

Patient- and Therapist-Related Risk Factors for Adverse Events in Acupuncture and Moxibustion in Japan: Multicenter Survey of Acupuncture and Moxibustion Teaching Clinics

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ABSTRACT

Background/Objective: To investigate the patient- and therapist-related factors underlying adverse events (AEs) in acupuncture and moxibustion (A&M).

Design: Retrospective study using data from medical records.

Subjects: Patients who underwent A&M therapy in 4 clinics providing A&M over a 6-month period and their therapists.

Main Outcome Measures: Survey items included the number of patients, age, sex, number of sessions, number and type of AEs, patients' underlying disease, and the therapist's years of clinical experience. The chi-squared test was used for intergroup comparisons. Spearman's rank correlation coefficient was used to analyze the correlations between the number of sessions and AEs. Logistic regression analysis was performed with AEs as the objective variable to investigate the relationships between the various parameters and AEs.

Results: The analysis included 615 patients and 113 therapists. A total of 421 AEs occurred in a total of 4,369 sessions (9.6%). The number of sessions and number of AEs were significantly and positively correlated with patients ($r=0.47$, $P<0.001$) and therapists ($r=0.65$, $P<0.001$). Logistic analysis identified patient sex (adjusted odds ratio: 1.78, 95% confidence interval: [1.39–2.30]), liver disease (0.40, [0.19–0.84]), and years of clinical experience (to a cutoff of 2 or fewer years, 2–4 years: 0.65, [0.48–0.88], 5–9 years: 0.62, [0.44–0.87], 10 years or more: 0.50, [0.37–0.68]) as significant variables.

Conclusions: Female sex and fewer years of clinical experience were factors that increased the risk of AEs, and underlying liver disease was a factor that decreased the risk of AEs.

Keywords: adverse events, acupuncture, retrospective study, risk factor, logistic regression analysis, Japan

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INTRODUCTION

ADVERSE REACTIONS AND adverse events (AEs) are undesirable events that inevitably occur during medical procedures. AEs occurring in hospitals are most frequently related to surgeries and drugs. de Vries et al. reported a 9.2% incidence of AEs in their investigation of medical records of 74,485 patients, and they further reported that 7.4% of such AEs were fatal.¹

Complete elimination of AEs related to acupuncture and moxibustion (A&M) is difficult because the procedure causes damage to biologic tissues. Witt et al. investigated AEs in A&M treatments for 229,230 patients and reported that they occurred in 8.6% of patients.² However, they concluded that A&M is relatively safe since most AEs were mild, and serious events such as pneumothorax and nerve damage were extremely rare. Other studies have reported similar findings.^{3–5} In Japan, however, there is no standardized system for reporting A&M-related AEs, and most known AEs are only reported as case studies. Such reports include deaths,^{6,7} but this may be a publication bias since only serious AEs are typically reported in cases.^{8,9} Moreover, a few studies on AEs were descriptive epidemiologic studies focused on the details of AEs,^{10–14} not analytical studies delving into their causes. Furuse et al. conducted a multi-center study involving the largest number of sessions and facilities in Japan,¹⁴ but it was a descriptive study providing details and incidence of AEs with no mention of their causes.

Thus, this study focused on exploring the factors involved in the onset of AEs. We investigated both patient and therapist data, that is, age, sex, underlying disease, number of sessions, and the therapist's clinical experience, and their relationships with AE incidence.

MATERIALS AND METHODS

Participants and Survey Period

We obtained the data for patients and therapists participating in A&M therapy sessions at the following teaching clinics of the Kuretake College of Medical Arts & Sciences between June 1 and November 30, 2016: Tokyo Therapeutic Institute, Oriental Medicine Clinical Institute (Tokyo Metropolitan), Kuretake School of Oriental Medicine (Kanagawa Prefecture), and Kuretake School of Integrative Medicine (Saitama Prefecture). This study was approved by the Medical Ethics Committee of Showa University School of Medicine (approval no. 2973) and the Ethics Committee of Kuretake College of Medical Arts & Sciences (no. 19-004).

Methods

In this retrospective study, we obtained data from AE report forms (hereinafter, report forms) and medical re-

ports. Similar to a previous study of A&M,¹⁴ AEs were defined as “any untoward medical occurrence in a patient who underwent acupuncture therapy, and which does not necessarily have a causal relationship with this treatment (Supplementary Data).”

The report forms were filled by the therapist at each session as they wrote in the patient's medical record. Therapists noted the patient ID, date of therapy, therapist ID, AEs, and type of AE while completing the report form. The therapies were not modified or restricted in this investigation. After each session, the therapist checked for any AEs and their details by visual inspection, palpation, and interviews. As previously reported,¹⁴ AE types were classified as minor/subcutaneous bleeding, bleeding over 10 seconds, pain on insertion, residual pain of insertion points, discomfort, burn injury, aggravation of symptoms, both cutaneous and subcutaneous tissue inflammation, forgotten needles, and others.

