Kampo medicine prescriptions for hospitalized patients in Tohoku University Hospital

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ABSTRACT
Aim: Traditional Japanese medicine (Kampo medicine; KM) is widely used together with modern medicine in clinical settings. However, KM prescription trends during hospitalization has never been reported for Japanese university hospitals. This study aimed to investigate the KM prescription trends for hospitalized patients at a university hospital in Japan. The present study was conducted in a ‘Problem-based Learning’ workshop in a second-grade class at the Tohoku University School of Medicine.

Methods: Using the drug prescription data of Tohoku University Hospital between October 2017 and September 2018, we identified hospitalized patients who were prescribed KM, which included 17 formulations. We investigated the prescription trends, sex, and age distribution of patients, and diseases for which KMs were prescribed.

Results: Of the 19,249 patients, 1,229 patients (6.4%) were newly prescribed KM during admission. The average age was 60.2 ± 18.8 years, and female patients accounted for 51.4%. The most prescribed KM was daikenchuto (485 patients), mainly for post-operative patients in the surgical departments and psychosomatic patients with gastrointestinal symptoms in the psychiatric departments. Yokukansan was used for dementia patients in the geriatric medicine department and for delirium patients in the intensive care unit. Rikkunshito was administered to patients after gastric cancer surgery and to patients with anorexia nervosa. Daikenchuto and shakuyakukanzoto were more frequently prescribed to men, and goreisan and goshajinkigan were more frequently prescribed to women.

Conclusion: Kampo Medicines were prescribed for specific diseases or conditions at various inpatient departments in the university hospital.

KEY WORDS: inpatient, Kampo medicine, problem-based learning, trends in prescription, university hospital

INTRODUCTION
Traditional Japanese (Kampo) medicine, available as 148 Kampo formulations, is widely prescribed under the national health care insurance system in Japan. Even non-specialists in Kampo medicine (KM) can use them in Western medical practice [1,2]. Actually, a prescription survey at a tertiary-care hospital showed that 87% of non-specialists had prescribed KM [3]. Kampo formulations were more frequently prescribed for outpatients (92.9%) than for inpatients (7.0%), as shown by analyzing the national health care claim records [4]. However, the recent prescription trends of KM for hospitalized patients have not yet been reported.

In the Tohoku University Medical Department, a KM education program has been developed and is offered in a multiple-grade curriculum [5]. Students in the 2nd grade take a ‘Problem-based Learning’ class, which is a small-group practice to identify clinical problems and search for solutions. Three of the authors of this article (RS, YK, and DK) are medical students and took this class in 2018 and raised the question ‘What kinds of KM are used for what kind of diseases in what departments of our hospital?’

The purpose of this study was to investigate the prescription trends of KM in Tohoku University Hospital (TUH) for hospitalized patients, and to examine the association between prescriptions and diseases.

METHODS
This study is a medical record review and analysis of patients hospitalized at TUH, Sendai, Japan. TUH is the largest core hospital in northeast Japan, and it consists of
Table 1 | Background characteristics of the hospitalized patients prescribed Kampo medicine in Tohoku University Hospital

