

## Characteristics of the Prevention and Treatment of Gynecological Cancer in Japan

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Various interactions between biological, psychological, and social factors should be considered for the prevention of cancer. Endometrial cancer, which is a common gynecological cancer worldwide, ranks 6th among all cancers in women when the incidence has been age-adjusted [1]. The rate of incidence of endometrial cancer was 6.5 (per 100,000 women) in 2015, which is a four- to five-fold increase over the past 3 decades [2]. A large variation among the incidence rates internationally has been reported and the incidence rate in Japan is lower than that in Western countries; however, the incidence of endometrial cancer has increased 1.5-fold among the Japanese migrants in the United States and three- to four-fold among the Japanese Americans born in the United States when compared that of Japanese women living in Japan [3]. These findings suggest that a health-related lifestyle is related to the risk of endometrial cancer and epidemiological studies have investigated the dietary effects on endometrial cancer [4]. Thus, we have investigated the food intake frequency for the patients and healthy volunteers by using a frequency questionnaire. Results of a case-control study showed that the consumption of green tea and coffee were negatively associated with the risk of endometrial endometrioid adenocarcinoma (EEA) [5]. Furthermore, our study suggested that a higher intake of vegetables, peanuts, fish, and boiled eggs was associated with a reduced risk of EEA. A higher intake of instant noodles, instant food items, and deep-fried foods was associated with an increased risk of EEA when compared that of Japanese women who have a lower intake [6]. These findings suggest that foods containing polyphenols with antioxidant properties, omega-3 fatty acids [7], and vitamin D [8] could play a role in prevention, while instant foods that are high in rich fatty acids could increase the risk of EEA. Also, it is reported that Japanese foods are rich in these nutrients [9,10]. Thus, the intake of traditional Japanese foods, which is characterized by the relatively high amounts of fish and vegetables when compared to that of the Western diet, might be appropriate for the prevention of EEA in Japanese women.

The other characteristics of Japanese medicine in gynecological cancers are supportive cancer treatments and care. Surgery, radiotherapy, and chemotherapy along with anticancer drugs are the standard treatments for cancer. In addition, physicians can use Western-style medicine and traditional Japanese herbal (Kampo) medicine to manage patients in Japan. One hundred-forty-eight Kampo medicines were permitted into the health insurance system in Japan. Kampo medicine includes multi crude drugs; therefore each Kampo medication has effects on more than one system including the central nervous system, autonomic nervous system, immune system, absorption-metabolism, inflammation, circulation, as well as harmonization of the whole body. Multidisciplinary treatment can achieve the effects of holistic medicine through the integration of Western medicine and Kampo. The investigation showed that one-fourth of Japanese gynecological cancer patients take Kampo medicine [11]. A national survey showed that over 90% of physicians in the cancer treatment hospitals have prescribed Kampo medicine; over 70% of those physicians use Kampo medicine for patients with cancer [12].

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There were some reports in which Kampo medicine was used to control cancer-related symptoms. Daikenchuto (see STORK [13,14]) can improve abdominal pain and ileus that occurs after abdominal surgery. It supports movement and microcirculation of the bowel by promoting the secretion of motilin [15-19], substance P [18-21], calcitonin gene-related peptide [19-21], and adrenomedullin [22-25], as well as by activating the transient receptor potential vanilloid [26,27]. Rikkunshito (see STORK [13,14]) can reduce nausea and vomiting and alleviate the loss of appetite during chemotherapy by antagonizing the 5-HT<sub>3</sub>, 5-HT<sub>2B</sub>, and 5-HT<sub>2C</sub> receptors, resulting in the prevention of the cisplatin-induced decrease in ghrelin levels and the restoration of food intake [28,29]. Taxanes and platinum analogs are used for chemotherapy in gynecological cancer treatment and these agents can cause chemotherapy-induced peripheral neuropathy. Goshajinkigan (see STORK [13,14]) reduces the symptoms of chemotherapy-induced peripheral neuropathy and improves the quality of life during the treatment of cancer. Several mechanisms have been suggested by which goshajinkigan may alleviate peripheral neuropathy; it improves numbness/pallesthesia via the opioid system with the release of dynorphin and it improves the circulation and the blood supply to the nerves by promoting the production of nitric oxide [30,31]. Another report shows that goshajinkigan reduced the transmitter proteins and sensory receptors associated with C-fiber activation [32]; this effect may be a mechanism for the prevention of oxaliplatin-induced neuropathy. The oral administration or topical application of hangeshashinto (see STORK [13,14]) can improve stomatitis, a complication of chemotherapy, by directly inhibiting PGE<sub>2</sub> production [33]. Several reports suggest that some ingredients of hangeshashinto inhibit PGE<sub>2</sub> production and/or COX-2 expression [34,35]. Fatigue and malaise frequently occurs during palliative care stage. Hochuekkito (see STORK [13,14]), juzentaihoto (see STORK [13,14]), and ninjin'yoeito (see STORK [13,14]) supports vitality and harmony between the body and mind. Kampo medicine was used

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for the treatment of cancer-related numbness, constipation, anorexia, muscle cramps, and fatigue [36].