We extracted data on sex, age, and underlying diseases from the medical records. The underlying diseases were classified as allergic diseases, bleeding tendency, susceptibility to infection, liver diseases, and psychiatric diseases, similar to a previous study.¹⁴ Patients and therapists were assigned ID numbers for the study by a third party to de-identify the data. The research participants were notified using the opt-out method and had the choice to refuse the use of their data.

The survey items included the number of patients, age, sex, number of sessions, underlying diseases, and both the number and type of AEs. The number of therapies, age, number of sessions, number of AEs, type of AEs, and clinical experience was used for analyses. Patient age was categorized into 10-year groups, and clinical experience was classified into 4 categories: <2 years (<2 years), 2–4 years (<5 years), 5–9 years (<10 years), and ≥10 years (≥10 years). This is because the 2-year period after obtaining a license is regarded as a nonmandatory postgraduate clinical training period in Japan; a clinical training instructor qualification is awarded after 5 years or more of clinical experience, and teachers are required to have 10 years or more of clinical experience. Using the data obtained, we investigated the effects of patient gender, age, underlying disease, therapist gender, and clinical experience on AEs.

Statistical Analysis

Normally distributed data are presented as mean ± standard deviation, and non-normally distributed data are presented as medians (interquartile range: IQR). The chi-squared test or Fisher's exact test was used for intergroup comparisons. Spearman's rank correlation coefficient was used to analyze the correlations of patient factors and the number of therapist sessions with the number of AEs. Logistic regression analysis with AEs as the objective variable was performed to investigate the relationships between patient and therapist parameters and AEs, and the odds ratios (ORs) for each item were calculated. The adjusted OR was

TABLE 1. SUMMARY OF PATIENT CHARACTERISTICS

Age/number of patients	Male	Female	Total	P
Age (years) ^a	51 (36–67), 19, 87	49 (35–65), 18, 87	50 (36–66), 18, 87	0.357
<30 (18–29)	31 (5.0%)	66 (10.7%)	97 (15.7%)	
30s (30–39)	36 (5.9%)	52 (8.5%)	88 (14.4%)	
40s (40–49)	34 (5.5%)	81 (13.2%)	115 (18.7%)	
50s (50–59)	36 (5.9%)	63 (10.2%)	99 (16.1%)	
60s (60–69)	33 (5.4%)	72 (11.7%)	105 (17.1%)	
70s (70–79)	29 (4.7%)	49 (8.0%)	78 (12.7%)	
80s (80–89)	18 (2.9%)	15 (2.4%)	33 (5.3%)	
Total	217 (35.3%)	398 (64.7%)	615	0.148
Number of patients with underlying disease and type of underlying disease ^b	72 (11.7%)	194 (31.5%)	266 (43.2%)	<0.001
Bleeding tendency	6 (1.0%)	13 (2.1%)	19 (3.1%)	0.812
Susceptibility to infection	12 (2.0%)	7 (1.1%)	19 (3.1%)	0.014
Allergic diseases	56 (9.1%)	173 (28.1%)	229 (37.2%)	<0.001
Psychiatric diseases	1 (0.2%)	10 (1.6%)	11 (1.8%)	0.108
Liver diseases	7 (1.1%)	9 (1.5%)	16 (2.6%)	0.597

Bleeding tendency: under anticoagulant/antiplatelet therapy, 10; congenital, 1; unknown, 8. Susceptibility to infection: diabetes, 14; long-term steroid therapy, 1; unknown, 4. Allergic diseases: atopic dermatitis, 24; allergic rhinitis, 163; allergies to disinfecting alcohol, 7; allergies to metals, 23; others, 12. Psychiatric diseases: bipolar disorder, 2; depression, 7; schizophrenia, 1; other, 1. Liver diseases: hepatitis A, 1; hepatitis B, 2; hepatitis C, 6; unknown viral hepatitis, 1; drug-induced fulminant hepatitis, 1; acute hepatitis, 1; fatty liver, 1; benign hepatoma, 1; liver abscess, 1; liver cirrhosis, 1.

Bold means statistically significant ($p < 0.05$).

^aMedian (25%–75%), minimum, maximum.

^bDoes not equal the number of patients with underlying diseases since some patients had more than 1.

also calculated including sex, age group, underlying disease, and clinical experience. JMP Pro 15.2 (SAS Institute) was used for statistical analysis. Differences were considered statistically significant when P -values were < 0.05 .

RESULTS

Participants

A total of 617 patients (217 men, 398 women, and 2 unknown) were included in the analysis. Two patients of unknown sex were excluded from the study, and the remaining 615 were included in the analysis. The basic patient data are presented in Table 1. The patients' median age

was 50 (IQR 30) years. No significant sex-related differences were observed in patient age ($P = 0.357$), and no significant difference was observed among the age categories ($P = 0.148$). Underlying diseases were observed in 266 patients, and their incidence showed significant sex-related differences ($P < 0.001$). Significant sex-related differences were also observed in susceptibility to infection and allergic diseases ($P = 0.014$ and $P < 0.001$, respectively).

