Concise Report

What’s in season for rheumatoid arthritis patients?
Seasonal fluctuations in disease activity

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Introduction

Environmental factors are known to affect rheumatoid arthritis (RA). The notion that weather or seasonal changes affect rheumatic diseases, especially symptoms of RA, has been prevalent and are often suggested by patients as causes for changes in joint related symptoms. Yet, there are few studies that have found significant associations with RA and weather [1–6] or season [6–8]. And even when changes are observed, there has been no previous study that encompasses an overview of both subjective and objective evaluations of RA disease activities, especially those associated with seasonal changes [9–19].

Since it is not uncommon for arthritis patients to assume that seasonal changes affect the signs and symptoms of RA, it is important to take into account these fluctuations when examining patients. The purpose of this study is to examine whether a seasonal fluctuation exists with RA activity and to analyse seasonal effects of varying components that express disease activity in RA patients.

Patients and methods

Cohort database

This large non-interventional observational cohort study [Institute of Rheumatology RA (IORRA) cohort] was started in October 2000, in which all RA patients visiting the out-patient clinic of the Institute of Rheumatology, Tokyo Women’s Medical University, were asked to answer a validated questionnaire every six months. The questionnaires assess variables such as disability level, pain, global assessment of disease activity, use of medication, adverse events, health care utilization, and satisfaction of care. Further database includes physician’s assessments, patient-reported data and laboratory data. Approximately 4500 RA patients were included per study, and a response-rate of over 97% was achieved each time. The near-perfect response allows for a practical and high quality of epidemiological data on rheumatic diseases in Japan.

Patients and assessment

Data and information from 10 consecutive surveys from October 2000 to April 2005, bi-annually (October/November and April/May), were used for this study. In all, 1665 RA patients (81.7% females, average age 57.2 ± 11.2 yrs, disease duration 9.9 ± 8.1 yrs), falling under the diagnostic criteria according to the American College of Rheumatology, whose data were available for 10 consecutive phases were evaluated. Time of onset, disease stage and therapy were not specified for this study. Among 50.9% of the patient population was given oral corticosteroids, 39.5% methotrexate and the average methotrexate dose was 5.8 ± 3.2 mg/week. The following 10 criteria were collected and analysed in this study: DAS 28 (disease activity score), HAQ (health assessment questionnaire), TJC 28 (tender joint count), SJC 28 (swollen joint count), patient’s assessment of pain on a visual analogue scale (patient’s pain VAS), patient’s global assessment of disease activity (patient’s global VAS), physician’s global assessment of disease activity (physician’s global VAS), CRP (C-reactive protein), ESR (erythrocyte sedimentation rate) and RF (rheumatoid factor).

Statistical analysis

Analysis of variance (ANOVA) was used to assess the seasonality of each variable. The effects of patient and seasonality were included in the ANOVA model, namely repeated measures analysis. The effect of seasonality was tested for each variable, a significance level was set at 0.05 and multiple comparisons were carried out using the Bonferroni’s procedure.

Results

Due to the nature of our cohort study, where bi-annual studies were conducted, we were able to obtain results of two seasons. The April/May study represented spring, and October/November represented fall. Variables were compared using ANOVA and
Bonferroni’s procedure. An overall type I error rate of 0.05 was preserved using this procedure.

DAS 28 and HAQ showed higher RA disease activity in the spring compared to the fall (Table 1). The differences between the two seasons were significant. This was also seen in the other variables, where fall showed lower disease activity, while spring revealed higher disease activity. In addition, seasonal magnitudes of disease activity were significantly different between the two seasons. The one exception to this was the physician’s global assessment of disease activity, which was slightly higher during fall compared to spring. Furthermore, there was no significant difference in the scores between the two seasons for the physician’s global VAS.

Our results showed that for almost all criteria, there was more RA disease activity in spring compared with fall.

**Discussion**

The bi-annual evaluation of this observational cohort study revealed that seasonal fluctuation of RA disease activity does indeed exist, and that this fluctuation can be seen both subjectively and objectively. Most previous studies concerning seasonality are based either on patient complaints of pain and stiffness, providing only a subjective approach to the disease, or they are based on laboratory data, providing only an objective approach. Variables such as TJC 28, SJC 28, patient- and physician-oriented VASs, functional disability indices such as the HAQ, quality of life assessment and laboratory data are all vital to the evaluation of disease activity.

Our study evaluated seasonal change of RA, using both subjective and objective RA disease variables. A more thorough overview of the disease and its relation to seasonality were obtained because of the adequate number of patients and length of study. Because the difference in values between fall and spring are small, the true clinical relevance needs to be further assessed. However, our results showed that there was a decreased disease activity in fall, and an increased disease activity in spring, and these differences were significant.

