



## Classification of patients with cold sensation by a review of systems database: A single-centre observational study



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### ABSTRACT

**Objectives:** In Kampo medicine, a traditional medicine pattern<sup>(TM1)</sup> refers to the complete clinical presentation of the patient at a given moment in time. Candidate herbal formulas are chosen for a chief complaint, and an appropriate formula is determined on the basis of the pattern<sup>(TM1)</sup> diagnosis. In this study, we demonstrated the importance of accompanying symptoms in diagnosing traditional medicine patterns<sup>(TM1)</sup>.

**Design:** Single centre observational study.

**Setting:** We analysed data from 524 new patients with a hypersensitivity to cold sensation as their primary diagnosis (mean age 51.6 ± 17.8 years; female ratio 82.1%) who visited the Keio University Hospital Kampo Clinic between 2008 and 2013.

**Main outcome measures:** Accompanying symptoms were recorded on the browser-based e-questionnaire system, which contained 128 items. The Japan Society for Oriental Medicine's board certified Kampo specialists diagnosed the traditional medicine patterns<sup>(TM1)</sup>.

**Results:** When participants were classified according to the origin of their cold sensation, there were no differences in their traditional medicine patterns. In contrast, when patients were classified based on the number of accompanying symptoms, a significant difference in the patterns was identified. An increasing number of accompanying symptoms was associated with more frequent qi stagnation and blood stasis pattern<sup>(TM1)</sup>. Patients with a qi stagnation pattern had higher rates of depression and insomnia. In contrast, patients with a blood stasis pattern<sup>(TM1)</sup>, had higher rates of acne, body stiffness, and menstrual abnormality.

**Conclusions:** Qi stagnation and blood stasis patterns<sup>(TM1)</sup> are related to a number of different accompanying symptoms in the patients with hypersensitivity to cold sensation.

### 1. Introduction

The Eleventh edition of the International Classification of Diseases (ICD-11) was released in June 2018. This version of the ICD included a chapter on traditional medicine. In traditional Kampo medicine, there are two types of diagnoses: 1) traditional medicine disorders<sup>(TM1)</sup>, and 2) traditional medicine patterns<sup>(TM1)</sup>.<sup>1,2</sup> A traditional medicine disorder<sup>(TM1)</sup> refers to a set of dysfunctions in any of the body systems, which presents with associated manifestations. A traditional medicine pattern<sup>(TM1)</sup> refers to the complete clinical presentation of the patient at a given moment in time.

In Japan, there is only one official license for physicians. A separated license for Kampo medicine physicians is not available. Therefore, in Japan, Kampo medicine is a medical subspecialty. Kampo specialists are physicians who attained further education in Kampo medicine after finishing Western medicine residency. Kampo specialists are skilled at using various kinds of traditional Kampo formulas for different traditional medicine patterns<sup>(TM1)</sup>. As a result of their medical education, Kampo specialists often refer to Western diagnoses,<sup>3</sup> rather than traditional medicine disorders<sup>(TM1)</sup>. In addition, approximately 90% of physicians in Japan are not Kampo specialists, but have some experience in prescribing Kampo formula in their daily practices.<sup>3</sup> However, it

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is difficult for most Japanese physicians who are not Kampo medicine specialists to select the appropriate Kampo formula on the basis of a specific traditional medicine pattern<sup>(TM1)</sup>.<sup>3</sup>

History taking was divided into three parts: 1) chief complaint, 2) review of the systems, and 3) patient background, including past medical history or social history. A chief complaint is the most crucial part of making a disease diagnosis in Western medicine and a disorder<sup>(TM1)</sup> diagnosis in traditional Kampo medicine. For example, a chief complaint of pain may include details regarding its location, intensity, quality, onset, radiation, alleviating factors, and aggravating factors. The information relating to chief complaints are similar between patients if the patients share the same diagnosis. In a previous study, we reported how Kampo specialists selected an appropriate Kampo formula for patients with dysmenorrhea.<sup>4</sup> We were able to show that menstrual pain as the chief complaint and other details describing menstruation, did not contribute to the selection of the appropriate Kampo formula.<sup>4</sup>

Review of systems is a systematic questioning of accompanying symptoms along with asking about the chief complaint. In Kampo medicine, it is important for determining the traditional medicine pattern<sup>(TM1)</sup>. Review of the systems is usually collected via a questionnaire, while the chief complaint is usually collected verbally by taking a history with the patient.<sup>5</sup> In this study, we focused on review of the systems in patients with a diagnosis of hypersensitivity to cold sensations which is a very common symptom in traditional Japanese Kampo medicine clinic.<sup>6</sup> To undertake a review of the systems, information relating to accompanying symptoms was obtained systematically, via an e-questionnaire. Associations between the traditional medicine patterns<sup>(TM1)</sup> and review of systems were determined statistically. The findings of this study demonstrated the importance of accompany symptoms in diagnosing a traditional medicine pattern<sup>(TM1)</sup>.

