

Original Article

The Relationship between Joint Pain and Climate Conditions in Japan

Kimihiko Tokumori^{a,b*}, Da-Hong Wang^b, Tomoko Takigawa^b, Jiro Takaki^b, and Keiki Ogino^b

^aDepartment of Physical Therapy, Hiroshima International University, Faculty of Health Sciences, Higashihiroshima, Hiroshima 739-2695, Japan, and ^bDepartment of Public Health, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

This study aimed to determine whether there was any association between the regional climate and the proportion of people with joint pain. Regional climate data between 1971 and 2000 were obtained from the Japan Meteorological Agency. The variables used in the cluster analysis included sunlight hours, amount of precipitation, number of days with precipitation, and temperature. The regional proportion of people with joint pain was obtained from the National Survey for Health in 2001. After performing a cluster analysis, one-way ANOVA and Welch's test were used to determine whether the climate characteristics of the clusters were significantly different. Within each cluster, stepwise multiple linear regression analyses were performed. We found that sunlight hours showed a direct, negative association with the proportion of people with joint pain (adjusted $R^2 = 0.532$, $p = 0.016$) in cluster 1, which was characterized as the region with the fewest total hours of sunlight, less precipitation, a modest number of rainy days, and low temperature. In the other clusters, the regional female population rate (cluster 2) and the senior population rate (cluster 3, 4) were the primary predictors. We concluded that the degree of exposure to sunlight may play a crucial role in prevention of joint pain. This finding should encourage people to set aside some time for staying outdoors in their daily lives.

Key words: climate, joint pain, sunlight hours, cluster analysis

Joint pain is a prevalent complaint among the middle-aged and elderly. Japan, country with one of the longest life expectancies, is having to pay great medical expenses for the treatment of joint pain.

Joint pain is the chief symptom of patients with osteoarthritis (OA) and rheumatoid arthritis (RA), and in many cases, its pain causes major impediments in performing ADLs (Activities of Daily Living), e.g. difficulty in walking and climbing stairs. Osteoarthritis has a high prevalence particularly among the elderly, its etiologies mainly include abnormalities in

bone alignment [1-6], aging [7], excessive mechanical stress on joints due to obesity [8, 9], genetic factors [10-13], vitamin D deficiency [14], and womanhood [15, 16]; however, it is still unclear which is the decisive cause of osteoarthritis.

The influence of climate on osteoarthritic pain has also been reported [17-21]. Patients who have joint pain are known to be susceptible to weather changes [17]. In the West, studies on the relationships between weather and joint pain have been conducted for a long time. Although these studies have demonstrated that sudden changes of barometric pressure exacerbates joint pain [17], and climatic conditions such as frigid temperature and high humidity increase the prevalence of joint pain [18], the importance of

the relationships between weather and joint pain has not yet been decided. Moreover, the studies that have indicated the relationships between joint pain and frigid temperature/high humidity employed no more than 5 years of weather-condition data [21]; so far no study has examined the long-term climatic effects on joint pain.

The present study used sunlight hours, amount of precipitation, number of days with precipitation, and temperature as weather indices to classify the areas of Japan into several climatic areas. The objective of the study was to examine the relationships between the distinctive climates of these climatic areas (excluding Hokkaido) and the proportion of people with joint pain based on the climate data of a 29-year period issued by the Meteorological Agency of Japan.

In this study, we hypothesized that differences in climate characterized by sunlight hours, amount of precipitation, number of days with precipitation, and temperature would be associated with the proportion of people with joint pain.

Materials and Methods

Twenty-nine years' (1971–2000) worth of regional meteorological climate data (acquired by AMeDAS) from "Normal Values 2nd Edition" compiled by the Bureau of Statistics of the Japan Meteorological Agency was employed in this study. The variables used to characterize climate included sunlight hours, amount of precipitation, number of days with precipitation, and temperature. Data of each variable were the monthly mean value collected at the site of the fixed-point observation in each prefecture (607 points for sunlight hours, 907 points for amount of precipitation, 908 points for the number of days with precipitation, and 670 points for temperature). The data of Hokkaido were excluded from the analysis because Hokkaido is wide from the west to the east, and climate conditions differ markedly within that prefecture.

