

SOY, ISOFLAVONE, AND BREAST CANCER RISK IN JAPAN

The results from the JPHC Study

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We will introduce here some of the results from the JPHC Study recently published in the *Journal of the National Cancer Institute* (Yamamoto S, et al. 2003;95-906-13), which is concerned with female breast cancer

Background

Breast cancer incidence is higher in western countries than in Asian countries. In addition, migrant populations from Asia to the United States are known to have increased incidence of breast cancer. As for Japan, breast cancer mortality is higher in the metropolitan areas, but shows steadily increasing trends for all the prefectures. This evidence suggests that the difference in life style between the western countries and Asia, in particular, the difference in eating habits, may be associated with the difference in incidence of breast cancer. Among the food items, attention has been paid to soybean products since they are widely consumed in Asia but rarely consumed in western countries (at least, until quite recently). One report gives a 700-fold difference in consumption

between Japan and the United States. In addition, isoflavones, plant estrogens found mainly in soybean products, have been shown to have anticarcinogenic effects on hormone-related cancers in experimental studies, perhaps because of the similarity of the isoflavone structure to that of estrogens. Other possible mechanisms for anticarcinogenic effects are also suggested by experimental studies. Contrary to them, epidemiological studies did not provide consistent evidence for an association between isoflavone intake and breast cancer incidence.

JPHC Study

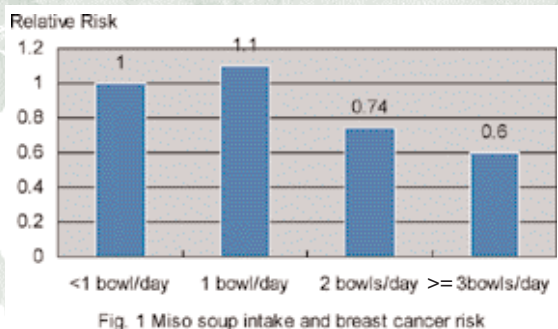
The JPHC Study (Japan Public Health Center-based prospective study on Cancer and Cardiovascular Diseases) is a multipurpose epidemiological study to investigate the

risk and consumption of soybean products. This study drew attention since it is the first prospective study to show the inverse association between breast cancer incidence and soyfood/isoflavone intake.

association between various life styles and diseases such as cancer, stroke, myocardial infarction, and other life-style related diseases (Supported by a grant from the Ministry of Health, Labour, and Welfare of Japan, Principle Investigator: Dr. Seiichiro Tsugane, National Cancer Center Japan). Study subjects for the JPHC Study include more than 140,000 men and women from all over Japan. The results presented here are for the subsample which includes 21,858 40-59-year-old women who lived in Iwate, Akita, Nagano and Okinawa prefectures. We investigated the association between individual food intake, as measured by the baseline questionnaire in 1990, and breast cancer incidence for the subsequent 10 years of follow-up, during which 179 cases of breast cancer were diagnosed. The questionnaire includes two items for soybean products, "miso-soup" and "soy, tofu, fried-tofu, and natto" where miso is a fermented soybean paste, tofu is a soybean curd, and natto is a fermented soybean. Isoflavone intake was calculated using these two items, which covers 90% of total soybean intake.

Main results

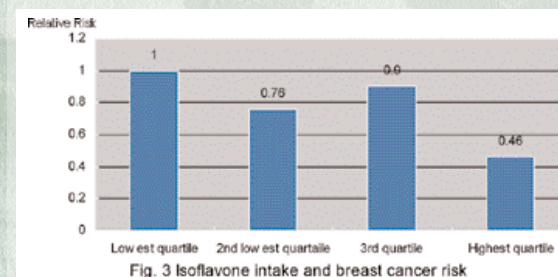
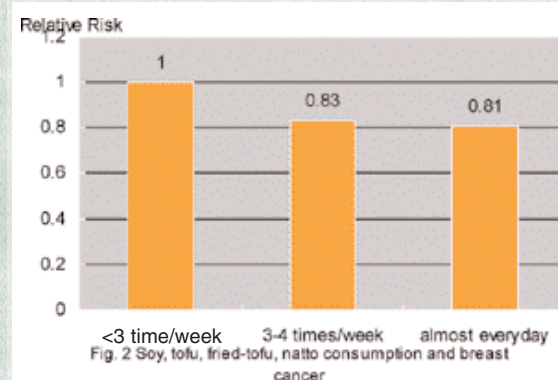
The results for miso-soup intake and breast cancer incidence are shown in Fig. 1. The vertical axis shows relative risk for breast cancer, that is, the ratio of risk compared to that for the lowest consumption subgroup. The breast cancer risk, for those who drink more than three bowls per day of miso-soup decreased by 60%



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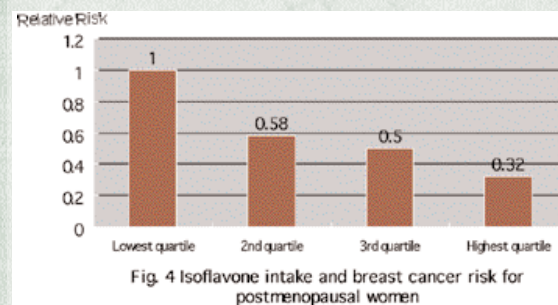
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relative to those who drink less than one bowl per day. Miso soup consumption and breast cancer risk shows a clear inverse association, while consumption of soy, tofu, fried-tofu, and natto and breast cancer risk does not (Fig. 2). The breast cancer risk by isoflavone consumption is shown in Fig. 3. Isoflavone consumption is divided into four categories according to the value calcu-

lated from the above two items. High consumers have lower risk of breast cancer than do low consumers. These results are adjusted for other factors related to breast cancer risk such as reproductive history, family history of breast cancer, other dietary factors and hormonal drug use. Further analysis was conducted by menopausal status using information from the questionnaire. A



more clear inverse association between isoflavone consumption and breast cancer risk was observed for women who had experienced menopause (Fig. 4). This association was also observed for soy, tofu, fried-tofu, and natto consumption and breast cancer risk. This observation may explain the larger difference in breast cancer incidence, between Asia and western countries, for postmenopausal women than for premenopausal women.

Discussion

So far, 13 epidemiological studies have been conducted for Asian populations and western populations to evaluate the association between soy or isoflavone consumption and breast cancer risk. Among them, 4 prospective cohort studies did not show an inverse association and 9 retrospective case-control studies showed inconsistent results. Our study is the first one to show an inverse association in a prospective study. One advantage of our study is a large variation of soybean consumption among the subjects. Among the subjects, some maintain the Japanese traditional eating habits in which a lot of soyfoods are consumed and others have changed their habits completely to the westernized style where soyfoods are rarely consumed. In addition, breast cancer incidence is steadily increasing in Japan. This study may have given us a unique chance to detect the association between isoflavone consumption and breast cancer risk. On the other hand, our study has several limitations. We could only evaluate two soyfood categories ("miso-soup" and "soy, tofu, fried-tofu, and natto"). The effect of isoflavone may vary among the types of soyfoods since the difference in cooking methods and the form of isoflavones (β -glucoside conjugates vs. aglucones) may lead to differences in bioavailability. Furthermore, there remains the possibility that other Japanese traditional eating habits may play a role in preventing breast cancer, although we controlled for as many potential confounding factors as possible. To investigate the direct relationship between isoflavone consumption and breast cancer risk, it will be very useful to examine biomarkers such as serum isoflavone. We plan to conduct further analyses for the JPHC Study, using more extensive questionnaires, additional biomarkers, and additional cases, in the near future.

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