## 2. Methods

### 2.1. Participant enrolment and the e-questionnaire system

Patients with a diagnosis of hypersensitivity to cold sensations who made their first visit to the Keio University Hospital Kampo Clinic between May 2008 and March 2013 were included in this study. Hypersensitivity to cold sensations is a very common symptom in traditional Japanese Kampo medicine clinic.<sup>6</sup> Hypersensitivity to cold sensations is a condition in which patients suffer from cold sensations in any part of body. Exclusion criteria included: unwillingness to participate in the study, and missing data e.g. age and/or sex. Participants who only described their lifestyle were also excluded. All registered participants provided a written or digital informed consent, and the study design was approved by the appropriate institutional review board at Keio University School of Medicine (approval no. 2010-0144 and 2014-0191).

Assessment of subjective symptoms has been described previously.<sup>7</sup> In brief, we collected information relating to participants' subjective symptoms, using a 128- question binary questionnaire. The 128 items on this questionnaire were first consensually selected by our institutional specialists, and confirmed after discussions with specialists from several Japanese institutions. Kampo specialists certified by the Japan Society for Oriental Medicine provided a pattern<sup>(TM1)</sup> for participants and entered the diagnosis into the e-questionnaire system. Each participant was assessed by a single Kampo specialist from among the numerous assessors who were Kampo specialists, with experience varying from approximately 10–30 years. Principle-based patterns<sup>(TM1)</sup> including Excess-deficiency and heat-cold are exclusive meaning that only one could be selected from 5 available categories for excess-deficiency and 4 for heat-cold. In contrast, body constituent patterns<sup>(TM1)</sup> are not exclusive and one or more categories could be selected.

### 2.2. Classification by the location of cold sensation

Initially, we classified the participants' data according to the location of their cold sensation, that is, classification by the chief complaint. Four parts in the body where participants feel cold sensation were included in our e-questionnaire system: general, hands, legs, and lower back. All of the locations could be overlapped. The frequency of overlap was reported in our previous analysis.<sup>7</sup> We compared sex ratio, mean age, number of accompanying symptoms, and the traditional medicine pattern<sup>(TM1)</sup> for each group.

### 2.3. Classification by the number of accompanying symptoms

Next, we classified the participants' data by review of the systems. The number of positive symptoms in review of the systems has been reported to have a predictive value on several mental disorders with somatization.<sup>8–14</sup> We previously reported the severity of some symptoms in participants with hypersensitivity to cold sensation.<sup>7</sup> Therefore, without weighting individual symptoms, we focused on the number of accompanying symptoms presented in association with cold sensation. In order to calculate proportions of each pattern<sup>(TM1)</sup> diagnosis, we classified the participants' data into five groups according to the number of accompanying symptoms; from 0–10, 11–20, 21–30, 31–40, and 41 or more. For each group, we compared sex ratio, mean age, and the traditional medicine pattern<sup>(TM1)</sup> for each group.

As a sensitivity analysis, we stratified female participants' data according to their age groups. In our previous analysis,<sup>15</sup> we reported the importance of sex and age in the classification of patients with hypersensitivity to cold sensation. We compared the traditional medicine pattern<sup>(TM1)</sup> for each group. We could not perform this analysis with male participants' data due to inadequate numbers for stratification.

### 2.4. Specific pattern<sup>(TM1)</sup> diagnosis

After specifying several traditional medicine patterns<sup>(TM1)</sup> which related to the number of positive symptoms in review of the systems, we divided the participants' data according to the existence of each pattern<sup>(TM1)</sup>. We compared sex ratio, mean age, number of accompanying symptoms, and significantly more or less frequent symptoms for each pattern<sup>(TM1)</sup> diagnosis.