The 29-year monthly mean values of each variable were then calculated by dividing the sum of the monthly mean values of each prefecture by the number of fixed observation points. Finally, the annual mean values (climatic values) were obtained by dividing the 12-month sums of the 29-year monthly mean values by the number of months (12 months).

The proportion of people with joint pain was calculated based on the data of the National Livelihood Survey (health polling) [22] implemented in 2001. The proportion of people with joint pain in each prefecture was calculated as

$$\frac{\text{\# of people (estimate) who answered "yes" to "limb joints hurt"}}{\text{total population}}$$

:

Four variables—sunlight hours, amount of precipitation, number of days with precipitation, and temperature—were used to divide Japan into 4 clusters (areas) on the basis of similarities among the climatic characteristics using cluster analysis.

The hierarchical cluster analysis technique organizes information about variables so that relatively homogeneous groups (clusters) can be formed. Although it can produce any number of clusters, the clusters formed should be highly internally homogeneous in the same cluster and highly externally heterogeneous among clusters. We performed a hierarchical clustering procedure using the Ward's Method and Squared Euclidean measure. These classified 4 clusters were the minimum clusters among which significant differences were observed in any of the climate variables (sunlight hours, amount of precipitation number of days with precipitation, and temperature). After the cluster analysis, we conducted a one-way analysis of variance (Tukey HSD multiple comparison) and Welch's test (Games-Howell multiple comparison) and then determined the climatic characteristics of each cluster (area). In order to examine the relationship between the climate in each cluster and joint pain, we performed a multiple linear regression analysis (stepwise method) with the dependent variable being the proportion of people with joint pain in each prefecture and the independent variables, as possible non-climatic factors related to joint pain, being the regional female population rate, regional senior population rate, rate of individuals with the regular exercise habit (these three data were from the National Livelihood Survey, 2001), and rate of primary industry workers from the 2000 census (Ministry of Internal Affairs and Communications; <http://www.stat.go.jp/data/kokusei/2000/kihon2/00/mokuji.htm>). Data with skewed distributions were converted into logarithms. The inclusion and exclusion criteria were set at $p < 0.05$ and $p > 0.10$, respectively. The

software employed was SPSS Statistics 17.0 for Windows.

Results

Table 1 shows the climate data and the proportion of people with joint pain in each prefecture of Japan. As a result of the cluster analysis and analysis of variance, the entire country was classified into 4 clusters based on climatic characteristics (Table 2). Significant differences in sunlight hours were observed between clusters 1 and 3, clusters 1 and 4, clusters 2 and 3, and clusters 2 and 4 (Fig. 1) while the differences between clusters 1 and 2, and clusters 3 and 4 were not significant. With respect to the amount of precipitation, there were significant differences between clusters 1 and 2, clusters 1 and 4, clusters 2 and 3, and clusters 3 and 4 (Fig. 2). With respect to the number of days with precipitation, significant differences were observed between clusters 1 and 2, clusters 1 and 3, clusters 2 and 3, and clusters 2 and 4 (Fig. 3). Finally, with respect to temperature, significant differences were observed between clusters 1 and 3 and clusters 1 and 4 (Fig. 4). Table 3 shows the climatic characteristics of each cluster by sunlight hours, amount of precipitation, number of days with precipitation, and temperature.

