Spondyloarthropathies in Japan: Nationwide Questionnaire Survey Performed by The Japan Ankylosing Spondylitis Society

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ABSTRACT. ***Objective.*** The Japan Ankylosing Spondylitis Society conducted a nationwide questionnaire survey of spondyloarthropathies (SpA) in 1990 and 1997, (1) to estimate the prevalence and incidence, and (2) to validate the criteria of Amor and the European Spondylarthropathy Study Group (ESSG) in Japan.

Methods. Japan was divided into 9 districts, to each of which a survey supervisor was assigned. According to unified criteria, each supervisor selected all the clinics and hospitals with potential for SpA patients in the district. The study population consisted of all patients with SpA seen at these institutes during a 5 year period (1985–89) for the 1st survey and a 7 year period (1990–96) for the 2nd survey.

Results. The 1st survey recruited 426 and the 2nd survey 638 cases, 74 of which were registered in both studies. The total number of patients with SpA identified 1985–96 was 990 (760 men, 227 women). They consisted of patients with ankylosing spondylitis (68.3%), psoriatic arthritis (12.7%), reactive arthritis (4.0%), undifferentiated SpA (5.4%), inflammatory bowel disease (2.2%), pustulosis palmaris et plantaris (4.7%), and others (polyenthesitis, etc.) (0.8%). The maximum onset number per year was 49. With the assumption that at least one-tenth of the Japanese population with SpA was recruited, incidence and prevalence were estimated not to exceed 0.48/100,000 and 9.5/100,000 person-years, respectively. The sensitivity was 84.0% for Amor criteria and 84.6 for ESSG criteria.

Conclusion. The incidence and prevalence of SpA in Japanese were estimated to be less than 1/10 and 1/200, respectively, of those among Caucasians. The adaptability of the Amor and ESSG criteria was validated for the Japanese population. (J Rheumatol 2001;28:554–9)

Key Indexing Terms:
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Ankylosing spondylitis (AS) and related spondyloarthropathies (SpA) are strongly associated with HLA-B27 in every country, including Japan. Frequency of HLA-B27, however, is different from race to race; it is found in 7% of Caucasians, but in less than 1% of the Japanese population. Since AS and related SpA are extremely rare in Japan, its incidence and prevalence are almost unknown. Shichikawa and others have estimated the prevalence of AS in Japan to be 0.04% by multiplying the prevalence of AS among the patients in a low back pain clinic by the prevalence of low back pain within a community[1,2]. In 1990 The Japanese AS Society was established by orthopedists and rheumatologists to improve knowledge of the disease among medical professionals and the public. The society has performed a nationwide questionnaire survey twice: (1) to assess the prevalence and incidence of this ailment in Japan and (2) to validate the criteria of Amor, *et al*[3,4] and the European Spondylarthropathy Study Group

(ESSG)[5] in Japan. The 2 surveys are described here. This is the first epidemiological study of AS and related SpA performed in Japan.

MATERIALS AND METHODS

Japan was divided into 9 districts, to each of which a local orthopedist or rheumatologist was assigned as a survey supervisor. Each survey supervisor selected all the clinics and hospitals with potential to be attended by patients with SpA in the district. The selection criterion was the institution to which at least one orthopedic rheumatologist licensed by the Japanese Orthopaedic Association and/or rheumatologist licensed by the Japan Rheumatism Association was posted. Questionnaire forms for medical record abstracts were sent to these institutions from The Japan AS Society. The physicians at the institutes were requested to answer the questionnaires by reviewing the medical records of patients with SpA attending their institutes. Diagnosis of SpA was performed by the physicians at the institutes according to either the Rome criteria or New York criteria for AS and, for other subsets of SpA, being based on ordinary clinical and roentgenographic features. Radiographic examination of the sacroiliac joint and the whole spinal column was mandatory and that of the appendicular skeleton was also performed as appropriate. However, no attempt was made to standardize the diagnostic standard among the institutes. The study population consisted of all SpA patients who attended those institutes during a 5 year period (1985–89) for the first survey and a 7 year period (1990–96) for the second survey.

The items surveyed in both studies included sex, birth year, SpA subset, year of onset, and Amor criteria. ESSG criteria, surgical treatments, and functional assessments including Schober test, occiput–wall test (both for spinal mobility), and Steinbrocker RA classification (for global function) were added to the second survey.