### 2.5. Statistical analysis

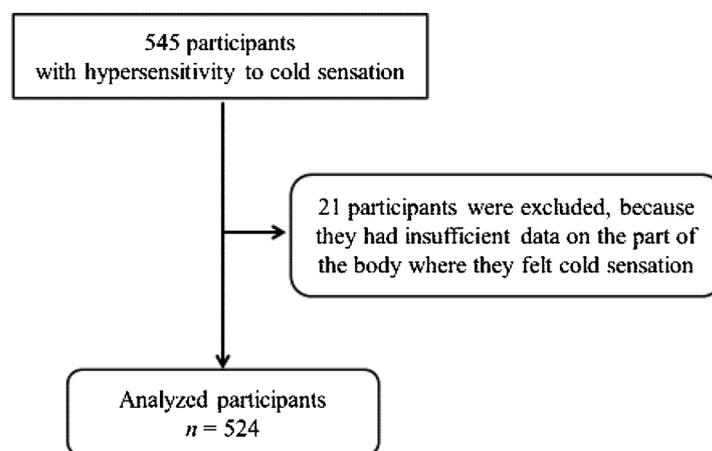
All statistical analyses were conducted using the R software, version 3.5.1 (The R Foundation for Statistical Computing (Jul 2, 2018, Austria). Data are shown as the means  $\pm$  SD. Differences between the groups were analyzed by the test for equal proportions or Cochran-Armitage trend test. The significant level was set at 5% for all tests.

## 3. Results

### 3.1. Participant information

A total of 545 participants were included in this study. Of these, 21 were excluded because of missing data on the part of the body affected by cold sensation, in spite of a diagnosis of hypersensitivity to cold sensations (Fig. 1).

Basic characteristics of the 524 participants were shown in Table 1. The mean age was  $51.6 \pm 17.8$  years old, and there were 430 women (percentage of women: 82.1%). With regard to the number of accompanying symptoms, mean number was  $23.1 \pm 11.4$  (Fig. 2). Common comorbidities were constipation (10.9%), insomnia (10.3%), and dysmenorrhea (8.0%).



**Fig. 1.** Flowchart for exclusion of participants from the study. A total of 545 participants were initially enrolled in the study; 21 of whom were excluded in spite of a diagnosis of hypersensitivity to cold sensations because of missing data regarding the part of the body where the cold sensation was experienced.

**Table 1**

Basic characteristics of the participants.

	Overall (n = 524)	Men (n = 94)	Women(n = 430)
Mean Age (years) ± SD	51.6 ± 17.8	58.9 ± 17.6	50.0 ± 17.5
Mean Number of Symptoms ± SD	23.1 ± 11.4	18.6 ± 10.8	24.1 ± 11.3
Principle-based pattern <sup>(TM1)</sup>			
Excess-Deficiency			
Excess	12 (2.3%)	7 (7.4%)	5 (1.2%)
Slight Excess	41 (7.8%)	15 (16.0%)	26 (6.0%)
Medium (Excess/Deficiency)	246 (46.9%)	44 (46.8%)	202 (47.0%)
Slight Deficient	114 (21.8%)	15 (16.0%)	99 (23.0%)
Deficient	111 (21.2%)	13 (13.8%)	98 (22.8%)
Heat-Cold			
Heat	3 (0.6%)	0 (0.0%)	3 (0.7%)
Moderate (Heat/Cold)	5 (1.0%)	2 (2.1%)	3 (0.7%)
Cold	437 (83.4%)	79 (84.0%)	358 (83.3%)
Tangled cold and heat	70 (13.4%)	11 (11.7%)	59 (13.7%)
Not available	9 (1.7%)	2 (2.1%)	7 (1.6%)
Body constituents pattern <sup>(TM1)</sup>			
Not applicable	15 (2.9%)	3 (3.2%)	12 (2.8%)
Qi deficiency	145 (27.7%)	31 (33.0%)	114 (26.5%)
Qi stagnation	115 (21.9%)	12 (12.8%)	103 (24.0%)
Qi uprising	26 (5.0%)	2 (2.1%)	24 (5.6%)
Blood deficiency	80 (15.3%)	9 (9.6%)	71 (16.5%)
Blood stasis	183 (34.9%)	19 (20.2%)	164 (38.1%)
Fluid disturbance	132 (25.2%)	16 (17.0%)	116 (27.0%)
Fluid deficiency	1 (0.2%)	0 (0.0%)	1 (0.2%)

SD: standard deviation.

The term, "medium" for Excess/Deficiency and "Moderate" for Heat/Cold have been defined in ICD-11.<sup>2</sup> Heat-cold pattern diagnosis is exclusive, and "Not available" means missing data of this diagnosis. In contrast, "Not applicable" has the active meaning for not having the body constituent pattern.