The therapists' basic data are shown in Table 2. The study assessed a total of 113 therapists (57 men and 56 women; mean age, 41 ± 10 years). No significant sex-related differences were observed among the therapists ($P = 0.189$). The median clinical experience was 3 years (IQR 8). Experience levels showed a significant sex-related difference ($P = 0.036$). Although the differences among the clinical

TABLE 2. NUMBER OF THERAPISTS AND YEARS OF CLINICAL EXPERIENCE

	Male	Female	Total	P
Mean age \pm SD (years)	42.7 \pm 9.4	40.2 \pm 9.4	41.4 \pm 9.9	0.189
Years of clinical experience ^a	5 (2–10), 1, 34	2 (1–4), 1, 22	3 (1–9), 1, 34	0.036
Number of therapists by years of experience (categories)				
<2 years	20 (17.7%)	31 (27.4%)	51 (45.1%)	
2–4 years	10 (8.9%)	12 (10.6%)	22 (19.5%)	
5–9 years	13 (11.5%)	5 (4.4%)	18 (15.9%)	
≥ 10 years	14 (12.4%)	8 (7.1%)	22 (19.5%)	
Total	57 (50.4%)	56 (49.6%)	113	0.053

Bold means statistically significant ($p < 0.05$).

^aMedian (25%–75%), minimum, maximum.

SD, standard deviation.

experience subgroups were not significant ($P=0.053$), the proportion of therapists with <2 years of experience was the greatest (45.1% of all therapists).

Number of Sessions and AEs

The reported AEs are shown in Table 3. A total of 421 AEs were reported across 4,369 sessions, indicating an AE incidence of 9.6%. A significant sex-related difference was observed in the number of AEs ($P<0.001$). The median number of sessions per patient was 6 (IQR 9). The frequency of treatment showed a significant sex-related intergroup difference ($P<0.001$).

The median number of AEs per patient was 0 (IQR 1), with 212 patients experiencing at least 1 AE. A significant sex-related difference was observed in the number of AEs among the age groups ($P=0.035$). No significant sex-related difference was observed in the number of AEs in patients with underlying diseases. The most frequently observed AE was minor bleeding ($n=221$; 50.4% of all AEs). A significant sex-related difference was observed only for mild bleeding ($P<0.001$). No serious AEs, such as pneumothorax or central nerve injury, were reported.

The number of sessions by male and female therapists was 2,141 and 2,228, respectively, and 163 and 258 AEs occurred in sessions by male and female therapists, respectively, showing a significant difference ($P<0.001$). The median number of sessions conducted per therapist was 30 (IQR 32). The mean number of sessions per therapist by years of clinical experience was 40.5, 32.5, 19.8, and 43.4 for those with <2 years' experience, 2–5 years' experience, 5–9 years' experience, and 10 or more years of experience, respectively. Significant sex-related differences were observed in the number of sessions among the groups ($P<0.001$).

The median number of AEs per therapist was 2 (IQR 6). Ten therapists reported no AEs, while 103 therapists reported one or more AEs, accounting for 91.1% of all therapists. The number of AEs was 257, 58, 47, and 59 for those with <2 years of experience (5.9% of all sessions), <5 years of experience (1.3%), <10 years of experience (1.1%), and ≥ 10 years of experience (1.4%), respectively. A significant sex-related difference was observed in the incidence of AEs among categories based on clinical experience ($P<0.001$).

The Spearman's ranked correlation coefficient for patients' number of sessions and number of AEs was $r=0.47$ ($P<0.001$), while that for therapists' number of sessions and number of AEs was $r=0.65$ ($P<0.001$); significant positive correlations were observed for both.

Risk Factors of AEs

The analyzed risk factors for AEs are shown in Table 4. The number of AEs was significantly higher in female patients ($P<0.001$). Among patients with underlying diseases, those with liver disease experienced significantly fewer AEs

than those without liver disease ($P=0.018$). The number of AEs was significantly higher in sessions conducted by female therapists ($P<0.001$). Therapists with fewer years of clinical experience experienced significantly more AEs ($P<0.001$).

Logistic analysis with the presence or absence of AEs as the objective variable showed that patient sex (adjusted OR: 1.78, 95% confidence interval [CI]: 1.39–2.30), presence of liver disease (adjusted OR: 0.40, 95% CI: 0.19–0.84), and clinical experience (adjusted ORs and 95% CIs: 0.65, 0.48–0.88; 0.62, 0.44–0.87; and 0.50, 0.37–0.68 for <5 years, <10 years, and ≥ 10 years, respectively, with <2 years as a reference) were significant variables.

DISCUSSION

This observational study assessed AEs in multiple teaching clinics of a Japanese A&M training school, and extracted patient sex, presence of underlying liver diseases, and therapists' clinical experience as risk factors for AEs.