RESULTS

Referral institutes and response rate. In the first survey the number of referring institutes all over Japan reached 134, out of which 77 joined the survey (57.5%). In the second survey 100 out of 141 institutes responded (70.9%).

Characteristics of SpA patients. The total number of patients with SpA recruited during 12 years (1985–96) was 990: 760 men, 227 women (3 sex unknown) with a male/female ratio of 3.3/1. Ethnically they were almost all Japanese except 19 Koreans, 5 Caucasians, 4 Chinese, and one Indonesian. They were born during the period 1904 to 1985 and the onset year ranged from 1935 to 1988. The mean age at disease onset was 30.3 ± 14.5 years for men, 38.7 ± 15.6 years for women; the difference was statistically significant, $p < 0.0001$ by Student t test. The diagnostic delay was 5.8 ± 7.8 years on average, the longest being 57 years.

Estimation of incidence and prevalence of SpA. The maximum onset number per year was 49, in the year 1987. The Japanese population above 15 years of age was 101,100,000 at that time. With the assumption, based on the rationale described later, that at least one-tenth of the real SpA population was recruited by the survey, the annual incidence would have been estimated not to exceed 0.48/100,000 person-years. The total of 990 cases was recruited in this study and the prevalence similarly estimated would have not exceeded 9.5/100,000.

Validity of Amor criteria. Data for Amor criteria were collected in 962 cases; the frequency of each item is shown in Table 1A. Between the first and second survey, oligoarthritis and the effectiveness of nonsteroidal antiinflammatory drugs increased, while sacroiliitis decreased in frequency ($p < 0.0001$ by chi-square analysis). The total scores of the 12 items ranged from 0 to 21 with the average of 8.1 ± 2.9. The sensitivity rate (the rate of cases with score ≥ 6) was 84.0%.

The frequency of each item of the Amor criteria in different subsets of SpA is shown in Table 1B. The prevalence of HLA-B27/family history in the AS population was 64%, which was low in comparison to that reported among Caucasoid and Mongoloid populations[5a].

Validity of ESSG criteria. ESSG criteria were examined in 638 cases in the second survey, 540 of which had inflammatory back pain or arthritis in addition to at least one of the 7 other items. The sensitivity rate was 84.6% (Table 2A). The frequency of each item of the ESSG criteria in different SpA subsets is shown in Table 2B.

SpA subsets. We adopted the classification of SpA subsets diagnosed by the physicians of the referring institutes. They consisted of AS (68.3%), psoriatic arthritis (12.7%), reactive arthritis (4.0%), undifferentiated SpA (5.4%), inflammatory bowel disease (IBD) (2.2%), pustulosis palmaris et plantaris (4.7%), SAPHO (0.3%), and others (polyenthesitis in 6 cases, juvenile RA and Behçet's disease in one each; 0.8%). Subset diagnosis was not specified in 14 cases (1.4%) (Table 3). Both the Amor and ESSG criteria showed the highest sensitivity in AS and the lowest in pustulosis palmaris et plantaris.

DISCUSSION

Comparison of first and second survey. Only 74 out of 426 patients recruited in the first survey were registered again in the second. No information was available on the fate of the remaining 352 patients. Some stopped attending medical services for unknown reasons or were thought to have died during the period of the second survey. Most were more likely intentionally excluded by the physicians who knew of their registration in the first survey.

The male/female ratio decreased (4.5 to 3.0; $p = 0.0116$) and the mean age at onset increased (30.7 to 32.4 yrs; $p = 0.0553$) between the 2 surveys. The same tendency was observed when the present study, in which male/female ratio was 5.4 and mean onset age in the AS subset was 28.9 years, was compared with an earlier study of AS[1], in which they were 12 and 25.4 years, respectively.

Estimation of prevalence and incidence. This study had several drawbacks in its survey method: neglect of the patient population with no hospital record; bias in the selection of the referring institutions (although about half of the licensed rheumatologists in Japan work for private clinics, over 80% of our referral institutions belonged to university hospitals and national or other public hospitals); and the low

Table 1. A. Frequency (%) of each item of the Amor criteria in 962 cases.

