joint pain. Patients consented to the storage and use of their anonymised data for future scientific purposes. Although emergency department visits account for less than 0.1% of visits, only patients who came for a scheduled appointment were selected for the study to avoid referral bias.

For each patient, regional weather data on average temperature and relative humidity on the day of the examination and the 5 days before the examination were determined at the zip code level. In order to be able to compare the influences, patient-related clinical data were subsequently modelled using a generalised additive mixed model (GAMM). In the GAMM, the number of swollen joints (SJC) or the number of tender joints (TJC) was used as the dependent variable, an intercept was adjusted for each patient, and temperature or relative humidity was used as a fixed effect. Due to the overdispersion of the data, a negative binomial distribution was assumed. In addition, sensitivity analyses were performed to test the robustness of our results. First, the temperature and humidity values on the day of the examination were replaced by the average temperature or humidity values of the 5 days prior to the examination. Second, we adjusted the analysis for potential confounders, gender and age at the day of the examination. Third, an analysis was performed in the subcohorts of patients with a maximum of at least two swollen joints. All analyses were performed using R version 4.2.1.

Results

A total of 17,256 follow-up visits with SJC and TJC were documented, 14,785 visits for 1,672 RA patients and 2,471 visits for 444 SpA patients between 2004 and 2022. The mean age at presentation was 55 years for RA patients and 50 years for SpA patients. Disease activity was quite low with 66% of patients being in remission. Only 34% of the patients in the RA and SpA groups had at least one swollen joint. C-reactive protein was normal (<0.5mg/dl) in the majority of patients and the 28-joint Disease Activity Score (DAS28) showed low (<3.2) or no (<2.6) activity in the vast majority of patients with RA. A more detailed description of the cohorts is provided in Table I.

The median temperature at the patients' residence was approximately 11.1°C with a range of -10°C to 31°C, and the median relative humidity was 77% with a range of 33% to 99% for the RA and SpA groups. Temperature and humidity were moderately correlated as shown in Figure 1.

For the RA cohort, GAMM analysis showed a temperature-dependent, moderate linear increase in the number of swollen finger joints over the range -10°C to +30°C. For each 10°C increase in temperature, the number of

Table I. Comprehensive description of the rheumatoid arthritis (RA) and apondyloarthritis (SpA) cohorts.

	RA (n=1.672, 14.785 visits)	SpA (n=444, 2.471 visits)
Age (mean (SD))	55.5 (16.8)	49.7 (14.7)
Female (%)	1332 (73.6%)	228 (51.4%)
Disease duration in years (median [25%,75%])	5.02 [1.0, 12.6]	6.53 [0.0, 15.3]
C-reactive protein mg/dl (mean (SD); median, [25%,75%])	0.8 (2.3); 0.3 [0.2, 0.7]	0.7 (1.7); 0.3 [0.2, 0.8]
Disease activity score DAS28 (mean (SD); median, [25%,75%])	2.98 (1.06); 2.79 [2.08, 3.55]	-
At least 1 swollen finger joint (%)	560 (33.5%)	149 (33.5%)
Numbers swollen finger joints (mean (SD); median, [25%,75%])	1.4 (2.8); 0 [0, 3]	0.9 (1.9); 0 [0, 3]
At least 1 painful finger joint (%)	590 (35.3%)	171 (38.6%)
Number painful finger joints (mean; median, [25%,75%])	1.6 (3.2); 0 [0, 3]	1.4 (2.7); 0 [0, 4]
Temperature (°C) (median [25%,75%])	11.1 [5.9, 16.8]	11.8 [6.3, 16.7]
Relative humidity (%) (median [25%,75%])	77.0 [68.0, 84.6]	77.0 [68.0, 84.0]