The results by the multiple linear regression analysis revealed that only the sunlight hours had a significant relationship (adjusted $R^2 = .532$, standardized $\beta = -.768$, $p = .016$) with the proportion of people with joint pain in cluster 1 (an area with short sunlight hours, a small amount of precipitation, low temperature, and low median number of days with precipitation). The ratio of women was significantly related to the proportion of people with joint pain in cluster 2 (adjusted $R^2 = .768$, standardized $\beta = .891$, $p = .001$), and the proportions of elderly and of primary industry workers were significantly related to the proportion of people with joint pain in cluster 3 (adjusted $R^2 = .627$, standardized $\beta = 1.088$, $-.475$, $p = .046$). The proportion of the elderly and the number of days with precipitation were significantly related with the proportion of people with joint pain in cluster 4 (adjusted $R^2 = .831$, standardized $\beta = 1.021$, $-.493$, $p = .014$) (Table 4).

Discussion

In comparison with factors such as age, sex, occupation, exercise habits, amount of precipitation, number of days with precipitation, and temperature, the hours of sunlight had a greater influence over the fluctuation of the proportion of people with joint pain in areas with short annual mean sunlight hours (cluster 1). This might imply that an increase in one's exposure time to the sunlight could decrease the development of joint pain (or vice versa) in areas with fewer hours of sunlight. Patberg *et al.* [23] reported that staying outdoors for 2h or more per day decreased the pain score of RA patients.

Although the present results cannot elucidate the detailed mechanism governing pain alleviation by sunlight, vitamin D might be involved in this mechanism as it is the most common substance to be activated by exposure to the sunlight. Polymorphisms of the vitamin D receptor (VDR) gene were also suggested as one of the etiologies of OA [13]. In the present study, if people who are more genetically susceptible to OA happened to inhabit the areas with higher proportions of people with joint pain, sunlight hours could be considered a confounder. However, according to the report by Huang *et al.* [24], the Japanese predominantly have certain genotypes (TT or Tt) of the VDR polymorphism that are equally conducive for developing OA. On the other hand, the preventive genotype 'tt' is hardly detectable in Japanese people. We therefore presume that the influence, if any, of the aforementioned VDR gene on the present results would be very limited.

Cluster 2 also includes areas with as few sunlight hours as cluster 1, and the ratio of women was significantly associated with the fluctuations in the proportion of people with joint pain. In general, arthropathies such as RA and OA are more prevalent among women; accordingly, the proportion of people with joint pain had been expected to be higher among women. The present result was consistent with the finding by Hanna *et al.* [16].

In cluster 3, the proportions of elderly people and of the primary industry workers were significantly associated with the proportion of people with joint pain. In cluster 4, the proportions of elderly people and number of days with precipitation were significantly associated with the proportion of people with

Table 1 The climatic values and the proportion of people with joint pain in each prefecture