The physician’s assessment was the only exception to this. The reason for this is not clear but it is quite evident that season has nothing to do with the physician’s perception or assessment of the disease. Perhaps physicians would rather believe that their evaluation of the disease, choices of medication, provision of medical attention are constant throughout the year. This is further suggested by the fact that overall VAS was much lower for the physicians’ assessment compared with the patients’.

Studies concerning seasonal association with RA are quite scarce while there are numerous reports of other environmental variables. RA and its association with weather variables such as temperature, barometric pressure, relative humidity, water vapour pressure, sunshine, cloud cover, wind speed and precipitation have been reported [1–6, 9–19]. The length and magnitude of exposure of subjects to weather, duration of study, uniformity of participants, use of warming/cooling devices, geographical region of the study and the difficulty of monitoring weather variables cause discrepancies between studies [20]. The few that do report about seasons do not show significant seasonality differences in RA [6, 7], and those that do report differences reveal winter months to be when patients claim their symptoms to be the worst [11, 21, 22]. In general, weather variables of temperature and humidity are factors that seem to affect perceptions of seasonal effects in RA patients. High temperature increases absolute humidity (summer) which is apparently unfavourable to symptoms and disease activity of RA, but due to less clothing and air conditioning, there is lower vapour pressure on the skin, allowing for better outcome for RA symptoms [20]. Also, shifts in pressure and humidity are more pronounced in winter compared with warmer months, perhaps a contributing factor to the perception by some RA patients that the summer months are more favourable [6].

Since seasonality primarily concerns the length of daylight, solar effects on circadian rhythm and RA need to be considered. Recent studies have suggested relations between daylight and pro-inflammatory cytokine production [23–30]. In addition, some studies have shown that an increase in vitamin D intake and increased photosynthized vitamin D are associated with decreased risk of developing RA [31, 32]. These findings suggest that less sunshine and less light may be the cause RA activity exacerbation.

In Japan, there is an overall understanding that symptoms are worse during the rainy season (June, July) when humidity is high and during the cold winter months. However, during the time of our study, no significant differences were observed in average barometric pressure, average temperature, average relative humidity and average sunlight in Tokyo during fall and spring (Japanese Meteorological Agency, 2005). Although previous studies have claimed differences in these variables as the cause of seasonality, our study showed seasonal fluctuation of disease activity without significant differences of these meteorological variables between the two seasons.

Along with other environmental factors, seasonal fluctuation is a contributing factor to RA disease activity. Due to the difficult nature of monitoring these factors, discrepancies between studies exist. Using our observational cohort study, we were able to observe a large number of RA patients and analyse both subjective and objective disease variables. The absolute differences between fall and spring were significant but minimal and may not truly reflect relevant clinical differences. However, our study did show a fluctuating pattern between seasons for disease activity. It is important to keep in mind that seasonality can affect RA and that they may bring about varying complaints, symptoms, laboratory data, and disease activity of patients at each hospital visit.

### Table 1. Comparison of disease activity variables between two seasons

<table>
<thead>
<tr>
<th></th>
<th>Fall (mean ± SE)</th>
<th>Spring (mean ± SE)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS 28</td>
<td>3.68 ± 0.02</td>
<td>3.80 ± 0.09</td>
<td>9.4 × 10^{-7}</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.75 ± 0.02</td>
<td>0.78 ± 0.02</td>
<td>3.0 × 10^{-5}</td>
</tr>
<tr>
<td>TJC 28</td>
<td>2.13 ± 0.06</td>
<td>2.30 ± 0.06</td>
<td>3.3 × 10^{-5}</td>
</tr>
<tr>
<td>SJC 28</td>
<td>2.32 ± 0.06</td>
<td>2.50 ± 0.06</td>
<td>2.57 × 10^{-7}</td>
</tr>
<tr>
<td>Patient’s pain VAS</td>
<td>31.3 ± 0.50</td>
<td>34.0 ± 0.83</td>
<td>2.04 × 10^{-7}</td>
</tr>
<tr>
<td>Patient’s global VAS</td>
<td>32.6 ± 0.47</td>
<td>35.6 ± 0.87</td>
<td>9.30 × 10^{-4}</td>
</tr>
<tr>
<td>Physician’s global VAS</td>
<td>18.2 ± 0.29</td>
<td>18.1 ± 0.44</td>
<td>9.842</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>1.22 ± 0.30</td>
<td>1.28 ± 0.03</td>
<td>0.003*</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>35.1 ± 0.47</td>
<td>36.3 ± 0.89</td>
<td>4.50 × 10^{-9}</td>
</tr>
<tr>
<td>RF (IU/ml)</td>
<td>128.2 ± 5.20</td>
<td>140.5 ± 3.44</td>
<td>2.93 × 10^{-9}</td>
</tr>
</tbody>
</table>

*statistical significance.

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**Rheumatology key message**

- Seasonal changes do affect RA and should be considered when evaluating disease activity.
Acknowledgements

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References