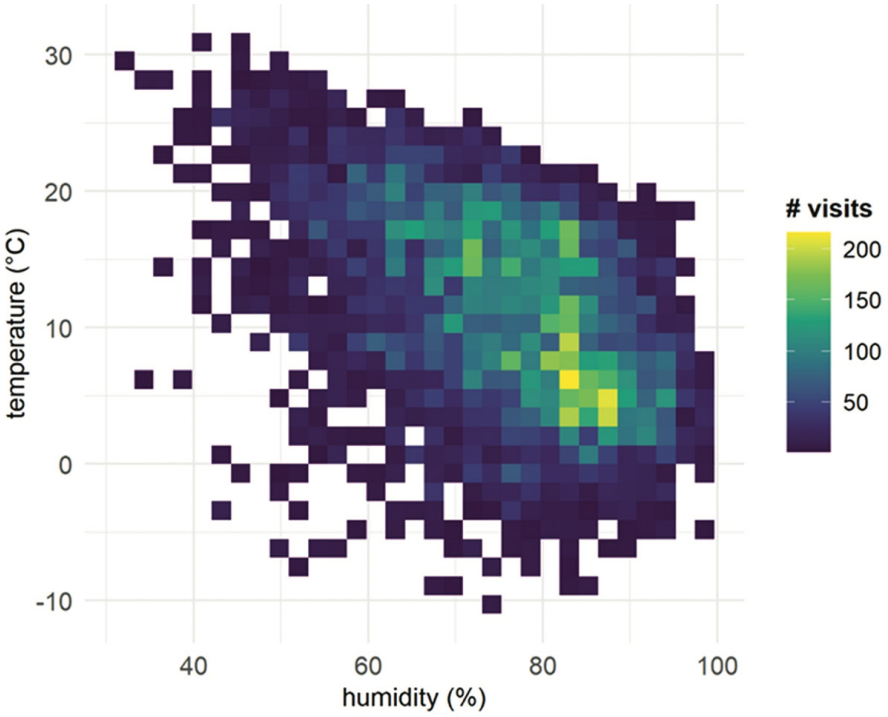

Fig. 1. The plot shows the distribution of the temperature and humidity values at visit date for all patients.

swollen joints increased by a factor of 1.05. In contrast to swollen joints, the number of painful finger joints, CRP, or DAS28 were not significantly affected by temperature. For humidity, we see a linear decrease in the number of painful and swollen finger joints with increasing relative humidity. For a 10% increase in relative humidity, the number of swollen joints decreases by a factor of 0.96. The confidence interval for all effects in the RA cohort is narrow, even at quite extreme temperatures (<0°C or ~30°C) or humidity (<40% or >90%), as shown in Figure 2.

For the SpA cohort, we found no trend in the number of swollen finger joints and CRP as a function of temperature. A slight increase in the number of swollen joints was found at higher relative humidity.

Similar results were found in terms of the effect of temperature and relative humidity on the number of painful joints. Again, no clear trend was found with respect to temperature. With regard to humidity, a small decrease in the number of painful joints was found with respect to humidity. However, the confidence intervals for both effects are wide, especially for extreme temperature (<0°C or ~30°C) or humidity (<40% or >90%) values. Therefore, there is a large uncertainty regarding these effects.

In addition, sensitivity analyses were performed to test the robustness of our results. First, the temperature and humidity values on the day of the examination were replaced by the average temperature or humidity values of the 5 days prior to the examination. Second, we adjusted the analysis for potential confounders, gender and age at the day of the examination. Third, an analysis was performed in the sub-cohorts of patients with a maximum of at least two swollen joints.

All sensitivity analyses confirmed the results of our primary analysis and indicate robust results.

Discussion

Temperature and humidity have a predictable effect on patients with RMDs. The majority of people tend to complain about cold and humid weather, and more people with musculoskeletal complaints seek medical attention during these periods as shown for many countries (1-3, 5, 11, 12). In regions with stable seasonal weather conditions, such as the Mediterranean region with warm dry summers and cool wet winters, seasonal differences in the manifestation and severity of RA are evident (15). Such stable seasonal weather does not exist in our region, and even in midsummer there are numerous wet and cold days. We have therefore chosen a more detailed approach to the evaluation that is directly related to temperature and humidity. This enabled us to show a linear increase in swollen finger joints as a function of increasing ambient temperature and decreasing relative humidity with temperature and humidity for our long-term followed and standardized documented RA outpatient cohort.