Prefecture	Population (Thousand)	Estimate Population of joint pain in extremities (Thousand)	Proportion of people with joint pain	Sunlight hours/month (h)	Amount of precipitation/month (mm)	Number of days with precipitation/month (days)	Temperature/month (°C)
Aomori	1,469	92	0.063	120.0	108.5	9.0	9.4
Iwate	1,408	88	0.063	121.8	111.3	9.3	9.5
Miyagi	2,355	120	0.051	132.6	112.7	9.4	11.0
Akita	1,181	85	0.072	108.5	152.0	12.7	10.3
Yamagata	1,235	76	0.062	111.6	162.1	13.5	10.7
Fukushima	2,114	117	0.055	126.6	116.2	9.7	10.6
Ibaraki	2,956	134	0.045	147.9	114.2	9.5	13.2
Tochigi	1,984	104	0.052	138.4	126.9	10.6	11.4
Gunma	1,997	102	0.051	140.4	114.4	9.5	11.4
Saitama	6,898	343	0.050	147.9	113.3	9.4	14.1
Chiba	5,894	306	0.052	147.2	135.4	11.3	15.0
Tokyo	11,896	688	0.058	143.6	151.2	12.6	16.1
Kanagawa	8,442	408	0.048	149.6	155.4	12.9	15.4
Niigata	2,461	148	0.060	110.9	193.9	16.2	12.6
Toyama	1,112	74	0.067	120.3	211.2	17.6	13.2
Ishikawa	1,174	71	0.060	122.9	189.7	15.8	13.5
Fukui	818	55	0.067	116.4	188.9	15.7	14.1
Yamanashi	877	48	0.055	154.9	128.4	10.7	12.5
Nagano	2,182	158	0.072	146.2	132.1	11.0	10.0
Gifu	2,080	122	0.059	129.2	186.6	15.6	12.3
Shizuoka	3,716	206	0.055	157.2	188.6	15.7	15.2
Aichi	6,950	388	0.056	158.1	140.3	11.7	14.9
Mie	1,834	117	0.064	155.2	180.0	15.0	15.3
Shiga	1,330	78	0.059	129.1	144.0	12.0	13.7
Kyoto	2,598	177	0.068	119.7	136.8	11.4	14.1
Osaka	8,638	580	0.067	146.2	113.6	9.5	14.8
Hyogo	5,479	364	0.066	134.6	127.7	10.6	14.3
Nara	1,433	84	0.059	125.0	140.3	11.7	13.3
Wakayama	1,062	74	0.070	146.1	191.0	15.9	14.9
Tottori	609	37	0.061	126.0	165.4	13.8	13.9
Shimane	755	58	0.077	122.4	155.7	13.0	13.6
Okayama	1,938	117	0.060	135.2	116.2	9.7	13.6
Hiroshima	2,853	190	0.067	140.1	130.9	10.9	13.7
Yamaguchi	1,511	94	0.062	146.0	156.5	13.0	14.7
Tokushima	820	56	0.068	143.8	179.3	14.9	14.9
Kagawa	1,016	76	0.075	154.3	97.3	8.1	15.4
Ehime	1,486	105	0.071	144.6	137.3	11.4	15.4
Kochi	810	61	0.075	150.8	226.9	18.9	15.5
Fukuoka	4,991	279	0.056	142.2	160.4	13.4	15.6
Saga	873	51	0.058	144.6	171.9	14.3	15.4
Nagasaki	1,507	108	0.072	150.5	172.2	14.3	15.9
Kumamoto	1,853	112	0.060	145.3	192.0	16.0	15.1
Oita	1,215	74	0.061	145.9	151.6	12.6	15.0
Miyazaki	1,165	72	0.062	150.5	225.1	18.8	16.1
Kagoshima	1,778	111	0.062	143.1	207.9	17.3	18.1
Okinawa	1,318	62	0.047	137.1	174.8	14.6	22.8

The proportion of people with joint pain was calculated by dividing the number of people who had chosen the answer “the limb joints hurt” in the total number (estimate number) of symptoms in the National Livelihood Survey (health polling) implemented in 2001 by the population of each prefecture. As the climatic data, we used 29 years (1971–2000) worth of regional meteorological data (acquired by AMeDAS) from “Normal Values 2nd Edition” edited by the Bureau of Statistics of the Japan Meteorological Agency.

Table 2 The four areas after the cluster analysis

Cluster 1 (n=9)	Aomori, Iwate, Miyagi, Fukushima, Gunma, Shiga, Kyoto, Nara, Okayama
Cluster 2 (n=10)	Akita, Yamagata, Niigata, Toyama, Ishikawa, Fukui, Gifu, Tottori, Shimane, Okinawa
Cluster 3 (n=17)	Ibaraki, Tochigi, Saitama, Chiba, Tokyo, Kanagawa, Yamanashi, Nagano, Aichi, Osaka, Hyogo, Hiroshima, Yamaguchi, Kagawa, Ehime, Fukuoka, Oita
Cluster 4 (n=10)	Shizuoka, Mie, Wakayama, Tokushima, Kochi, Saga, Nagasaki, Kumamoto, Miyazaki, Kagoshima

Table 3 The climatic characteristics of each cluster

Cluster	The climatic characteristics			
	Sunlight hours	Amount of precipitation	Number of days with precipitation	Temperature
1	Short	Few	Moderate	Low
2	Short	Many	Frequent	Moderate
3	Long	Few	Few	Comparative high
4	Long	Many	Few	High