### 3.2. Classification by the location of cold sensation

We classified the participants' data according to the location of their cold sensation, that is, classification by the chief complaint. We analyzed sex, mean age, number of symptoms, and the pattern<sup>(TM1)</sup> for each group (Table 2). We could not find any specific differences in the proportions of different pattern<sup>(TM1)</sup> between the groups, except for a higher ratio of the tangled cold and heat pattern<sup>(TM1)</sup> in the lower back group. There was only 3 participants who were diagnosed as having the heat pattern<sup>(TM1)</sup>, and 5 participants, the moderate (heat/cold) pattern<sup>(TM1)</sup>. Most of the participants were diagnosed as having the cold pattern<sup>(TM1)</sup>, or the tangled cold and heat pattern<sup>(TM1)</sup>.

### 3.3. Classification by the number of accompanying symptoms

We classified participants' data into five groups according to the number of accompanying symptoms; from 0–10, 11–20, 21–30, 31–40, and 41 or more. An increasing number of accompanying symptoms was significantly associated with a higher female ratio. With a higher female ratio, the excess or slight excess pattern<sup>(TM1)</sup> became significantly less frequent. In contrast, the tangled cold and heat pattern<sup>(TM1)</sup>, qi stagnation pattern<sup>(TM1)</sup>, qi uprising pattern<sup>(TM1)</sup>, and blood stasis pattern<sup>(TM1)</sup> significantly increased (Table 3). We stratified female participants' data according to their age group as a sensitivity analysis, and were able to confirm the same trend in each age group (Supplementary Table 1).

The numbers of participants who were diagnosed as the tangled cold and heat, and qi uprising patterns<sup>(TM1)</sup> were too small for further analysis. In future research, we will aim to further explore the qi stagnation and blood stasis patterns<sup>(TM1)</sup>.

### 3.4. Specific pattern<sup>(TM1)</sup> diagnosis

We divided participants' data according to a diagnosis of the qi stagnation pattern<sup>(TM1)</sup> or blood stasis pattern<sup>(TM1)</sup>. Participants with the qi stagnation pattern<sup>(TM1)</sup> (n = 115; female 103 (89.6%); Mean age ± SD 51.0 ± 15.7 years) had a significantly greater number of positive symptoms compared with participants who did not (n = 409; female 327 (80.0%); Mean age ± SD 51.7 ± 18.4 years). The mean number of symptoms reported by participants with the qi stagnation pattern and those who did not, was 26.3 ± 11.0 and 22.2 ± 11.3, respectively. Several symptoms were reported more frequently in participants with the qi stagnation pattern<sup>(TM1)</sup> (Fig. 3). These symptoms were reported significantly more frequently by participants with the qi stagnation pattern<sup>(TM1)</sup> possibly because these participants had greater numbers of positive symptoms. Therefore, we stratified the participants' data according to the number of accompanying symptoms. We were able to confirm that the frequency of most of these symptoms were significantly higher in participants with the qi stagnation pattern<sup>(TM1)</sup> at least in one group (Supplementary Table 2).

Similarly, participants with the blood stasis pattern<sup>(TM1)</sup> (n = 183; female 164 (89.6%); Mean age ± SD 45.7 ± 16.2 years) had significantly greater numbers of symptoms compared with participants who did not (n = 341; female 266 (78.0%); Mean age ± SD 54.8 ± 17.9 years). The mean number of positive symptoms reported by participants with the blood stasis pattern and those who did not were 26.0 ± 11.5 and 21.6 ± 11.0, respectively. Several symptoms were more frequent in participants with the blood stasis pattern<sup>(TM1)</sup> (Fig. 4). We stratified the participants' data according to the number of

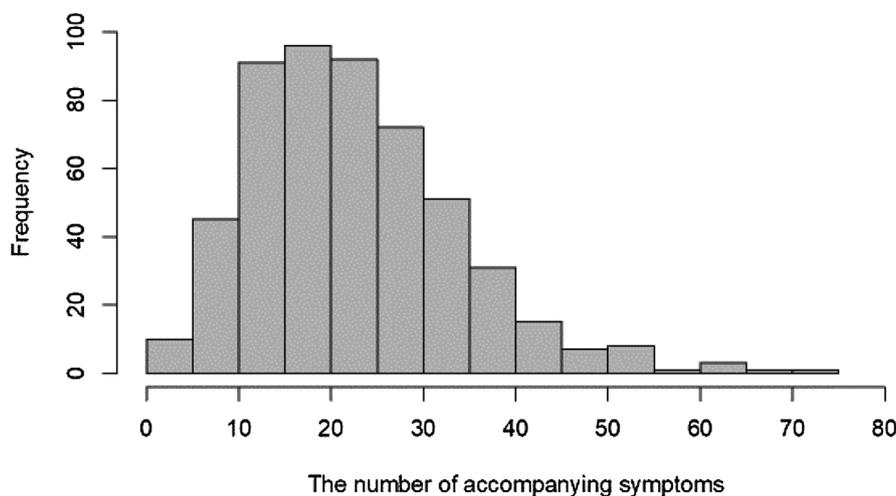


Fig. 2. A histogram of the number of accompanying symptoms of the 524 participants. Mean number was  $23.1 \pm 11.4$ , and median number was 22 with range from 3 to 72.

