



Kampo medicine in ICUs in Japan between 2010 and 2020

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To the Editor

Kampo medicine is used empirically in Japan for critically ill patients admitted to the intensive care unit (ICU). According to information obtained from non-ICU patients, Daikenchuto is used for gastrointestinal motility [1–3], Yokukansan for delirium [4, 5], Rikkunshito for upper gastrointestinal symptoms [6, 7], and Shakuyakukanzoto for muscle cramps [8]. Considering their mechanism of action, Kampo medicine is expected to improve patient outcomes and reduce ICU costs. However, despite their possible efficacy and empirical use, details regarding the recent practice patterns of Kampo medicine in Japanese ICUs are lacking. Knowledge of nationwide trends and practice patterns of Kampo medicine in Japan is important to understand its influence on ICU practices. Moreover, it would also aid in establishing evidence-based medicine in the future. Therefore, the present study aimed to assess the recent practice patterns of Kampo medicine in ICUs in Japan.

We used the Japanese Diagnosis Procedure Combination database, which contains discharge abstract and administrative claims data from more than 1400 acute-care hospitals that voluntarily contribute to the database. The database covers approximately 75% of all ICU beds in Japan [9, 10]. All patients admitted to the ICU between July 2010 and March 2021 were included in this study. The definition of ICU in this study was a separate unit providing critical care services with at least one physician on-site 24 h per day, at least two intensivists working full-time, around-the-clock nursing, the equipment necessary to care for critically ill patients, and a nurse-to-patient ratio of 1:2, as defined by

Japanese procedure codes A3002, A3004, and A301 [10]. We identified patients who were prescribed at least one Kampo medicine during their ICU stay. Number of patients prescribed Kampo medicine per 1000 ICU admissions was calculated. Overall and top five used Kampo medicines were described by fiscal year, and their trends were tested using Cochran–Armitage test [11]. Patient characteristics and outcomes of ICU patients treated with and without Kampo medicine were compared using standardized mean differences, and absolute standardized mean difference of > 10% was considered to indicate a statistically significant difference between the two groups [12]. Characteristics of the patients who were prescribed the top five Kampo medicines in the ICU were also reported. All analyses were performed using STATA/SE software version 17.0 (STATA Corp, College Station, TX, USA). All hypothesis tests were two sided, and the level of significance was set at 0.05.

A total of 3,661,079 patients admitted to the ICU from 724 hospitals were identified during the study period. Of these, 207,448 (5.7%) received at least one Kampo medicine during their ICU stay. The overall number of patients who were prescribed Kampo medicine per 1000 ICU admissions was 56.7. Moreover, a significant increasing trend was observed in the number of ICU patients who were prescribed Kampo medicine, with the number increasing from 25.8 in 2010 to 84.3 in 2020 (P for trend < 0.001) (Fig. 1). The most prescribed Kampo medicine was Daikenchuto (65.0%), followed by Yokukansan (15.3%), Rikkunshito (14.5%), Shakuyakukanzoto (5.1%), and Goreisan (5.0%). A significant increasing trend was observed in the use of all of the aforementioned Kampo medicines from 2010 to 2020 (P < 0.001). Patients treated with Kampo medicine were more likely to be admitted for emergency surgery, undergo invasive treatments during ICU stay, and have longer hospital and ICU stays in comparison to those not treated with Kampo medicine (Online Resource 1). Characteristics of the patients who were prescribed the top five Kampo medicines in ICUs are shown in Online Resource 2. Median (interquartile range) length of prescribed days during hospital and ICU stays were 8

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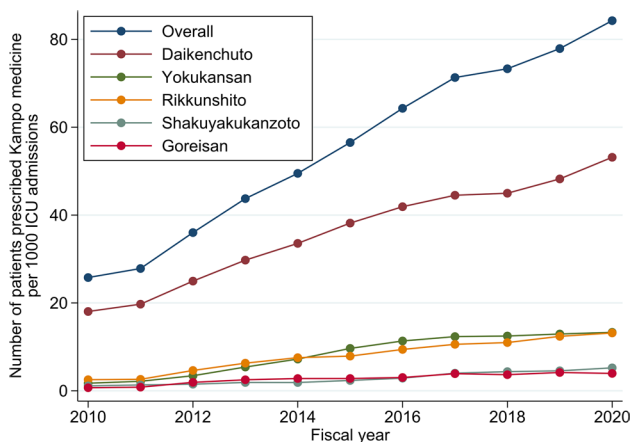


Fig. 1 Trends in the number of patients prescribed Kampo medicine per 1000 ICU admissions from 2010 to 2020. Each fiscal year started on April 01 and ended on March 31. ICU, intensive care unit

(3–19) and 2 (1–4), respectively. Daikenchuto and Rikkunshito were prescribed mainly for patients with invasive mechanical ventilation and enteral nutrition, Yokukansan and Shakuyakukanzoto were prescribed for older patients, and Goreisan for trauma patients.