| Department                                      | Frequency of Kampo prescription (%) | Patients prescribed Kampo medicine (N) | Hospitalized patients (N) | Age (mean ± SD) | Female (%) |
|------------------------------------------------|-------------------------------------|---------------------------------------|---------------------------|-----------------|------------|
| 1 Geriatric med. & neuroimaging              | 36.2                                | 47                                    | 130                       | 81.2 ± 8.1      | 63.8       |
| 2 Psychosomatic med.                          | 26.7                                | 23                                    | 86                        | 45.6 ± 20.4     | 78.3       |
| 3 Gynecology                                  | 23.6                                | 163                                   | 690                       | 57.1 ± 13.1     | 100        |
| 4 Cardiovascular surg.                        | 22.1                                | 67                                    | 303                       | 62.4 ± 16.3     | 22.4       |
| 5 General surg.                               | 13.5                                | 274                                   | 2029                      | 64.8 ± 14.4     | 36.5       |
| 6 Internal med. & rehabilitation sci.         | 13.2                                | 10                                    | 76                        | 63.4 ± 15.3     | 50         |
| 7 Psychiatry                                  | 12.6                                | 24                                    | 191                       | 53.3 ± 19.4     | 70.8       |
| 8 Pediatric surg.                             | 12.1                                | 29                                    | 240                       | 11.6 ± 12.5     | 58.6       |
| 9 Therapeutic radiology                       | 11.2                                | 28                                    | 251                       | 70.1 ± 10.3     | 3.6        |
| 10 Neurosurgery                               | 10.6                                | 38                                    | 359                       | 58.5 ± 17.8     | 36.8       |
| 11 Emergency & critical care med.             | 10.5                                | 78                                    | 743                       | 67.6 ± 17.8     | 34.6       |
| 12 Hematology & rheumatology                  | 9.6                                 | 40                                    | 417                       | 55.5 ± 15.6     | 60         |
| 13 Urology                                    | 8.0                                 | 43                                    | 538                       | 65.1 ± 15.0     | 23.3       |
| 14 Palliative med.                            | 7.1                                 | 19                                    | 266                       | 70.4 ± 16.3     | 52.6       |
| 15 Medical oncology                           | 7.0                                 | 28                                    | 401                       | 63.8 ± 11.5     | 42.9       |
| 16 Obstetrics                                 | 6.6                                 | 75                                    | 1140                      | 34.7 ± 6.7      | 100        |
| 17 Otolaryngology-head & neck surg.           | 6.1                                 | 45                                    | 743                       | 65.9 ± 11.5     | 15.6       |
| 18 Neurology                                  | 5.8                                 | 22                                    | 381                       | 63.7 ± 15.3     | 36.4       |
| 19 Respiratory med.                           | 4.2                                 | 38                                    | 909                       | 66.3 ± 13.5     | 42.1       |
| 20 Rehabilitation med.                       | 4.2                                 | 2                                     | 48                        | 30.0 ± 19.8     | 50         |
| 21 Neuropsychology                            | 4.1                                 | 5                                     | 121                       | 75.4 ± 5.5      | 20         |
| 22 Orthopedic surg.                           | 2.7                                 | 16                                    | 592                       | 64.2 ± 16.5     | 56.3       |
| 23 Thoracic surg.                             | 2.3                                 | 10                                    | 434                       | 63.6 ± 19.4     | 20         |
| 24 Cardiovascular med.                        | 2.3                                 | 29                                    | 1272                      | 66.8 ± 14.6     | 48.3       |
| 25 Gastroenterology                           | 2.2                                 | 25                                    | 1127                      | 61.5 ± 17.1     | 36         |
| 26 Dermatology                                | 1.6                                 | 8                                     | 512                       | 75.8 ± 8.8      | 50         |
| 27 Diabetes & metabolism                      | 1.3                                 | 4                                     | 308                       | 67.3 ± 8.5      | 0          |
| 28 Plastic & reconstructive surg.             | 1.2                                 | 4                                     | 332                       | 58.5 ± 20.4     | 50         |
| 29 Nephrology, endocrinology, & vascular med. | 0.7                                 | 4                                     | 538                       | 65.3 ± 14.6     | 25         |
| 30 Pediatrics                                 | 0.7                                 | 6                                     | 867                       | 10.8 ± 7.1      | 66.7       |
| 31 Oral & maxillofacial surg.                 | 0.6                                 | 5                                     | 887                       | 61.6 ± 18.6     | 60         |
| 32 Ophthalmology                              | 0.3                                 | 6                                     | 2018                      | 68.0 ± 20.3     | 83.3       |
| 33 Kampo med.                                 | †                                   | 2                                     | 0                         | 44.5 ± 0.7      | 100        |
| 34 Anesthesiology                             | †                                   | 12                                    | 1                         | 56.0 ± 18.6     | 50         |
| 35 General med.                               | 0.0                                 | 0                                     | 1                         | —               | —          |
| 36 Clinical infectious diseases               | 0.0                                 | 0                                     | 5                         | —               | —          |
| 37 Pediatric surg. oncology                   | 0.0                                 | 0                                     | 1                         | —               | —          |
| 38 Epileptology                               | 0.0                                 | 0                                     | 150                       | —               | —          |
| 39 Diagnostic radiology                       | 0.0                                 | 0                                     | 64                        | —               | —          |
39 medical and three dental inpatient departments with 1225 care beds. The operational status of TUH was as follows: average length of stay, 15.0 days; bed occupancy rate, 82.0%; referral rate, 78.5%; reverse referral rate, 47.2%; and total number of surgeries, 9395 during this research period.