Item		1st Survey	2nd Survey	Total	p
1.	Back pain	85	79	80	NS
2.	Oligoarthritis	39	62	55	< 0.0001
3.	Buttock pain	44	38	40	NS
4.	Sausage digit	6	6	6	NS
5.	Enthesopathy	19	22	21	NS
6.	Iritis	17	17	17	NS
7.	Urethritis/cervicitis	2	2	2	NS
8.	Acute diarrhea	3	3	3	NS
9.	Psoriasis/balanitis/enteritis	14	19	17	NS
10.	Sacroiliitis	82	66	70	< 0.0001
11.	HLA-B27/family history	54	67	47	NS
12.	NSAID effect	56	67	62	< 0.0001
Score		8.0 ± 2.6	8.1 ± 3.0	8.1 ± 2.9	NS
Sensitivity		86.3	83.5	84.0	NS

Table 1. B. Frequency (%) of each item of the Amor criteria in different SpA subsets.

		AS	PsA	ReA	IBD	PPP	SAPHO	USpA	Others	Total
1.	Back pain	91	44	50	68	55	100	72	75	80
2.	Oligoarthritis	47	79	88	68	61	100	74	50	55
3.	Buttock pain	47	16	27	27	12	33	49	50	40
4.	Sausage digit	2	22	5	0	4	0	17	0	6
5.	Enthesopathy	17	21	51	9	19	0	50	50	21
6.	Iritis	21	2	2	22	2	33	9	25	17
7.	Urethritis/cervicitis	1	0	30	0	0	0	3	0	2
8.	Acute diarrhea	1	0	5	22	2	33	3	0	3
9.	Psoriasis/balanitis/enteritis	2	97	19	81	12	33	3	0	17
10.	Sacroiliitis	90	17	21	50	19	100	52	12	71
11.	HLA-B27/family history	64	4	25	18	2	0	7	12	47
12.	NSAID effect	64	53	72	59	68	33	56	25	62

PsA: psoriatic arthritis, ReA: reactive arthritis, IBD: inflammatory bowel disease, PPP: pustulosis palmaris et plantaris, USpA: undifferentiated SpA.

response rate of the referral institutions. Those factors were supposed to have caused a considerable divergence of the patient population size.

Japan was divided into 9 districts for this study. The prevalence of SpA per district differed by 6 times between the highest (1.52/100,000 in Kinki district) and the lowest (0.26/100,000 in Northern Kyushu district). It was an unrealistic discrepancy in a small country like Japan, where a well developed transportation system covers the whole territory. If the 8 districts other than Kinki were assumed to have prevalences similar to it, the total prevalence would become 3 times greater. These considerations might support our presumption that the prevalence in the general Japanese population should not exceed 10 times the figure obtained in this study.

International comparison of prevalence and annual incidence (Tables 4 and 5). AS is considered to be the prototype of SpA. There are many epidemiologic data, most from Caucasian populations, on the frequency of AS. According to Khan[6], the prevalence of AS in adults in the general white population is close to 0.2%, and among B27 positive individuals it is 2%. Studies of non-Caucasians reveal that AS is extremely rare in black African populations[7]. The disease is less common among American blacks than in whites[8]. Among Asians, Chinese in Taiwan have a prevalence of AS between 0.19 and 0.54%, which is similar to that reported in Caucasians[9]. The prevalence of AS in an Inupiat population was found to be 0.2%[10]. In Japan it was estimated to be

Table 2. A. Frequency of items of the ESSG criteria in 638 cases.

Item	%
Inflammatory back pain/arthritis	94.0
Family history	6.7
Psoriasis	14.1
Inflammatory bowel disease	4.5
Urethritis/cervicitis/diarrhea	1.9
Buttock pain	23.8
Achilles/plantar enthesitis	17.2
Sacroiliitis	67.1
Sensitivity	84.6

Table 2. B. Frequency (%) of each item of the ESSG criteria in different SpA subsets.

	AS	PsA	ReA	IBD	PPP	SAPHO	USpA	Others	Total
Inflammatory back pain/arthritis	97.7	89.0	92.5	90.9	78.7	100	89.4	75.0	94.0
Family history	10.1	0	0	0	0	0	2.6	12.5	6.7
Psoriasis	1.2	98.7	3.7	0	2.1	33.3	0	0	14.1
Inflammatory bowel disease	1.7	0	0	100	0	0	0	0	4.5
Urethritis/cervicitis/diarrhea	0.4	0	25.9	0	0	0	5.2	0	1.8
Buttock pain	31.3	9.7	7.4	13.6	6.3	0	13.1	0	23.8
Achilles/plantal enthesitis	14.5	14.6	48.1	4.5	8.5	0	44.7	50.0	17.2
Sacroiliitis	88.8	20.7	14.8	45.4	17.0	100	52.6	12.5	67.0

PsA: psoriatic arthritis, ReA: reactive arthritis, IBD: inflammatory bowel disease, PPP: pustulosis palmaris et plantaris, USpA: undifferentiated SpA.