Of the 615 patients in the analysis, 398 were women (64.7%); thus, women were more numerous than men. Yamashita reported that female patients tend to use more A&M therapies more than males in a nationwide telephone survey on the use of complementary and alternative therapies.¹⁵ Another study reported that 56% of 5,008 users of acupuncture treatment were female.¹¹ These reports suggest that women use A&M treatment more frequently than men in Japan, and this study is consistent with previous reports.

Our analysis also showed that females are associated with a greater risk of AEs. Among individual AEs, minor bleeding occurred in 8.2% of men and 42.2% of women, resulting in a large sex-related difference. Since statistically significant differences were not observed in the other parameters, the overall sex-related differences in AEs can be attributed to the results for minor bleeding. MacPherson et al. reported that the incidence and risk ratio of AEs in acupuncture treatment was higher in women in a 3-month survey with 6,348 participants.¹⁶ The results of this study support this finding. However, this study did not show sex-related differences in the diseases underlying bleeding tendency. Since previous studies have not reported on this sex-related difference, to the best of the authors' knowledge, the cause of this finding is unknown.

Patients with underlying liver diseases had a lower risk of AE than those without underlying liver disease. We speculate that this is because the therapist knew the patient's underlying medical condition in advance and took special care to prevent infection by implementing measures to prevent blood exposure, such as shallow depth of needles, use of fine needles, and standard precautions. In the late 1980s, the spread of infectious diseases such as hepatitis and acquired immunodeficiency syndrome (AIDS) through blood became a social problem, and in 1987, the Ministry of Health, Labour, and Welfare issued warnings and