accompanying symptoms and confirmed that the frequency of most of these symptoms were significantly higher in participants with the blood stasis pattern<sup>(TM1)</sup> in at least one group (Supplementary Table 3).

4. Discussion

We reported the result of our statistical analysis using patients' subjective symptoms and showed the importance of accompanying symptoms in a pattern<sup>(TM1)</sup> diagnosis in Japanese Kampo medicine. Review of the systems has the potential of contributing to disease diagnosis in conventional medicine.<sup>16</sup> In contrast, positive items in a review of the systems are used to classify the patient according to traditional medicine patterns<sup>(TM1)</sup>.

Hypersensitivity to cold sensations is a commonly reported symptom in Japanese Kampo medicine clinic.<sup>6</sup> Hypersensitivity to cold

sensations is a condition in which patients suffer from cold sensations in any part of body. The term, hypersensitivity to cold sensations, is used as a diagnosis in Japan but its pathophysiology is not well understood. In Western medicine, the pathophysiology of chronic oversensitivity to cold is thought to be a disturbance of heat production or heat distribution.<sup>17</sup> Decreased activity, muscle volume, or thyroid hormone level are good examples of disturbed heat production. Decreased arterial flow due to atherosclerosis, or insufficient venous function are examples of disturbed heat distribution. In contrast, a change of thermal set point due to inflammatory cytokines plays an important role in acute cold sensations or chills.<sup>18</sup> In contrast, deficiency in yang qi (which warms the human body), or deficiency in nutritional blood, are thought to cause chronic cold sensation in Kampo medicine. In addition, the qi stagnation or blood stasis patterns may cause localized cold sensations. In the case of chills, the *cold-pathogen* is thought to be

Table 2  
Classification of participants according to the body part where the cold sensation was experienced.

	General (n = 210)	Hands (n = 221)	Legs(n = 396)	Lower back (n = 117)
Female(%)	182 (86.7%)	181 (81.9%)	312 (78.8%)	103 (88.0%)
Mean Age (years) ± SD	49.2 ± 17.2	48.4 ± 18.2	52.4 ± 18.2	51.6 ± 17.1
Mean Number of Symptoms ± SD	25.4 ± 12.4	24.8 ± 12.2	23.5 ± 11.8	28.9 ± 13.7
Principle-based pattern <sup>(TM1)</sup>				
Excess-Deficiency				
Excess	4 (1.9%)	2 (0.9%)	8 (2.0%)	2 (1.7%)
Slight Excess	17 (8.1%)	21 (9.5%)	32 (8.1%)	8 (6.8%)
Medium (Excess/Deficiency)	92 (43.8%)	106 (48.0%)	185 (46.7%)	57 (48.7%)
Slight Deficient	44 (21.0%)	42 (19.0%)	88 (22.2%)	25 (21.4%)
Deficient	53 (25.2%)	50 (22.6%)	83 (21.0%)	25 (21.4%)
Heat-Cold				
Heat	2 (1.0%)	1 (0.5%)	3 (0.8%)	1 (0.9%)
Moderate (Heat/Cold)	1 (0.5%)	2 (0.9%)	5 (1.3%)	1 (0.9%)
Cold	182 (86.7%)	187 (84.6%)	329 (83.1%)	90 (76.9%)
Tangled cold and heat	20 (9.5%)	27 (12.2%)	54 (13.6%)	24 (20.5%)
Not available	5 (2.4%)	4 (1.8%)	5 (1.3%)	1 (0.9%)
Body constituents pattern <sup>(TM1)</sup>				
Not applicable	5 (2.4%)	7 (3.2%)	12 (3.0%)	5 (4.3%)
Qi deficiency	62 (29.5%)	70 (31.7%)	113 (28.5%)	35 (29.9%)
Qi stagnation	49 (23.3%)	44 (19.9%)	88 (22.2%)	26 (22.2%)
Qi uprising	10 (4.8%)	13 (5.9%)	21 (5.3%)	6 (5.1%)
Blood deficiency	39 (18.6%)	32 (14.5%)	57 (14.4%)	17 (14.5%)
Blood stasis	82 (39.0%)	85 (38.5%)	137 (34.6%)	50 (42.7%)
Fluid disturbance	51 (24.3%)	52 (23.5%)	100 (25.3%)	23 (19.7%)
Fluid deficiency	0 (0.0%)	1 (0.5%)	1 (0.3%)	0 (0.0%)

SD: standard deviation.