To the best of our knowledge, this is the first nationwide study in Japan on trends and recent practices of Kampo medicine in ICUs. The results showed an increasing trend of use of Kampo medicine in ICU practice from 2010 to 2020, despite the lack of clear evidence. The observed increasing trend was remarkable, and the linear increase pattern suggested that prescriptions of Kampo medicines in ICUs would continue to increase in the future. Daikenchuto was the most prescribed Kampo medicine in the ICUs. Previous trials outside the ICU have suggested the beneficial effects of Daikenchuto on gastrointestinal motility in patients with postoperative adhesive small bowel obstruction and chronic constipation [1–3]. However, in the present study, Daikenchuto was administered to various ICU patients other than those who underwent abdominal surgery, suggesting that Daikenchuto was used empirically in ICU patients for gastrointestinal motility, for which there was no evidence. For the same reason, there is no evidence regarding the use of Yokukansan for treatment of ICU delirium or using Shakuyakukanzoto for hiccups during invasive mechanical ventilation [4, 5, 8]. The increasing impact and scant evidence regarding the use of Kampo medicine in ICU warrants future research.

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Data Availability The datasets analysed in the current study are not publicly available because of contracts with the hospitals providing data to the database.

Declarations

Conflict of interest The authors declare that they have no competing interests.

References

- Endo S, Nishida T, Nishikawa K, Nakajima K, Hasegawa J-I, Kitagawa T, Ito T, Matsuda H. Dai-kenchu-to, a Chinese herbal medicine, improves stasis of patients with total gastrectomy and jejunal pouch interposition. *Am J Surg*. 2006;192:9–13. <https://doi.org/10.1016/j.amjsurg.2006.01.022>.
- Yoshikawa K, Shimada M, Wakabayashi G, Ishida K, Kaiho T, Kitagawa Y, Sakamoto J, Shiraiishi N, Koeda K, Mochiki E, Saikawa Y, Yamaguchi K, Watanabe M, Morita S, Kitano S, Saji S, Kanematsu T, Kitajima M. Effect of Daikenchuto, a traditional Japanese herbal medicine, after total gastrectomy for gastric cancer: a multicenter, randomized, double-blind, placebo-controlled, Phase II trial. *J Am Coll Surg*. 2015;221:571–8. <https://doi.org/10.1016/j.jamcollsurg.2015.03.004>.
- Yuki M, Komazawa Y, Kobayashi Y, Kusunoki M, Takahashi Y, Nakashima S, Uno G, Ikuma I, Shizuku T, Kinoshita Y. Effects of Daikenchuto on abdominal bloating accompanied by chronic constipation: a prospective, single-center randomized open trial. *Curr Ther Res Clin Exp*. 2015;77:58–62. <https://doi.org/10.1016/j.curtheres.2015.04.002>.
- Iwasaki K, Satoh-Nakagawa T, Maruyama M, Monma Y, Nemoto M, Tomita N, Tanji H, Fujiwara H, Seki T, Fujii M, Arai H, Sasaki H. A randomized, observer-blind, controlled trial of the traditional Chinese medicine Yi-Gan San for improvement of behavioral and psychological symptoms and activities of daily living in dementia patients. *J Clin Psychiatry*. 2005;66:248–52. <https://doi.org/10.4088/jcp.v66n0214>.
- Mizukami K, Asada T, Kinoshita T, Tanaka K, Sonohara K, Nakai R, Yamaguchi K, Hanyu H, Kanaya K, Takao T, Okada M, Kudo S, Kotoku H, Iwakiri M, Kurita H, Miyamura T, Kawasaki Y, Omori K, Shiozaki K, Odawara T, Suzuki T, Yamada S, Nakamura Y, Toba K. A randomized cross-over study of a traditional Japanese medicine (kampo), yokukansan, in the treatment of the behavioural and psychological symptoms of dementia. *Int J Neuropsychopharmacol*. 2009;12:191–9. <https://doi.org/10.1017/S146114570800970X>.
- Tatsuta M, Iishi H. Effect of treatment with liu-jun-zi-tang (TJ-43) on gastric emptying and gastrointestinal symptoms in dyspeptic patients. *Aliment Pharmacol Ther*. 1993;7:459–62. <https://doi.org/10.1111/j.1365-2036.1993.tb00120.x>.

7. The traditional Japanese medicine rikkunshito improves upper gastrointestinal symptoms in patients with functional dyspepsia. Accessed 2023 Jan 4. <https://www.cochranelibrary.com/es/central/doi/https://doi.org/10.1002/central/CN-01722304/full>. Cochrane Library [Internet]
8. Ota K, Fukui K, Nakamura E, Oka M, Ota K, Sakaue M, Sano Y, Takasu A. Effect of Shakuyaku-kanzo-to in patients with muscle cramps: a systematic literature review. *J Gen Fam Med*. 2020;21:56–62. <https://doi.org/10.1002/jgf2.302>.
9. Yasunaga H. Real world data in Japan: chapter II the diagnosis procedure combination database. *Ann Clin Epidemiol*. 2019;1:76–9.
10. Ohbe H, Sasabuchi Y, Kumazawa R, Matsui H, Yasunaga H. Intensive care unit occupancy in Japan, 2015–2018: a nationwide inpatient database study. *J Epidemiol*. 2022;32:535–42. <https://doi.org/10.2188/jea.JE20210016>.
11. Armitage P. Tests for linear trends in proportions and frequencies. *Biometrics*. Wiley. Int Biom Soc. 1955;11:375–86. <https://doi.org/10.2307/3001775>.
12. Amrhein V, Greenland S, McShane B. Scientists rise up against statistical significance. *Nature*. 2019;567:305–7. <https://doi.org/10.1038/d41586-019-00857-9>.

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