Table 3. Distribution of SpA subsets and sensitivity of Amor and ESSG criteria in each subset.

Subset	Distribution (%)	Amor Sensitivity	ESSG Sensitivity*
AS	676 (68.3)	89.4	92.3
Psoriatic arthritis	126 (12.7)	77.2	89.0
Reactive arthritis	40 (4.0)	72.2	55.5
Undifferentiated SpA	54 (5.4)	84.3	84.2
IBD	22 (2.2)	81.8	90.9
Pustulosis palmaris et plantaris	47 (4.7)	42.5	26.0
SAPHO	3 (0.3)	100.0	100.0
Other (polyenthesitis, etc.)	8 (0.8)	25.0	62.5
Unknown	14 (1.4)	42.8	42.8

*Data from the 2nd survey only.

Table 4. International comparison of the prevalence of AS and SpA.

Disease	Race/Site	Report Year	Prevalence, %
AS	White[7]	1992	0.2
AS	Minnesota[17]	1992	0.13
AS	Finland[18]	1997	0.15
AS	Taiwan[9]	1995	0.19–0.54
AS	Eskimo[14]	1988	0.2
AS	Japan[11]	1973	0.04
AS	Japan	Present study	0.0065
SpA	Lebanon[12]	1997	8
SpA	Circumpolar[13]	1996	2–3.4
SpA	Thailand	1998	0.12
SpA	White[16]	1998	1.9
SpA	Japan	Present study	0.0095

Table 5. International comparison of the annual incidence of AS and SpA.

Disease	Site	Report Year	Incidence/100,000 person-years
AS	Minnesota[17]	1992	7.3
AS	Finland[18]	1997	6.9
SpA	Massachusetts[19]	1994	2.0
SpA	Japan	Present study	0.48

0.04% in the 1970s[1,2], although these estimates were not based on a direct population study. The prevalence of SpA estimated in our study was 9.5/100,000 or 0.0095%. Since AS was 68.3% of all SpA, the prevalence of definite AS was 6.5/100,000 or 0.0065%. This figure was 1/30th of that reported in Caucasians, Taiwanese, and Eskimos. The fact that HLA-B27 prevalence among Japanese is 0.5% or less[11], which is less than one-sixteenth of the prevalence among Caucasians, is likely to validate the low prevalence of AS we obtained.

The spectrum of SpA is thought to be much wider than previously realized, and there is tremendous overlap among the various subsets of SpA. By contrast with the abundance of epidemiologic data on AS, there are few studies on overall prevalence of SpA. Prevalence of SpA in Lebanon was reported to be around 8%, within which AS was 40.3%[12]. It was reported to be between 2% and 3.4% in indigenous circumpolar populations of Russia and Alaska[13,14]. In rural Thailand the prevalence of SpA and rheumatoid arthritis (RA) was reported to be 0.12% each[15]. Braun and colleagues estimated the prevalence of SpA among whites to be 1.9%, in which AS was 0.86%, undifferentiated SpA 0.67%, and psoriatic arthritis 0.29%[16]. Thus the estimated prevalence of SpA in our study (0.0095%) is around 1/10 of that in Thailand and 1/200 of that in Caucasians and Eskimos.

As far as we know, studies on the annual incidence of AS or SpA are scanty. The annual incidence of AS in Minnesota, USA, obtained by a longitudinal population study from 1935 to 1989 was 7.3 per 100,000 person-years[17], and that in Finland from 1974 to 1975 was 6.9 per 100,000 person-years[18]. The mean annual incidence of SpA among children referred to pediatric rheumatology centers in Massachusetts, USA, was reported to be 2.0 per 100,000 person-years[19]. The estimated annual incidence of SpA among adult Japanese in our study was 0.48 per 100,000 person-years, around one-tenth of those reported in North America and Finland.

International comparison of the distribution of SpA subsets (Table 6). In Lebanon[12] and Alaska[13] SpA is the most

Table 6. International comparison of the distribution of SpA subsets.