TABLE 3. REPORTED ADVERSE EVENTS

	Males	Females	Total	P
Patients				
Number of sessions (male–female ratio)	1,479 (33.9%)	2,890 (66.1%)	4,369	
Number of AEs (percentage of all sessions)	91 (2.1%)	330 (7.5%)	421 (9.6%)	<0.001
Number of sessions per patient ^a	5 (2–10), 1, 22	6 (2–11), 1, 34	6 (2–11), 1, 34	
Number of AEs per patient ^a	0 (0–1), 0, 5	0 (0–1), 0, 11	0 (0–1), 0, 11	
Patients with at least 1 AE (percentage of all patients)	64 (10.4%)	148 (24.1%)	212 (34.5%)	
Number of AEs by patient age category				
Top: number of sessions (mean number of sessions/patient, percentage of all sessions)				
Bottom: number of AEs (mean AEs/patient, percentage of all sessions)				
<30 years (18–29)	144 (4.6, 3.3%)	299 (4.5, 6.8%)	443 (4.6, 10.1%)	
	10 (0.3, 0.2%)	28 (0.4, 0.6%)	38 (0.4, 0.8%)	
30s (30–39)	148 (4.1, 3.4%)	322 (6.2, 7.4%)	470 (5.3, 10.8%)	
	14 (0.4, 0.3%)	34 (0.7, 0.8%)	48 (0.5, 1.1%)	
40s (40–49)	199 (5.9, 4.6%)	534 (6.6, 12.2%)	733 (6.4, 16.8%)	
	9 (0.3, 0.2%)	78 (1.0, 1.8%)	87 (0.8, 2.0%)	
50s (50–59)	267 (7.4, 6.1%)	432 (6.9, 9.9%)	699 (7.1, 16.0%)	
	16 (0.4, 0.4%)	41 (0.7, 0.9%)	57 (0.6, 1.3%)	
60s (60–69)	302 (9.2, 6.9%)	710 (9.9, 16.3%)	1,012 (9.6, 23.2%)	
	17 (0.5, 0.4%)	83 (1.2, 1.9%)	100 (1.0, 2.3%)	
70s (70–79)	229 (7.9, 5.2%)	440 (9.0, 10.1%)	669 (8.6, 15.3%)	
	19 (0.4, 0.4%)	46 (0.9, 1.1%)	65 (0.8, 1.5%)	
80s (80–89)	190 (10.6, 4.4%)	153 (10.2, 3.5%)	343 (10.4, 7.9%)	<0.001
	6 (0.3, 0.1%)	20 (1.3, 0.5%)	26 (0.8, 0.6%)	0.035
Number of AEs in patients with underlying diseases (percentage of all AEs)				
Bleeding tendency	8 (1.9%)	16 (3.8%)	24 (5.7%)	0.669
Susceptibility to infection	6 (1.4%)	5 (1.2%)	11 (2.6%)	0.350
Allergic diseases	76 (18.1%)	116 (27.6%)	192 (45.7%)	0.764
Psychiatric diseases	4 (1.0%)	10 (2.4%)	14 (3.4%)	0.580
Liver diseases	4 (1.0%)	4 (1.0%)	8 (2.0%)	0.716
Types of AEs ^b (percentage of all sessions, percentage of all AEs)				
Minor/subcutaneous bleeding	36 (0.8%, 8.2%)	185 (4.2%, 42.2%)	221 (5.1%, 50.4%)	<0.001
Bleeding over 10 seconds	5 (0.1%, 1.1%)	7 (0.2%, 1.6%)	12 (0.3%, 2.7%)	0.554
Pain on insertion (pain that required removal of needles during the session)	14 (0.3%, 3.2%)	27 (0.6%, 6.2%)	41 (0.9%, 9.4%)	1.000
Residual pain of insertion points	16 (0.4%, 3.8%)	37 (0.8%, 8.8%)	53 (1.2%, 12.6%)	0.662
Discomfort	13 (0.3%, 3.0%)	35 (0.8%, 8.0%)	48 (1.1%, 11.0%)	0.360
Burn injury	4 (0.1%, 0.9%)	12 (0.3%, 2.7%)	16 (0.4%, 3.6%)	0.600
Aggravation of symptoms	2 (0.1%, 0.5%)	9 (0.2%, 2.0%)	11 (0.3%, 2.5%)	0.353
Cutaneous inflammation and subcutaneous tissue inflammation	0	5 (0.1%, 1.1%)	5 (0.1%, 1.1%)	0.174
Forgotten needles	0	2 (0.1%, 0.5%)	2 (0.1%, 0.5%)	0.552
Others ^c	4 (0.1%, 0.9%)	8 (0.2%, 1.8%)	12 (0.3%, 2.7%)	1.000
Unknown ^d	7 (0.2%, 1.6%)	10 (0.2%, 2.3%)	17 (0.4%, 3.9%)	0.609
Total	101 (2.3%, 23.1%)	337 (7.7%, 76.9%)	438	
Therapist				
Number of sessions	2,141 (49.0%)	2,228 (51.0%)	4,369	
Number of AEs (percentage of all sessions)	163 (3.7%)	258 (5.9%)	421	<0.001
Number of sessions/therapist ^a	29 (11–47), 1, 231	35 (20–50), 1, 216	30 (16–48), 1, 231	
Number of AEs/therapist ^a	2 (0–4), 0, 15	2.5 (1–6), 0, 24	2 (0–6), 0, 24	
Therapist with at least 1 AE (percentage of all therapists)	39 (34.5%)	64 (56.6%)	103 (91.1%)	
Number of sessions by years of clinical experience (categories)				
Top: number of sessions (mean number of sessions/therapist, percentage of all sessions)				
Bottom: number of AE (mean number of AEs/therapist, percentage of all sessions)				
<2 years	701 (35.1, 16.0%)	1,362 (43.9, 31.2%)	2,063 (40.5, 47.2%)	
	65 (3.3, 1.5%)	192 (6.2, 4.4%)	257 (5.0, 5.9%)	
2–4 years	323 (32.3, 7.4%)	393 (32.8, 9.0%)	716 (32.5, 16.4%)	
	12 (1.2, 0.3%)	46 (3.8, 1.0%)	58 (2.6, 1.3%)	
5–9 years	499 (38.4, 11.4%)	137 (27.4, 3.1%)	636 (19.8, 14.5%)	
	38 (2.9, 0.9%)	9 (1.8, 0.2%)	47 (2.6, 1.1%)	
≥10 years	618 (44.1, 14.1%)	336 (42.0, 7.7%)	954 (43.4, 21.8%)	<0.001
	48 (3.4, 1.1%)	11 (1.4, 0.3%)	59 (2.7, 1.4%)	<0.001

Bold means statistically significant ($p < 0.05$).

^aMedian (25%–75%), minimum, maximum.

^bMultiple AEs can occur in a session, thus does not equal the number of AEs.

^cSluggishness, 4; pain in parts other than the insertion site, 3; post-A&M pain, 1; hot flashes, 1; redness after needle removal, 1.

^dYes to AE in the report form, but the type of AE unmarked.

AE, adverse event.

TABLE 4. NOMINAL LOGISTIC REGRESSION ANALYSIS FOR ADVERSE EVENTS IN NUMBER OF TREATMENTS ($n=4,369$)