Drug prescription data of patients hospitalized between 1 October 2017 and 30 September 2018 were identified in 42 departments. We extracted the following patients’ items from the database of TUH: sex, age, department of admission, names of KM prescriptions, prescription status, and names of diseases having the most paid medical expenses during hospitalization based on the Japanese diagnosis procedure combination (DPC) system according to the 10th edition of the International Statistical Classification of Diseases (ICD-10). In TUH, KMs usually prescribed for admitted patients are limited to the following 17 formulations: bakumondoto, daikenchuto (DKT), goreisan (GRS), goshajinkigan (GJG), hachimijiogan, hangeshashinto, hochuekkito, juzentaihoto, kakkonto (KKT), kamishoyosan, keishibukuryogan, rikkunshito (RKT), saireito, shakuyakukanzoto (SKT), shoseiryuto (SST), tokishakuyakusan, and yokukansan (YKS). Prescription status refers to the type of prescription and contains the following items: regular, temporary, continuous before admission, and after discharge. First, we excluded the data for continuous prescriptions before admission because these would be used for daily use, and would have little association with the medical procedure on admission. We then excluded duplicate prescription data from the same patients. We combined similar disease names for analysis.

We calculated the KM prescription ratio for each department and the total. The departments where the Kampo prescription ratio was double or higher than the average ratio over all departments we termed ‘the highlighted departments’, and additionally surveyed the top three disease names for which KM was frequently prescribed. For the diseases most frequently prescribed KMs, we surveyed the top two frequently prescribed KMs. Finally, we investigated the characteristics of patients for whom KMs were frequently prescribed.

Table 1 (continued)

| Department                             | Frequency of Kampo prescription (%) | Patients prescribed Kampo medicine (N) | Hospitalized patients (N) | Age (mean ± SD) | Female (%) |
|----------------------------------------|-------------------------------------|--------------------------------------|--------------------------|-----------------|------------|
| Oral anesthesia & pain management      | 0.0                                 | 0                                    | 14                       | —               | —          |
| Dentistry for disabilities            | 0.0                                 | 0                                    | 64                       | —               | —          |
| Total                                  | 6.4                                 | 1229                                 | 19 249                   | 60.2 ± 18.8     | 51.4       |

1 The Departments of Kampo Medicine and Anesthesiology have no hospital beds. The prescriptions were made for patients hospitalized in other departments.

Med., medicine; sci., science; surg., surgery.

After the investigation in this class, the students and tutors (ST and RA) additionally discussed the usage of each KM in our hospital and its clinical evidence, as part of the educational program in our department [5].

RESULTS

The total number of hospitalized patients in TUH was 19 249 and the total number of prescriptions for KM was 6293 during the research period. Data after excluding continuous prescriptions before admission showed that 1229 (6.4%) patients received KM (Table 1).

The departments with the highest proportion of patients prescribed KM were geriatric medicine and neuroimaging, 36.2%; psychosomatic medicine, 26.7%; gynecology, 23.6%;
cardiovascular surgery, 22.1%; general surgery, 13.5%; and internal medicine and rehabilitation science, 13.2%. The prescription ratio of these six departments was double or higher than the overall average (6.4%). The departments with the largest number of patients prescribed KM were general surgery, where gastrointestinal, hepato-biliary-pancreatic, breast, endocrine, peripheral vascular, and transplant surgeries (274 patients) are performed, gynecology (163 patients), and emergency medicine (78 patients). In the anesthesiology department, 12 patients were administered KM for post-anesthetic care. For example, YKS for the treatment of delirium in the intensive care unit, and GRS for the treatment of headache after lumbar anesthesia of delivery.

Including the prescriptions adopted for urgent care, 36 Kampo formulations were prescribed during the study period. The most frequent KMs and the numbers of patients were as follows: DKT, 485 patients (39.5%); YKS, 132 (10.7%); SKT, 109 (8.9%); RKT, 93 (7.6%); GRS, 90 (7.3%); and GJG, 66 (5.4%) (Fig. 1).