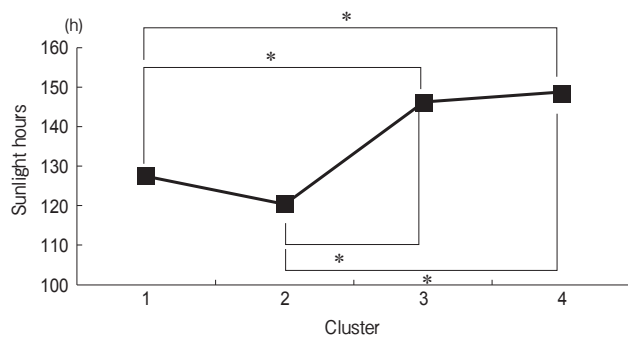


Fig. 1 Comparison of the annual mean sunlight hours between the clusters by Tukey HSD. Clusters 1 to 4 were determined by a hierarchical clustering procedure using the Ward's method and the squared Euclidean measure. * $p < 0.05$ by Tukey HSD after analysis of variance (one-way ANOVA).

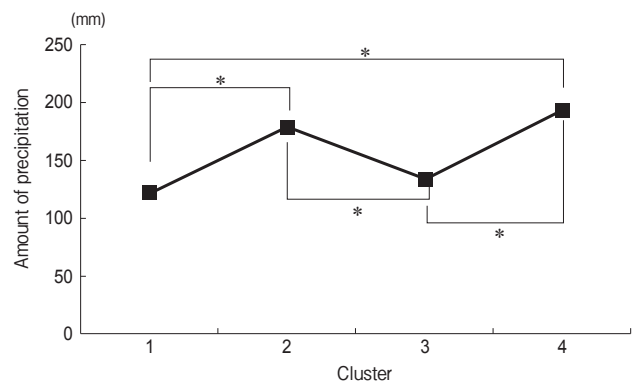


Fig. 2 Comparison of the annual mean amount of precipitation between the clusters by Tukey HSD. Clusters 1 to 4 were determined by a hierarchical clustering procedure using the Ward's method and the squared Euclidean measure. * $p < 0.05$ by Tukey HSD after one-way ANOVA, in which logarithm values were used.

joint pain, indicating that age had a great influence on the proportion of people with joint pain in areas with sufficient sunlight hours (cluster 3 and 4), that agrees with the results by Davies-Tuck *et al.* [7]. Surprisingly, we also found the proportion of people who engaged in the primary industry was negatively associated with the proportion of people with joint pain in cluster 3. It is known that working in primary industries includ-

ing farming, fishing, and forestry is physically demanding, and people working in primary industries generally bear a great physical burden to their joints; we assumed that the proportion of people with joint pain among them would be relatively high. However, the present results showed a decrease in the

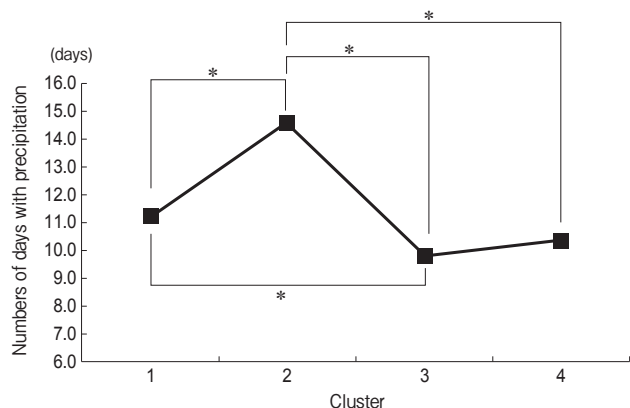


Fig. 3 Comparison of the annual mean number of days with precipitation between the clusters by Games-Howell. Clusters 1 to 4 were determined by a hierarchical clustering procedure using the Ward's method and the squared Euclidean measure. * $p < 0.05$ by Games-Howell after Welch's test.