<i>AEs</i>								
	<i>Number of treatment</i>	<i>No</i>	<i>Yes</i>	<i>P</i>	<i>OR (95% CI)</i>	<i>P</i>	<i>Adjusted OR (95% CI)</i>	<i>P</i>
Patients								
Sex								
Male	1,479	1,388 (93.9%)	91 (6.2%)		1		1	
Female	2,890	2,560 (88.6%)	330 (11.4%)	<0.001	1.97 (1.54–2.50)	<0.001	1.78 (1.39–2.30)	<0.001
Age group								
<30 years	443	405 (91.4%)	38 (8.6%)		1		1	
30s	470	422 (89.8%)	48 (10.2%)		1.21 (0.76–1.90)	0.399	1.26 (0.80–1.98)	0.317
40s	733	646 (88.1%)	87 (11.9%)		1.44 (0.96–2.14)	0.077	1.47 (0.98–2.21)	0.065
50s	699	642 (91.9%)	57 (8.2%)		0.95 (0.62–1.45)	0.801	1.06 (0.69–1.65)	0.078
60s	1,012	912 (90.1%)	100 (9.9%)		1.17 (0.79–1.73)	0.435	1.22 (0.82–1.81)	0.329
70s	669	604 (90.3%)	65 (9.7%)		1.15 (0.75–1.75)	0.522	1.32 (0.85–2.03)	0.213
80s	343	317 (92.4%)	26 (7.6%)	0.207	0.87 (0.52–1.47)	0.612	1.05 (0.59–1.86)	0.871
By underlying disease								
Bleeding tendency								
No	4,186	3,789 (90.5%)	397 (9.5%)		1		1	
Yes	183	159 (86.9%)	24 (13.1%)	0.123	1.44 (0.93–2.24)	0.105	1.53 (0.90–2.61)	0.116
Susceptibility to infection								
No	4,208	3,798 (90.3%)	410 (9.7%)		1		1	
Yes	161	150 (93.2%)	11 (6.8%)	0.275	0.68 (0.37–1.26)	0.222	0.77 (0.39–1.53)	0.459
Allergic diseases								
No	2,493	2,264 (90.8%)	229 (9.2%)		1		1	
Yes	1,876	1,684 (89.8%)	192 (10.2%)	0.255	1.13 (0.92–1.38)	0.245	1.05 (0.85–1.30)	0.634
Psychiatric diseases								
No	4,255	3,848 (90.4%)	407 (9.6%)		1		1	
Yes	114	100 (87.7%)	14 (12.3%)	0.333	1.32 (0.75–2.34)	0.334	1.08 (0.60–1.95)	0.794
Liver diseases								
No	4,195	3,782 (90.2%)	413 (9.9%)		1		1	
Yes	174	166 (95.4%)	8 (4.6%)	0.018	0.44 (0.22–0.90)	0.025	0.40 (0.19–0.84)	0.016
Therapists								
Sex								
Male	2,141	1,978 (92.4%)	163 (7.6%)		1		1	
Female	2,228	1,970 (88.4%)	258 (11.6%)	<0.001	1.59 (1.29–1.95)	<0.001	1.22 (0.98–1.53)	0.079
By years of clinical experience								
<2 years	2,063	1,806 (87.5%)	257 (12.5%)		1		1	
2–4 years	716	658 (91.9%)	58 (8.1%)		0.62 (0.46–0.83)	0.002	0.65 (0.48–0.88)	0.006
5–9 years	636	589 (92.6%)	47 (7.4%)		0.56 (0.41–0.78)	<0.001	0.62 (0.44–0.87)	0.006
≥10 years	954	895 (93.8%)	59 (6.2%)	<0.001	0.46 (0.35–0.62)	<0.001	0.50 (0.37–0.68)	<0.001

Bold means statistically significant ($p < 0.05$).

^aMedian (25%–75%).

CI, confidence interval; OR, odds ratio.

recommendations for the prevention of AIDS and other infectious diseases in A&M. The Clinical A&M Guidelines published subsequently^{17–20} also described infection measures, and these measures were in school education. Since then, it has become standard practice to use disposable needles and wear gloves in A&M training schools to prevent infectious diseases and educate people about them. In their review on acupuncture and hepatitis infection, Furuse et al. revealed that hepatitis infections have not been reported after acupuncture therapy since 1990 in Japan, and stated that infection control measures in acupuncture practices before and after 1990 should be discussed separately.²¹ It is possible that therapists who teach hepatitis infection control measures at school practice more caution in treating hepatitis patients than in patients without liver disease.

From the point of view of the therapists, bleeding consisted of over half of AEs, suggesting that therapists are exposed to a higher risk of blood-borne infections. Umeda et al. reported that hepatitis B and C viruses were detected in acupuncture needles after their removal.^{22,23} Since over 90% of all therapists experienced one or more AEs in this study, rigorous education of infection prevention measures is required for therapists.

Assuming less than 2 years as the referential period of clinical experience, the number of AEs per session tended to decrease with increasing clinical experience. Although the risk of onset was suggested to decrease with an increase in clinical experience, to the best of our knowledge, there are no similar previous reports. Greater experience in a particular area intuitively indicates higher skills and knowledge,

and this was the first study to identify that experience was a factor influencing AE occurrence.

Sex-related differences were observed in clinical experience, with male therapists showing more clinical experience. Although there were no significant differences among experience-level categories, therapists with <2 years of experience were the most numerous, accounting for 45.1% of all therapists in this analysis. This is presumably related to the fact that the participating clinics were affiliated with an A&M training school and likely included many graduating clinical trainees. Considering a cutoff experience of 5 years, which is the required benchmark for obtaining a license for instructing clinical practicum, those with <5 years of experience included 30 men and 43 women, and those with 5 or more years of experience included 27 men and 13 women. Although the data are not clear in this regard, it is possible that clinical instructors may have included more males than females. According to the 2016 survey of acupuncturists' employment status, fewer women are employed in therapeutic work between the ages of 25 and 39 than men, and the most common reasons for nonemployment are marriage, childbirth, and childcare, excluding "working in other business".²⁴ This may be the same reason why there are few female instructors in the teaching clinics.