We then analyzed the detailed prescriptions and diseases in the six highlighted departments where KM was most frequently prescribed. Figure 2 shows the largest number of Kampo prescriptions in the six departments. Daikenchuto was most frequently prescribed in psychosomatic medicine, gynecology, cardiovascular surgery, and general surgery. In geriatrics, YKS was the most frequently prescribed. Rikkunshito was the second most frequently prescribed in psychosomatic medicine and

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**Figure 2** | Number of Kampo prescriptions in the six departments where Kampo medicine was frequently prescribed. (a) Geriatric medicine; (b) psychosomatic medicine; (c) gynecology; (d) cardiovascular surgery; (e) general surgery; (f) internal rehabilitation.
general surgery. Shakuyakukanzoto was frequently prescribed in the cardiovascular and general surgery departments. In the internal medicine and rehabilitation science department, prescribed Kampo formulas varied because a wide variety of patients from other departments were treated there. Detailed prescription data in each department are shown in Table S1. The five departments with the highest number of Kampo prescriptions were surgical departments (general medicine, gynecology, emergency and critical care medicine, obstetrics, and cardiovascular surgery), and with the exception of obstetrics, DKT was the most prescribed medicine.

Table 2a lists the top-three diseases of for which medical expenses during hospitalization were paid most, and for which doctors frequently prescribed Kampo formulas in the highlighted departments. The most frequent KMs used for patients with these diseases are shown in Table 2b. In the geriatric department, YKS was most frequently prescribed for Alzheimer’s disease. In the psychosomatic medicine department, patients with anorexia nervosa received RKT or DKT. In the gynecology department, DKT and GJG were prescribed for patients with ovarian cancer. Among the 34 patients with aortic aneurysm or aortic dissection in the cardiovascular surgery department, 29 received DKT. In the general surgery department, 26 patients with gastric cancer were prescribed RKT.

We examined the distributions of the patients receiving the most frequently prescribed Kampo formulas (Fig. 3). KM was mainly prescribed to adult females (30s–70s) and to older men (50s–80s). Female patients were more common in obstetrics and gynecology (100%), and male patients were more frequent in therapeutic radiology (96.4%) and other surgical departments. Yokukansan was prescribed more to elderly patients. DKT and SKT were prescribed more to males than to females. On the other hand, GRS and GJG were prescribed more to females. The age distribution of patients receiving GRS showed the higher peak among women in their 30s. Goshajinkigan was mainly prescribed in women in their 40s–60s.

Table 2 | The diseases for which Kampo medicines were most prescribed, and Kampo medicines in the highlighted departments

| (a) Diseases for which Kampo medicines were prescribed. | 1st | 2nd | 3rd |
|--------------------------------------------------------|-----|-----|-----|
| Geriatric med. & neuroimaging (47) | Alzheimer’s disease (22) | Dementia with Lewy body (6) | Congestive heart failure/ Parkinson’s disease (2) |
| Psychosomatic med. (23) | Anorexia nervosa (12) | Chronic idiopathic pseudointestinal obstruction (3) | — |
| Gynecology (163) | Ovarian cancer (80) | Endometrial cancer (34) | Cervical cancer (21) |
| Cardiovascular surg. (67) | Aortic aneurysm and aortic dissection (34) | Valvular disease (7) | Ischemic cardiomyopathy (6) |
| General surg. (274) | Gastric cancer (35) | Gallbladder cancer and bile duct cancer (28) | Ileus and bowel obstruction (24) |
| Internal med. & rehabilitation sci. (10) | Aortic stenosis (2) | Others (1) | — |

| (b) Kampo medicines that were most prescribed for the top disease. | Disease name | 1st Kampo medicine | 2nd Kampo medicine |
|---------------------------------------------------------------|--------------|-------------------|--------------------|
| Geriatric med. & neuroimaging (47) | Alzheimer’s disease (22) | Yokukansan (20) | Hochuekkito/ninjin’yoeito (1) |
| Psychosomatic med. (23) | Anorexia nervosa (12) | Rikkunshito (4) | Daikenchuto (3) |
| Gynecology (163) | Ovarian cancer (80) | Daikenchuto (40) | Goshajinkigan (19) |
| Cardiovascular surg. (67) | Aortic aneurysm or aortic dissection (34) | Daikenchuto (29) | Shakuyakukanzoto (3) |
| General surg. (274) | Gastric cancer (35) | Rikkunshito (26) | Daikenchuto (5) |
| Internal med. & rehabilitation sci. (10) | Aortic stenosis (2) | Shoseiryuto (2) | — |