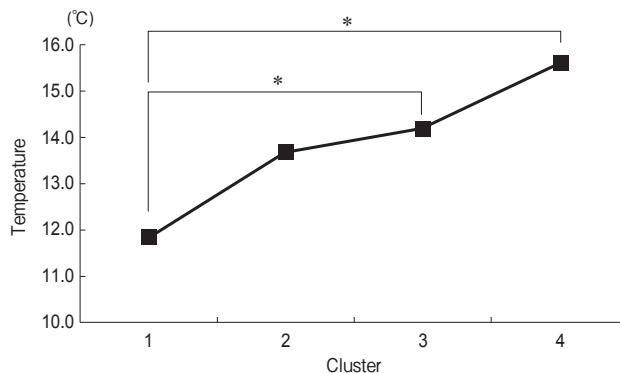


Fig. 4 Comparison of the annual mean temperature between the clusters by Tukey HSD. Clusters 1 to 4 were determined by a hierarchical clustering procedure using the Ward's method and the squared Euclidean measure. * $p < 0.05$ by Tukey HSD after one-way ANOVA, in which logarithm values were used.

Table 4 Multipul linear regression analysis for joint pain in each cluster

Cluster	Regression model	Independent variable	Adjusted R^2	Standardized β	Partial	p value
1	1 ^a	Sunlight hours	.532	-.768	-.768	.016
2	1 ^b	Proportion of female	.768	.891	.891	.001
	1 ^c	Proportion of the elderly	.534	.750	.750	.001
3	2 ^d	Proportion of the elderly and Proportion of people working in the primary industry	.627	1.088 -.475	.801 -.504	.000 .046
		1 ^e	Proportion of the elderly	.626	.817	.817
4	2 ^f	Proportion of the elderly and Number of days with precipitation	.831	1.021 -.493	.932 -.778	.000 .014

a Amount of precipitation, number of days with precipitation, temperature, rate of females, rate of elderly people, rate of people in primary industry and rate of individuals with regular exercise habits were excluded from the model.

b Sunlight hours, amount of precipitation, number of days with precipitation, temperature, rate of elderly people, rate of people in primary industry and rate of individuals with regular exercise habits were excluded from the model.

c Sunlight hours, amount of precipitation, number of days with precipitation, temperature, rate of females, rate of people in primary industry and rate of individuals with regular exercise habits were excluded from the model.

d Sunlight hours, amount of precipitation, number of days with precipitation, temperature, rate of females and rate of individuals with regular exercise habits were excluded from the model.

e Sunlight hours, amount of precipitation, number of days with precipitation, temperature, rate of females, rate of people in primary industry and rate of individuals with regular exercise habits were excluded from the model.

f Sunlight hours, amount of precipitation, temperature, rate of females, rate of people in primary industry and rate of individuals with regular exercise habits were excluded from the model.

proportion of people with joint pain among areas with a high proportion of people working in primary industries, possibly because workers in primary industries mainly work outdoors, which increases their exposure to sunlight.

On the other hand, the number of days with precipitation had a significant relationship with the proportion of people with joint pain in cluster 4. The areas in this cluster are characterized by fewer days of precipitation, a large amount of precipitation, more sunlight hours, and high temperature. In comparison with the other clusters, this cluster had a high proportion of people with joint pain and the highest proportion of all clusters of workers from the primary industry (data not shown). Hence, the climate of these areas might suit the primary industry like agriculture. Although this consideration might be contradictory to that of cluster 3, if the minimum time of sunlight exposure to people in these areas is secured, we may assume that a great physical burden to their joints by daily heavy work would have a stronger influence on the onset of joint pain in comparison with the suppressive effect by sunlight exposure.

In this study, we observed that residence in areas with shorter sunlight hours seemed to entail a higher risk of developing joint pain. However, the present data were collected at fixed observation points in each area, and do not represent anyone's actual exposure to sunlight. Therefore, it cannot be said that living in those particular areas would automatically increase the risk of developing joint pain. It would be rare for anyone to stay outdoors all day long; normal exposure ranges from a few hours at most to a few minutes. In other words, what matters is how many opportunities individuals have to be exposed directly to sunlight, and how often they take advantage of those opportunities.