In this study, AEs occurred in 421 out of 4,369 A&M sessions, equating to an incidence of 9.6%. Half of all AEs involved minor bleeding (50.4%), and no serious AEs such as pneumothorax or cranial nerve damage occurred. Shinbara et al. reported that subcutaneous and mild bleeding and pain on insertion were the leading AEs in their study on A&M clinics in Japanese cities (not teaching clinics).²⁵ Our findings were consistent with this study, which may suggest that the general trends in AEs were similar in clinics not affiliated with teaching institutions. Other previous studies have reported that serious AEs are rare in A&M treatments.^{2-5,10,14,16} Nevertheless, given that over 30% of all patients experienced an AE, it is necessary to disclose information on the expected AEs before administering A&M.

This study performed an analysis with the total number of AEs (421) occurring in 4,369 A&M sessions as the objective variable, while previous studies other than A&M analyzed "the number of patients who experienced any AEs." This is because the definition of AE differs between general clinical practice and A&M therapies. For general clinical practice, de Vries has defined AE as "an unintended injury or complication resulting in prolonged hospital stay, disability at the time of discharge or death and caused by healthcare management rather than by the patient's underlying disease process,"¹ so that once patients experience AE, they never suffer again. In contrast, AEs in A&M are defined as "any untoward medical occurrence in a patient who underwent acupuncture therapy," which could occur in all treatments. Therefore, when they are mild or within the range of tolerance for the patient, they do not necessarily indicate discontinuation or withdrawal of patients from A&M therapies.

Therefore, we analyzed AEs not by the number of patients, but by the number of sessions.

Despite this, our findings cannot be compared directly with other studies since the majority of previous studies on AEs in A&M were descriptive epidemiologic studies, as mentioned earlier; none aimed to analyze the related factors. The lack of a standardized AE reporting system in Japan further increases the value of the findings of this study on AE types and rates as well as the newly identified factors behind AEs.

This study had several limitations. First, since AE reporting involves some degree of subjectivity from both therapists and patients, the reporting bias of therapists and patients could not be eliminated completely. Second, the treatment methods were not standardized, so the treatment theories and methods used by the therapists are unknown. Also, we did not collect detailed data about each therapy session (e.g., puncture site, number of needles used, and needle insertion depth). Therefore, the extent to which these parameters affect AEs is unknown. The effect of these differences on AEs will be the subject of future research.

CONCLUSION

This study identified female sex and low therapist clinical experience as factors that increase the risk of AEs in A&M treatments, and underlying liver disease of patients was shown to decrease the risk. The significantly lower incidence of AEs in liver disease patients suggests the effectiveness of safety education and the importance of education on other AEs. These results provide new insights into the risk factors of AEs; however, a larger-scale survey is needed for detailed investigations on the rates and risks of AE onset, and early establishment of a standardized AE reporting system in Japan is also warranted.

AUTHORS' CONTRIBUTIONS

A.U. is the main author; statistical instruction by T.Y.; article correction by Y.K. and H.O.; search for articles by T.S., A.M., and H.D.; clinical supervision by A.S.; research supervision by A.K. All the authors have approved the final version of the article.