The knowledge of integrative medicine with Western and traditional medicines have been applied for the treatment and prevention of gynecological cancer in Japan. Further cohort or controlled studies will promote its use for disease control and support of the patient's quality of life.

### Conflict of Interest

Shin Takayama, Takehiro Numata, Minoru Ohsawa, and Tadashi Ishii, belong to the Department of Kampo and Integrative medicine, Tohoku University School of Medicine. The department received a grant from Tsumura, a Japanese manufacturer of Kampo medicine; however, the grant was used as per Tohoku University rules. This potential conflict of interests was addressed by the Tohoku University Benefit Reciprocity Committee and was managed appropriately.

### References

1. American Cancer Society (2012) Global cancer facts and figures. American Cancer Society, Atlanta, GA.
2. National Cancer Center, Japan: Center for Cancer Control and Information Services.
3. Liao CK, Rosenblatt KA, Schwartz SM, Weiss NS, et al. (2003) Endometrial cancer in Asian migrants to the United States and their descendants. *Cancer Causes Control* 14: 357-360.
4. Hirose K, Tajima K, Hamajima N, Takezaki T, Inoue M, et al. (1996) Subsite (cervix/uterus)-specific risk and protective factors in uterine cancer. *Jpn J Cancer Res* 87: 1001-1009.
5. Koizumi T, Nakaya N, Okamura C, Sato Y, Shimazu T, et al. (2008) Case-control study of coffee consumption and the risk of endometrial adenocarcinoma. *Eur J Cancer Prev* 17: 358-363.
6. Takayama S, Monma Y, Tsubota-Utsugi M, Nagase S, Tsubono Y, et al. (2013) Food Intake and the Risk of Endometrial Endometrioid in Japanese Women. *Nutr Cancer* 65: 954-960.
7. Komatsu W, Ishihara K, Murata M, Saito H, Shinohara K, et al. (2003) Docosahexaenoic acid suppresses nitric oxide production and inducible nitric oxide synthase expression in interferon-gamma plus lipopolysaccharide-stimulated murine macrophages by inhibiting the oxidative stress. *Free Radic Biol Med* 34: 1006-1016.
8. Holick MF (2007) Vitamin D deficiency. *N Engl J Med* 357: 266-81.
9. Ozawa M, Ninomiya T, Ohara T, Doi Y, Uchida K, et al. (2013) Dietary patterns and risk of dementia in an elderly Japanese population: the Hisayama Study. *Am J Clin Nutr* 97: 1076-1082.
10. Nanri A, Kimura Y, Matsushita Y, Ohta M, Sato M, et al. (2010) Dietary patterns and depressive symptoms among Japanese men and women. *Eur J Clin Nutr* 64: 832-839.
11. Takeda T, Yamaguchi T, and Yaegashi N (2012) Perceptions and attitudes of Japanese gynecologic cancer patients to Kampo (Japanese herbal) medicines. *Int J Clin Oncol* 17: 143-149.
12. Ito A, Munakata K, Imazu Y, Watanabe K (2012) First nationwide attitude survey of Japanese physicians on the use of traditional Japanese medicine (Kampo) in cancer treatment. *Evid Based Complement Alternat Med* 2012: 957082.
13. STORK. <http://kconsort.umin.jp/>, Department of Pharmacognosy, Phytochemistry and Narcotics (DPPN), National Institute of Health Sciences (NIHS) of Japan and National Institute of Biomedical Innovation, Health and Nutrition (NIBIOHN).
14. Motoo Y, Hakamatsuka T, Kawahara N, Arai I, Tsutani K, et al. (2017) Standards of Reporting Kampo Products (STORK) in research articles. *J Intergrat Med* 15: 182-185.
15. Nagano T, Itoh H, Takeyama M (1999) Effect of Dai-kenchu-to on levels of 3 brain-gut peptides (motilin, gastrin and somatostatin) in human plasma. *Biol Pharm Bull* 22: 1131-1133.
16. Satoh Y, Itoh H, Takeyama M (2010) Daikenchuto raises plasma levels of motilin in cancer patients with morphine-induced constipation. *Journal of Traditional Medicines* 27: 115-121.
17. Sato Y, Inoue S, Katagiri F, Itoh H, Takeyama M, et al. (2006) Effects of pirenzepine on Dai-kenchu-to-induced elevation of the plasma neuropeptide levels in humans. *Biol Pharm Bull* 29: 166-171.
18. Kono T, Koseki T, Chiba S, Ebisawa Y, Chisato N, et al. (2008) Colonic vascular conductance increased by Daikenchuto via calcitonin gene-related peptide and receptor-activity modifying protein 1. *JSurg Res* 150: 78-84.