Med., medicine; sci., science; surg., surgery.
Figure 3 | Age and sex distributions of all patients and patients receiving each Kampo formula. F, female; M, male. Age represents mean ± S.D. (a) total, (b) daikenchuto, (c) yokukansan, (d) shakuyakukanzoto, (e) rikkunshito, (f) goreisan, (g) goshajinkigan.
DISCUSSION

We investigated the trends in KM prescriptions for hospitalized patients in Western departments at TUH, a large-scale hospital. To our knowledge, this study is the first to reveal in detail prescription trends of KM in inpatients departments. KM was used for 6.4% of all hospitalized patients in TUH. The aggregate results per department showed that KM was frequently prescribed in the departments of surgery and psychiatry. On the other hand, few patients were prescribed KM in the departments where surgery in small areas was performed, such as dermatology, plastic and reconstructive surgery, and ophthalmology, where less post-operative care is needed. In the departments dealing with psychosomatic disorders, KM was frequently prescribed, suggesting that KM together with conventional treatment was used to treat intractable psychosomatic symptoms.

The mean age of the patients prescribed KM was relatively higher than of the total of hospitalized patients (60.2 vs 53.9 years). Older patients may have more complications and symptoms, and KM may be used as an additional treatment to alleviate these symptoms.

Frequent KM usage in each department is suggested to be based on accumulated clinical evidence. DKT was most frequently prescribed, particularly in surgical departments and psychosomatic medicine (Fig. 2, Table 2). DKT improves intestinal bowel dysfunction after surgery [6], and its use is associated with a short period till discharge and a small medical cost of hospitalization [7]. Moreover, DKT improves chronic constipation and abdominal bloating [8,9]. Clinical evidence has also been accumulated about YKS use in geriatrics [10], SKT for muscle cramp [11] and chemotherapy-induced hiccups [12], RKT for appetite loss and gastrointestinal symptoms [13,14], and GJG for peripheral neuropathy as a side effect of chemotherapy [15]. The results of our study indicate that KM was used complementarily with Western conventional therapy in evidence-based medicine.

Since 2013, the Japan Society for Oriental Medicine (JSOM) has annually released ‘Evidence reports of Kampo Treatment’ (EKAT) [16], which is a list of randomized controlled trials (RCTs) using KM. Analyzing EKAT showed that 28.1% of the RCTs aimed to investigate the complementary effects on Western medicine or alleviate its side effects [17]. The JSOM has also published clinical practice guidelines for Kampo products in Japan (KCPG) [18]. Future clinical evidence could change the prescription trend of KM.

The prescription trends differed from those described in previous studies [1–3], mainly due to the research setting including the factors outpatient/inpatient, hospital, available KMs, and research period. In particular, KM usage for inpatients and outpatients would be quite different. A recent survey using National Health Care Claims revealed that outpatient Kampo prescriptions were much more frequent than inpatient prescriptions [4], and KKT, SST, and maoto, usually used for the common cold, were most frequently prescribed in an outpatient setting [19]. In the general medicine department in TUH, 14% of outpatients received KM, and 53% of the patients prescribed KM showed improvement after treatment [20].

The limitations of this study are the result of the research setting. TUH is a special functioning hospital that provides advanced medical services, and relatively serious patients are admitted. Kampo prescription in TUH was limited to only 17 kinds of the 148 formulations approved under the national health care system. This surveillance took into account a one-year period and did not deal with changes over time. Further multi-center, longitudinal studies are needed to clarify the general transition of Kampo prescription trends. However, we could demonstrate that KMs were prescribed in various scenes in many departments in this study based on clinical evidence, and possibly helped to alleviate multiple symptoms of hospitalized patients.

CONCLUSIONS

KMs were prescribed for specific diseases or conditions at various inpatient departments in modern medicine, based on accumulated clinical evidence.

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CONFLICTS OF INTEREST

ST, AK, MO, and TI are associated to the Department of Kampo and Integrative Medicine, Tohoku University Graduate School of Medicine, which is a joint research institute with Tsumura & Co., Japan.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article:

**Table S1.** The three most frequent Kampo prescriptions in each department.