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SUPPLEMENTARY MATERIAL

Supplementary Data

REFERENCES

- de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boormeester MA. The incidence and nature of in-hospital adverse events: A systematic review. *Qual Saf Health Care*. 2008;17(3):216–223.
- Witt CM, Pach D, Brinkhaus B, et al. Safety of acupuncture: Results of a prospective observational study with 229,230 patients and introduction of a medical information and consent form. *Forsch Komplementmed*. 2009;16(2):91–97.
- Melchart D, Weidenhammer W, Streng A, et al. Prospective investigation of adverse effects of acupuncture in 97733 patients. *Arch Intern Med*. 2004;164(1):104–105.
- Endres HG, Molsberger A, Lungenhausen M, Trampisch HJ. An internal standard for verifying the accuracy of serious adverse event reporting: The example of an acupuncture study of 190,924 patients. *Eur J Med Res*. 2004;9(12):545–551.
- White A, Hayhoe S, Hart A, Ernst E. Adverse events following acupuncture: Prospective survey of 32 000 consultations with doctors and physiotherapists. *BMJ*. 2001;323(7311):485–486.
- Watanabe M, Unuma K, Fujii Y, Noritake K, Uemura K. An autopsy case of vagus nerve stimulation following acupuncture. *Leg Med*. 2015;17(2):120–122.
- Iwadate K, Ito H, Katsumura S, et al. An autopsy case of bilateral pneumothorax after acupuncture. *Leg Med*. 2003;5(3):170–174.
- Yamashita H, Tsukayama H, White AR, Tanno Y, Sugishita C, Ernst E. Systematic review of adverse events following acupuncture: The Japanese literature. *Complement Ther Med*. 2001;9(2):98–104.
- Furuse N, Uehara A, Sugawara M, Yamazaki T, Shinbara H, Yamashita H. Literature review on adverse events (2012–2015) associated with acupuncture and moxibustion [in Japanese]. *J Jpn Soc Acupunct Moxibust*. 2017;67(1):29–47.
- Yamashita H, Tsukayama H, Tanno Y, Nishijo K. Adverse events in acupuncture and moxibustion treatment: A six-year survey at a national clinic in Japan. *J Altern Complement Med*. 1999;5(3):229–236.
- Yamashita H, Tsukayama H, Hori N, Kimura T, Tanno Y. Incidence of adverse reactions associated with acupuncture. *J Altern Complement Med*. 2000;6(4):345–350.
- Yamashita H, Tsukayama H, Sugishita C. Local adverse reactions commonly seen in Japanese-style medical acupuncture practice. *Clin Acupunct Orient Med*. 2001;2(2):132–137.
- Shinbara H, Ogasawara C, Hayama S, Hino K, Taniguchi H, Sumiya E. A survey of adverse events at acupuncture clinics in Japan. *Jpn Acupunct Moxibust*. 2012;8(1):28–37.
- Furuse H, Shinbara H, Uehara A, et al. A multicenter prospective survey of adverse events associated with acupuncture and moxibustion in Japan. *Med Acupunct*. 2017;29(3):155–162.
- Yamashita H, Tsukayama H. Characteristics of acupuncture patients in Japan—data from nationwide survey on complementary and alternative medicine. *Jpn Acupunct Moxibust*. 2005;1(1):43–48.
- MacPherson H, Scullion A, Thomas KJ, Walters S. Patient reports of adverse events associated with acupuncture treatment: A prospective national survey. *Qual Saf Health Care*. 2004;13(5):349–355.
- Kobayashi H, supervision. Treatment and Safety Guidelines Committee, ed. [*Shinkyu chiryou ni okeru anzensei gaidorain iinkai hen*]. *Guidelines for Infection Prevention in Acupuncture and Moxibustion Therapy [Shinkyu chiryou ni okeru kansen boushi no shishin]*. [in Japanese]. Tokyo, Japan: Ishiyaku Pub, Inc.; 1993.
- World Health Organization. *Guidelines on Basic Training and Safety in Acupuncture*. WHO; 1999.
- Ozaki A. Acupuncture and Moxibustion Safety Committee, ed. [*Shinkyu anzen iinkai hen*]. *Acupuncture and Moxibustion Medical Safety Guidelines [Shinkyu iryou anzen gaidorain]*. [in Japanese]. Tokyo, Japan: Ishiyaku Pub, Inc.; 2007.
- Sakamoto A, Committee for Safe Acupuncture of JSAM. Safety Guidelines for Japanese Acupuncture and Moxibustion Practice 2020. Online document at: https://safety.jsam.jp/_src/6707/Safety%20Guidelines%20for%20Japanese%20Acupuncture%20and%20Moxibustion%20Practice%202020%20edited%20by%20JSAM.pdf Accessed June 12, 2021.
- Furuse N, Uchino Y, Yamashita H. Literature review on acupuncture and infection of hepatitis B and C [in Japanese]. *J Jpn Soc Acupunct Moxibust*. 2016;66(3):166–179.
- Umeda T, Kuribayashi K, Kasahara Y, Wakayama I. Hepatitis B virus is detected on the surface of acupuncture needles [in Japanese]. *J Jpn Soc Acupunct Moxibust*. 2002;52(2):137–140.
- Kasahara Y, Matsuo T, Okuda M, Umeda T, Kuribayashi K. Effect of wiping acupuncture needles with cotton on removing hepatitis C virus contaminating the needle surface [in Japanese]. *J Jpn Soc Acupunct Moxibust*. 2004;54(1):87–96.
- Japan College Association of Oriental Medicine [*toyo ryoho gakkou kyokai*]. *The 5th Questionnaire Survey Report on the Career Status of Licensed Massage, Acupuncture and Moxibustion Practitioners. Japan College Association of Oriental Medicine [Dai 5 kai anna massagi shiatsu-shi, hari-shi oyobi kyu-shi menkyo syutokusya no sinro joukyou. ankeito tyousa houkousyo]*. [in Japanese]; 2016. Online document at: https://www.toyoryoho.or.jp/book/an_05.pdf Accessed June 12, 2021.
- Shinbara H, Sumiya E, Taniguchi H, Kitade T. Present state of infection control in acupuncture and moxibustion -A questionnaire survey for practicing acupuncture in the Kinki region- [in Japanese]. *J Jpn Soc Acupunct Moxibust*. 2009;59(5):464–476.

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