Site	Report Year	AS, %	PsA, %	ReA, %	IBD, %	USpA, %
Lebanon	1997[12]	40.3	13.8	2.8	2.8	40
France	1995[3,4]	43.5	13.6	9.9	4.7	28
Circumpolar	1996[13]	20.3	1.6	37.3	—	40
Japan	Present study	68.3	12.7	4.0	2.2	5.4

PsA: psoriatic arthritis, ReA: reactive arthritis, IBD: inflammatory bowel disease, USpA: undifferentiated SpA.

common rheumatic disease, surpassing RA and osteoarthritis (OA), and undifferentiated SpA is the most common subset. In France AS is the most common SpA subset, followed by undifferentiated SpA[3]. This is quite different from Japan, where, as this study reveals, AS is the main subset of SpA, in contrast to the low frequency of undifferentiated SpA and reactive arthritis. These differences might result partly from the difference of genetic and environmental background and partly from insufficient knowledge of SpA classification among Japanese physicians, although some improvement was observed between the first survey and the second.

Validity of Amor and ESSG criteria for Japanese SpA. The sensitivities that the 2 sets of criteria showed for the Japanese population in our study were 84.0 for Amor and 84.6 for the ESSG. These figures are slightly low in comparison to those revealed for French[4] and Spanish[20] studies (Table 7). However, if the subset was limited to AS, the sensitivities of those criteria in the Japanese population were 89.4 and 92.3, respectively (Table 3), equivalent to those in France and Spain. It indicates that the adaptability of the 2 criteria sets to the Japanese population was validated.

Further comments. As noted, the prevalence of HLA-B27/family history in the AS population was 64%, which is low in comparison to reports among Caucasoid and Mongoloid populations. It suggests a possible contamination of the AS population with other SpA subsets in this study. To check this point, we analyzed the distribution of diagnosed subsets for each of the 12 items of the Amor criteria (Table 8). The patients with acute diarrhea were more often (42.8%) diagnosed as having AS than IBD (23.8%). Those with psoriasis were diagnosed as PsA in 68.6%, but also diagnosed as AS in 11.0%. These findings might support the above assumption. From another viewpoint, Table 8 also reveals the majority (94.2%) of patients with HLA-B27/family history were diagnosed with AS, implying that the present data are valid and that AS in Japanese is less strongly related to HLA and more strongly related to environmental factors than before.

In summary, the annual incidence of AS and SpA in Japan was estimated to be less than 1/10 of that among Caucasians. The prevalence of AS in Japan was less than 1/30 and the prevalence of SpA less than 1/200 of those among Caucasians. The usefulness of the Amor and ESSG criteria was validated for the Japanese population.

Table 7. International comparison of sensitivity of Amor and ESSG criteria.

Site	Report Year	Amor	ESSG
Spain	1995[20]	90.8	83.5
Lebanon	1997[12]	64.8	68.6
France	1991[3,4]	91.9	87.1
Japan	Present study	84.0	84.6

Table 8. Distribution of diagnosed SpA subsets for each of 12 items of the Amor criteria.

		AS	PsA	ReA	IBD	PPP	SAPHO	USpA	Others	Unknown
1.	Back pain	78.7	7.0	2.3	1.9	3.3	0.3	4.7	0.7	0.6
2.	Oligoarthritis	58.3	18.1	5.9	2.8	5.4	0.5	7.1	0.7	0.9
3.	Buttock pain	80.9	5.1	2.5	1.5	1.5	0.2	6.4	1.0	0.5
4.	Sausage digit	31.0	46.5	3.4	0	3.4	0	15.5	0	0
5.	Enthesopathy	57.4	12.8	8.9	0.9	4.4	0	12.8	1.9	0.4
6.	Iritis	88.8	1.8	0.6	3.1	0.6	0.6	3.1	1.2	0
7.	Urethritis/cervicitis	30.0	0	55.0	0	0	0	10.0	0	5.0
8.	Acute diarrhea	42.8	0	9.5	23.8	4.7	4.7	14.2	0	0
9.	Psoriasis/balanitis/enteritis	11.0	68.6	4.0	10.4	3.4	0.5	1.1	0	0.5
10.	Sacroiliitis	87.6	3.0	1.0	1.6	1.3	0.4	3.9	0.1	0.7
11.	HLA-B27/family history	94.2	1.3	1.9	0.8	0.2	0	0.8	0.2	0.2
12.	NSAID effect	71.0	10.9	4.3	2.1	5.2	0.1	4.8	0.3	0.9

PsA: psoriatic arthritis, ReA: reactive arthritis, IBD: inflammatory bowel disease, PPP: pustulosis palmaris et plantaris, USpA: undifferentiated SpA.

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