The authors thus postulate that proactively securing time to be exposed to the sunlight in the areas with fewer sunlight hours would contribute to lowering the risk of developing joint pain to the same extent as in the other areas. In fact, no relationships were observed between sunlight hours and the proportion of people with joint pain in cluster 2, despite this cluster having the fewest sunlight hours. The areas in cluster 2 had plenty of rainfall and many days with precipitation, leaving only a few sunny days. However, the main distinction between the areas in cluster 2 and

those in cluster 1 is that the former has more rainy days. Consequently, the residents in the areas of cluster 2 might have the habit of exposing themselves longer to the sunlight on the few sunny days that came at intervals between rainy days to supplement the shortage.

The present study has several potential limitations. First, it is a secondary data analysis using each prefecture's climate data. We divided the country into 4 areas using only 4 variables (sunlight hours, amount of precipitation, number of days with precipitation, and temperature) to examine the relationship between joint pain and climate conditions; nevertheless, further minute climate divisions with other variables (humidity or atmospheric pressure, *etc.*) that assumedly have relevance to joint pain might be needed. Second, data on people with joint pain was secondary data from the National Livelihood Survey implemented in 2001, not the actual number of patients. There are many disorders besides OA that cause joint pain; for example, RA, gout, and osteoporosis. Information on the disorders of the subjects, previous symptoms, extent of pain, and treatment history was not available in this study. Third, the climate data used in the present analyses were merely collected at fixed observation points in each area, they do not represent anyone's actual amount (time) of exposure to sunlight. In order to reveal the effect of the body's actual amount of exposure to light therapy using xenon equipment instead of sunlight, we are now carrying out experiments using animal models that can develop OA spontaneously.

In conclusion, the present results suggest that the degree of exposure to sunlight may play a crucial role in the prevention of joint pain, in some cases more influential than the factors generally considered to be so (aging, sex, occupation, *etc.*) on limb joints, particularly in regions with few sunlight hours, a small amount of precipitation, low temperature, and a medium number of days with precipitation (*i.e.*, cluster 1). Further investigation needs to be performed to provide direct supporting evidence.

Acknowledgments. This work was supported by Grant-in-Aid for Young Scientists (B) (20700453) from The Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