Some participants experienced cold sensation in multiple body parts. The term, "medium" for Excess/Deficiency and "Moderate" for Heat/Cold have been defined in ICD-11.<sup>2</sup> Heat-cold pattern diagnosis is exclusive, and "Not available" means missing data of this diagnosis. In contrast, "Not applicable" has the active meaning for not having the body constituent pattern.

**Table 3**  
Classification of participants according to the number of symptoms.

Number of symptoms	From 0 to 10 (n = 55)	From 11 to 20 (n = 187)	From 21 to 30 (n = 164)	From 31 to 40 (n = 82)	41 or more (n = 36)
Female(%)	34 (61.8%)	146 (78.1%)	141 (86.0%)	77 (93.9%)	32 (88.9%)
Mean Age (years) ± SD	51.3 ± 19.2	54.2 ± 18.4	51.2 ± 18.0	47.8 ± 15.4	49.1 ± 15.0
Principle-based pattern <sup>(TM1)</sup>					
Excess-Deficiency					
Excess	3 (5.5%)	5 (2.7%)	3 (1.8%)	1 (1.2%)	0 (0.0%)
Slight Excess	6 (10.9%)	18 (9.6%)	9 (5.5%)	6 (7.3%)	2 (5.6%)
Medium (Excess/Deficiency)	30 (54.5%)	90 (48.1%)	75 (45.7%)	35 (42.7%)	16 (44.4%)
Slight Deficient	5 (9.1%)	39 (20.9%)	41 (25.0%)	20 (24.4%)	9 (25.0%)
Deficient	11 (20.0%)	35 (18.7%)	36 (22.0%)	20 (24.4%)	9 (25.0%)
Heat-Cold					
Heat	0 (0.0%)	1 (0.5%)	1 (0.6%)	0 (0.0%)	1 (2.8%)
Moderate (Heat/Cold)	1 (1.8%)	1 (0.5%)	2 (1.2%)	0 (0.0%)	1 (2.8%)
Cold	48 (87.3%)	170 (90.9%)	135 (82.3%)	64 (78.0%)	20 (55.6%)
Tangled cold and heat	3 (5.5%)	14 (7.5%)	24 (14.6%)	16 (19.5%)	13 (36.1%)
Not available	3 (5.5%)	1 (0.5%)	2 (1.2%)	2 (2.4%)	1 (2.8%)
Body constituents pattern <sup>(TM1)</sup>					
Not applicable	3 (5.5%)	8 (4.3%)	3 (1.8%)	1 (1.2%)	0 (0.0%)
Qi deficiency	14 (25.5%)	47 (25.1%)	53 (32.3%)	24 (29.3%)	7 (19.4%)
Qi stagnation	5 (9.1%)	34 (18.2%)	37 (22.6%)	26 (31.7%)	13 (36.1%)
Qi uprising	1 (1.8%)	7 (3.7%)	10 (6.1%)	5 (6.1%)	3 (8.3%)
Blood deficiency	9 (16.4%)	24 (12.8%)	30 (18.3%)	11 (13.4%)	6 (16.7%)
Blood stasis	11 (20.0%)	58 (31.0%)	52 (31.7%)	40 (48.8%)	22 (61.1%)
Fluid disturbance	16 (29.1%)	42 (22.5%)	41 (25.0%)	23 (28.0%)	10 (27.8%)
Fluid deficiency	0 (0.0%)	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)

SD: standard deviation.