19. Murata P, Kase Y, Ishige A, Sasaki H, Kurosawa S, et al. (2002) The herbal medicine Dai-kenchu-to and one of its active components [6]-shogaol increase intestinal blood flow in rats. *Life Sciences* 70: 2061-2070.
20. Sato Y, Katagiri F, Inoue S, Itoh H, Takeyama M, et al. (2004) Dai-kenchu-to raises levels of calcitonin gene-related peptide and substance P in human plasma. *Biol Pharm Bull* 27: 1875-1877.
21. Suzuki Y, Itoh H, Yamamura R, Tatsuta R, Sato Y, et al. (2012) Significant increase in salivary substance P level after a single oral dose of Japanese herbal medicine Dai-kenchu-to in humans. *Biomedicine & Aging Pathology* 2: 81-84.
22. Kono T, Omiya Y, Hira Y, Kaneko A, Chiba S, et al. (2011) Daikenchuto (TU-100) ameliorates colon microvascular dysfunction via endogenous adrenomedullin in Crohn's disease rat model. *J Gastroenterol* 46: 1187-1196.
23. Kono T, Kaneko A, Omiya Y, Ohbuchi K, Ohno N, et al. (2013) Epithelial transient receptor potential ankyrin 1 (TRPA1)-dependent adrenomedullin upregulates blood flow in rat small intestine. *Am J Physiol Gastrointest Liver Physiol* 304: G428-G436.
24. Kaneko A, Kono T, Miura N, Tsuchiya N, Yamamoto M, et al. (2013) Preventive effect of TU-100 on a type-2 model of colitis in mice: possible involvement of enhancing adrenomedullin in intestinal epithelial cells. *Gastroenterol Res Pract* 2013: 384057.
25. Kono T, Omiya Y, Hira Y, Kaneko A, Chiba S, et al. (2010) Anti-colitis and -adhesion effects of Daikenchuto via endogenous adrenomedullin enhancement in Crohn's disease mouse model. *J CrohnsColitis* 4: 161-170.
26. Kikuchi D, Shibata C, Imoto H, Naitoh T, Miura K, et al. (2013) Intra-gastric Dai-Kenchu-To, a Japanese herbal medicine, stimulates colonic motility via transient receptor potential cation channel subfamily V member 1 in dogs. *Tohoku J Exp Med* 230: 197-204.
27. Tokita Y, Yamamoto M, Satoh K, Nishiyama M, Iizuka S, et al. (2011) Possible involvement of the transient receptor potential vanilloid type 1 channel in postoperative adhesive obstruction and its prevention by a kampo (traditional Japanese) medicine, Daikenchuto. *J Pharmacol Sci* 115: 75-83.
28. Tominaga K, Kido T, Ochi M, Sadakane C, Mase A, et al. (2011) The traditional Japanese medicine rikkunshito promotes gastric emptying via the antagonistic action of the 5-HT(3) receptor pathway in rats. *Evid Based Complement Alternat Med* 2011: 248481.
29. Takeda H, Sadakane C, Hattori T, Katsurada T, Ohkawara T, et al. (2008) Rikkunshito, an herbal medicine, suppresses cisplatin-induced anorexia in rats via 5-HT2 receptor antagonism. *Gastroenterology* 134: 2004-2013.
30. Yamada K, Suzuki E, Nakaki T, Watanabe S, Kanba S, et al. (2005) Aconiti tuber increases plasma nitrite and nitrate levels in humans. *J Ethnopharmacol* 96: 165-169.
31. Gotoh A, Goto K, Sengoku A, Shirakawa T, Akao Y, et al. (2004) Inhibition mechanism of Goshajinki-gan on the micturition reflex in rats. *J Pharmacol* 96: 115-123.
32. Imamura T, Ishizuka O, Aizawa N, Zhong C, Ogawa T, et al. (2008) Goshajinki-gan reduces transmitter proteins and sensory receptors associated with C fiber activation induced by acetic acid in rat urinary bladder. *Neurourol Urodyn* 27: 832-837.
33. Nakazono Y, Ara T, Fujinami Y, Hattori T, Wang PL (2010) Preventive effects of a Kampo medicine, hangeshashinto on inflammatory responses in lipopolysaccharide-treated human gingival fibroblasts. *J Hard Tissue Biol* 19: 43-50.
34. Pan MH, Hsieh MC, Hsu PC, Ho SY, Lai CS, et al. (2008) 6-Shogaol suppressed lipopolysaccharide-induced up-expression of iNOS and COX-2 in murine macrophages. *Mol Nutr Food Res* 52: 1467-1477.

35. Feng AW, Yu C, Mao Q, Li N, Li QR, et al. (2011) Berberine hydrochloride attenuates cyclooxygenase-2 expression in rat small intestinal mucosa during acute endotoxemia. *Fitoterapia* 82: 976-982.
36. Iwase S, Yamaguchi T, Miyaji T, Terawaki S, Inui A, et al. (2012) The clinical use of Kampo medicines (traditional Japanese herbal treatments) for controlling cancer patients' symptoms in Japan: a national cross-sectional survey. *BMC Complement Altern Med* 20: 222.