- Teichtahl AJ, Wluka AE and Cicuttini FM: Frontal plane knee alignment is associated with a longitudinal reduction in patella cartilage volume in people with knee osteoarthritis. *Osteoarthritis Cartilage* (2008) 16: 851–854.
- Jackson BD, Wluka AE, Teichtahl AJ, Morris ME and Cicuttini FM: Reviewing knee osteoarthritis—a biomechanical perspective. *J Sci Med Sport* (2004) 7: 347–357.
- Davies-Tuck M, Teichtahl AJ, Wluka AE, Wang Y, Urquhart DM, Cui J and Cicuttini FM: Femoral sulcus angle and increased patella facet cartilage volume in an osteoarthritic population. *Osteoarthritis Cartilage* (2008) 16: 131–135.
- Teichtahl AJ, Davies-Tuck ML, Wluka AE, Jones G and Cicuttini FM: Change in knee angle influences the rate of medial tibial cartilage volume loss in knee osteoarthritis. *Osteoarthritis Cartilage* (2009) 17: 8–11.
- Cicuttini F, Wluka AE, Hankin J and Wang Y: Longitudinal study of the relationship between knee angle and tibiofemoral cartilage volume in subjects with knee osteoarthritis. *Rheumatology Oxford* (2004) 43: 321–324.
- Chang A, Hayes K, Dunlop D, Hurwitz D, Song J, Cahue S, Genge R and Sharma L: Thrust during ambulation and the progression of knee osteoarthritis. *Arthritis Rheum* (2004) 50: 3897–3903.
- Davies-Tuck ML, Wluka AE, Wang Y, Teichtahl AJ, Jones G, Ding C and Cicuttini FM: The natural history of cartilage defects in people with knee osteoarthritis. *Osteoarthritis Cartilage* (2008) 16: 337–342.
- Teichtahl AJ, Wluka AE, Wang Y, Hanna F, English DR, Giles GG and Cicuttini FM: Obesity and adiposity are associated with the rate of patella cartilage volume loss over 2 years in adults without knee osteoarthritis. *Ann Rheum Dis* (2009) 68: 909–913.
- Powell A, Teichtahl AJ, Wluka AE and Cicuttini FM: Obesity: a preventable risk factor for large joint osteoarthritis which may act through biomechanical factors. *Br J Sports Med* (2005) 39: 4–5.
- Valdes AM, Hart DJ, Jones KA, Surdulescu G, Swarbrick P, Doyle DV, Schafer AJ and Spector TD: Association study of candidate genes for the prevalence and progression of knee osteoarthritis. *Arthritis Rheum* (2004) 50: 2497–2507.
- Valdes AM, Van Oene M, Hart DJ, Surdulescu GL, Loughlin J, Doherty M and Spector TD: Reproducible genetic associations between candidate genes and clinical knee osteoarthritis in men and women. *Arthritis Rheum* (2006) 54: 533–539.
- Valdes AM, Doherty M and Spector TD: The additive effect of individual genes in predicting risk of knee osteoarthritis. *Ann Rheum Dis* (2008) 67: 124–127.
- Keen RW, Hart DJ, Lanchbury JS and Spector TD: Association of early osteoarthritis of the knee with A Taq 1 polymorphism of the vitamin D receptor gene. *Arthritis Rheum* (1997) 40: 1444–1449.
- Heike A, Bischoff-ferrari, Yuqing Z, Douglas PK and David T: Positive association between serum 25-hydroxyvitamin D level and bone density in osteoarthritis. *Arthritis Rheum* (2005) 53: 821–826.
- Teichtahl AJ, Wluka AE, Proietto J and Cicuttini FM: Obesity and the female sex, risk factors for knee osteoarthritis that may be attributable to systemic or local leptin biosynthesis and its cellular effects. *Med Hypotheses* (2005) 65: 312–315.
- Hanna FS, Teichtahl AJ, Wluka AE, Wang Y, Urquhart DM, English DR, Giles GG and Cicuttini FM: Women have increased rates of cartilage loss and progression of cartilage defects at the knee than men: a gender study of adults without clinical knee osteoarthritis. *Menopause* (2009) 16: 666–670.
- Wilder FV, Hall BJ and Barrett JP: Osteoarthritis pain and weather. *Rheumatology Oxford* (2003) 42: 955–958.
- Patberg WR and Rasker JJ: Weather effects in rheumatoid arthritis: from controversy to consensus. A review. *J Rheumatol* (2004) 31: 1327–1334.
- Guedj D and Weinberger A: Effect of weather conditions on rheumatic patient. *Ann Rheum Dis* (1990) 49: 158–159.
- Laborde JM, Dando WA and Powers MJ: Influence of weather on osteoarthritis. *Soc Sci Med* (1986) 23: 549–554.
- Patberg WR: Effect of temperature and humidity on daily pain score in a patient with rheumatoid arthritis. *Arthritis Rheum* (1989) 32: 1627–1629.
- National Livelihood Survey, Ministry of Health, Labour and Welfare, Tokyo (2001) pp385–431 (in Japanese).
- Patberg WR and Rasker JJ: Beneficial effect of being outdoors in rheumatoid arthritis (letter). *J Rheumatol* (2002) 29: 202–204.
- Huang J, Ushiyama T, Inoue K, Kawasaki T and Hukuda S: Vitamin D receptor gene polymorphisms and osteoarthritis of the hand, hip, and knee: a case-control study in Japan. *Rheumatology* (2000) 39: 79–84.