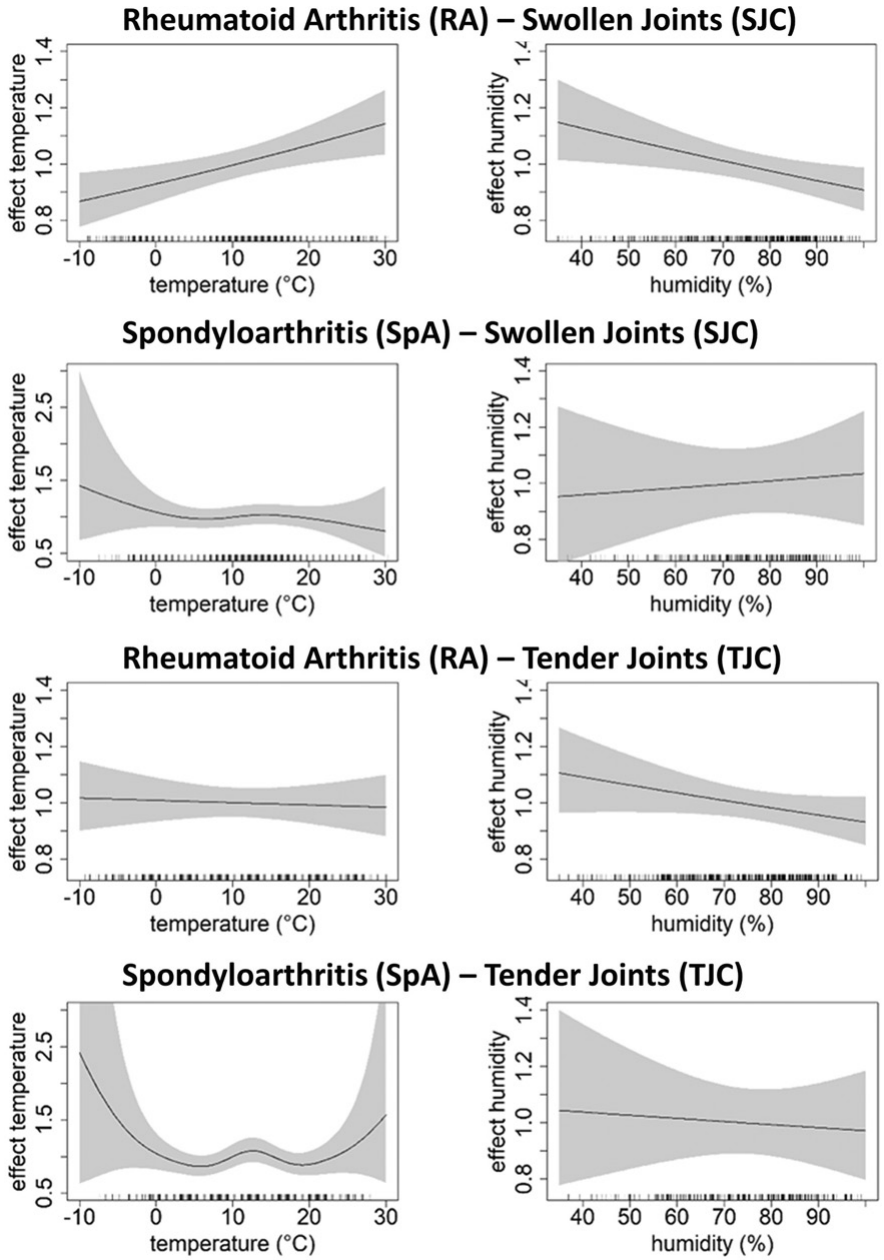

Fig. 2. The graphs show the results of a mixed additive model with a negative binomial distribution for the influence of temperature (left) and relative humidity (right) on the number of swollen (SJC) and tender joints (TJC) and the corresponding confidence interval (grey area) in the cohort with rheumatoid arthritis (RA) and spondyloarthritis (SpA).

This is indicative of an acute increase in joint related inflammatory activity even in generally well controlled disease. As expected, we are not able to detect any influence of recent temperature on CRP levels, joint pain or DAS28. Joint pain in RA is often multifactorial and is influenced not only by inflammation but also by secondary osteoarthritis, general pain level and increased muscle tone, all factors that are more likely to improve with dry heat. Thus, the expected increase in pain due to heat-induced increased joint inflammation can be reduced by pain relief due to a reduction in osteoarthritis pain (7). The health effects of a short-term increase in temperature may be mitigated by behavioural changes, such as not exercising or staying in a cool place; long-term effects may lead to other adaptive behavioural or physiological changes that we could not detect. An impending rise in temperature and prolonged dry spells raise concerns about an increase in systemic RA disease activity, especially during the summer months, and a possible increase in secondary damage such as joint destruction. However, current experience from warm and dry areas in summer contradicts this fear (15). Negative effects of the average temperature increase on rheumatoid arthritis may have been mitigated by the therapeutic advances of the last two decades, but the therapeutic effect of modern therapy may also be reduced by the increase in temperature. After all, we were able to demonstrate the same temperature effect with an increase in the number of swollen joints even in RA patients in remission. In contrast to patients with RA, the SpA cohort showed an increase in swollen joints with humidity and a slight decrease with temperature. This demonstrates disease-related effects of temperature and humidity. Observer- or location-related effects were not detected. This short-term effect does not suggest any benefit of climate change for patients with SpA.

Other long-term consequences of the expected climate crisis, such as increased infection rates, psychological stress, and lack of exercise, could not be captured by our study.

To make valid predictions, large cohorts, long follow-up periods and standardised settings are required. We therefore selected only the most common disease groups and were able to include 2,116 patients with 17,256 visits in the calculation, outperforming other publications. In addition, we restricted the evaluation to limited and robust parameters to avoid random effects. The comparison of the confidence intervals of the RA and SpA cohorts depicts the need for large sample sizes. In smaller subgroups or for rarer diseases, we were unable to obtain reliable results. In addition, our predictions cannot be generalised and should be confirmed in other cohorts, but especially in other climatic regions. We should all strengthen our measures against climate change to protect ourselves and our patients from possible and probable consequences. In addition, we need more in-depth studies on the pathophysiological effects of changing climatic conditions on RMDs and strategies to control them. Further

multivariate analyses and follow-up of our outpatient cohorts and the NAKO cohort (16), which includes over 200,000 subjects and is representative of the German population, are planned.

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