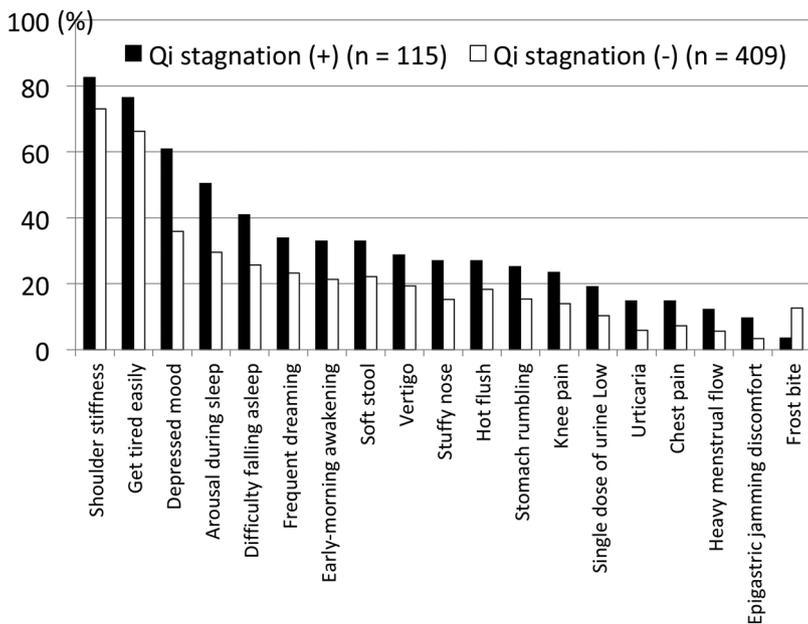
The term, "medium" for Excess/Deficiency and "Moderate" for Heat/Cold have been defined in ICD-11.<sup>2</sup> Heat-cold pattern diagnosis is exclusive, and "Not available" means missing data of this diagnosis. In contrast, "Not applicable" has the active meaning for not having the body constituent pattern.

an important cause of acute cold sensations. They are based on totally different medical concepts. In Japanese Kampo medicine, pattern<sup>(TM1)</sup> diagnoses are often used to label patients independently from the "traditional pathophysiology".<sup>3</sup> Disorder<sup>(TM1)</sup> or determination of traditional pathophysiology is not mandatory in current Kampo medicine. This situation enables Japanese non-specialist physicians to select an appropriate pattern<sup>(TM1)</sup> and herbal formula via accompanying symptoms.

There are some limitations to consider in interpreting our results. We analyzed data from only one institution in Japan. The diagnosis of hypersensitivity to cold sensations was based on patients' subjective complaints and there was no standardized criterion for diagnosing this condition. We cannot exclude the possibility that this condition may be a form of somatic symptoms disorder. Consistency in the diagnosis of

the patterns<sup>(TM1)</sup> among Kampo specialists is uncertain. This study was performed as an observational study in the usual clinical setting, and therefore it was not possible to evaluate the consistency in patterns<sup>(TM1)</sup> diagnosis among the contributing physicians. Diagnosis in traditional medicine should be based on the patterns of the key component symptoms (or weighting of symptoms) instead of only the number of accompanying symptoms.

We already reported that the distribution of subjective cold sensation could be divided into two categories; general and peripheral.<sup>7</sup> The peripheral distribution could be further divided into two subcategories; peripheral extremities (hands and legs) or lower body (lower back and legs). General distribution of cold sensation could be related to the pathogenesis of a disturbance of heat production. On the other hand, peripheral distribution of cold sensation could be related to a



**Fig. 3.** Frequency of symptoms in participants with (black bar) or without (white bar) a diagnosis of qi stagnation pattern<sup>(TM1)</sup>. Participants with qi stagnation pattern<sup>(TM1)</sup> (n = 115) had a significantly greater number of positive symptoms (26.3 ± 11.0) than those without (n = 409; 22.2 ± 11.3). Several symptoms were significantly more frequent in participants with the qi stagnation pattern<sup>(TM1)</sup>. Items with P ≥ 0.05 in the test for equal proportions have been excluded from this figure.

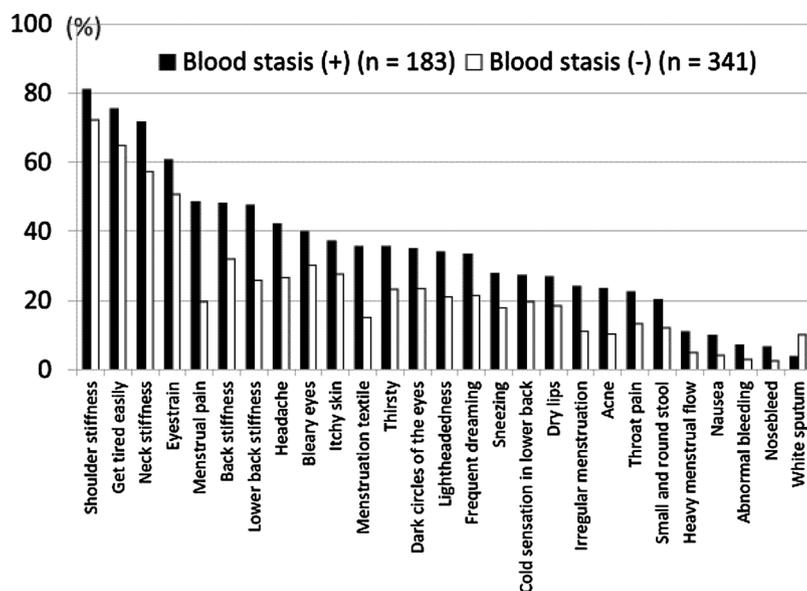


Fig. 4. Frequency of symptoms in participants with (black bar) or without (white bar) a diagnosis of blood stasis pattern<sup>(TM1)</sup>. Participants with blood stasis pattern<sup>(TM1)</sup> (n = 183) had a significantly greater number of positive symptoms (26.0 ± 11.5) than those without (n = 341; 21.6 ± 11.0). Several symptoms were significantly more frequent in participants with the blood stasis pattern<sup>(TM1)</sup>. Items with P ≥ 0.05 in the test for equal proportions have been excluded from this figure.

disturbance of heat distribution. However, the yield of this categorization in classifying patients into different patterns<sup>(TM1)</sup> is unclear in this analysis. Our results suggest the importance of a review of the systems, rather than a chief complaint, in a pattern<sup>(TM1)</sup> diagnosis.

When we divided participants' data by the number of accompanying symptoms, female ratio was higher in the groups with many symptoms. According to the basic background classification, we showed that women have more accompanying symptoms. The tangled head-cold pattern<sup>(TM1)</sup> is mainly used for patients with cold sensation and hot flush or heat sensation in their upper body. It is reasonable that such patients have more symptoms than the patients without hot flush or heat sensation in their upper body.

We also showed that the qi stagnation pattern<sup>(TM1)</sup>, qi uprising pattern<sup>(TM1)</sup>, and blood stasis pattern<sup>(TM1)</sup> increased as the accompanying symptoms increased. Okitsu et al.<sup>22</sup> reported a questionnaire for the diagnosis of the qi stagnation pattern<sup>(TM1)</sup>. Terasawa et al., Park et al., and Kang et al.<sup>19–21</sup> also reported a questionnaire for the diagnosis of the blood stasis pattern<sup>(TM1)</sup>. Their questionnaires only have positive-scored items, and patients with scores higher than a cutoff point would be diagnosed as the pattern<sup>(TM1)</sup>. The more symptoms the patient have, the more likely the patients are diagnosed using the pattern<sup>(TM1)</sup> diagnoses. Our results concur with these previous articles. Frequent symptoms in participants with the qi stagnation pattern<sup>(TM1)</sup> are similar to the symptoms, included in the final version of the questionnaire reported by Okitsu et al.,<sup>22</sup> namely, abdominal fullness, fatigue, diarrhea, inhibited urination, systemic body pain, chillness, aversion to cold, indigestion, and chest and rib-side pain. Our results support the inclusion of these items. In the same way, frequent symptoms in participants with the blood stasis pattern<sup>(TM1)</sup> are similar to the symptoms included in the questionnaires reported previously.<sup>19–21</sup> Although these questionnaires for determining the blood stasis pattern<sup>(TM1)</sup> also included many objective findings, these questionnaires included: chronic body pain, lower abdominal pain, dark circles under the eyes, dizziness, dysmenorrhea, and scaly and rough skin, as symptoms. These items are also compatible with our result.

In contrast, we found almost stable ratio of the qi deficiency pattern<sup>(TM1)</sup>, blood deficiency pattern<sup>(TM1)</sup>, and fluid disturbance pattern<sup>(TM1)</sup>. When we predict these pattern<sup>(TM1)</sup> diagnoses with the patients' symptoms database, we may need to include negative-scored items, which are non-specifically present in diagnoses (e.g. shoulder stiffness and fatigue), or items frequented only in patients with several accompanying symptoms. Otherwise, we may need apply objective findings. Several questionnaires have reported on qi deficiency, blood

deficiency, or the fluid disturbance pattern<sup>(TM1)</sup>.<sup>23–27</sup> They were determined by expert consensus and consisted only of positive-scored items. We could not find any papers that validated the predictive power of these questionnaires for pattern<sup>(TM1)</sup> diagnoses.

## 5. Conclusion

Our result showed the importance of accompanying symptoms in diagnosing a pattern<sup>(TM1)</sup> in Japanese Kampo medicine. We also showed the importance of the number of accompanying symptoms in diagnosing a pattern<sup>(TM1)</sup>.

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## Declaration of interest

No competing financial interests exist.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ctim.2019.05.011>.

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