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Soy and isoflavone intake associated with reduced risk of ovarian cancer in southern Chinese women

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ABSTRACT

Isoflavones, mainly found in soy, have been shown to inhibit ovarian cancer cell proliferation. We hypothesized that soy consumption and isoflavone intake are related to the risk of ovarian cancer. A case–control study was conducted in southern China to ascertain this hypothesis. Five hundred incident patients with histologically confirmed cancer of the ovary and 500 controls (mean age 59 years) were recruited from four public hospitals in Guangzhou. Information on habitual consumption of soy foods, including soybean, soy milk, fresh tofu, dried tofu, and soybean sprout, was obtained face-to-face from participants through a validated and reliable semi-quantitative food frequency questionnaire. Isoflavone intakes were then estimated using the USDA nutrient database. The ovarian cancer patients reported lower consumption levels of individual and total soy foods (75.3 ± 53.6 g/day) compared to the controls (110.7 ± 88.8 g/day). Logistic regression analyses showed that regular intake of soy foods could reduce the ovarian cancer risk, the adjusted odds ratio being 0.29 (95% confidence interval 0.20 to 0.42) for women who consumed at least 120 g/day relative to those less than 61 g/day. Similarly, isoflavone intakes were inversely associated with the ovarian cancer risk, with significant dose–response relationships ($P < 0.001$). We concluded that consumption of soy foods is associated with a reduced risk of ovarian cancer in southern Chinese women.

1. Introduction

Ovarian cancer has the eighth highest incidence of all cancers in women [1], and is the second most common gynecological malignancy [2]. The 5-year prevalence rate for ovarian cancer has exceeded half a million cases worldwide [1]. Considerable geographic variations exist in the incidence of ovarian cancer, with higher rates reported in developed countries. The age-standardized rates in Europe and the United States are 10.1 and 8.8 per 100,000 women, respectively, but only 3.8 per 100,000 women in China [1]. The difference in incidence rates between countries has generated interest in the role of dietary and lifestyle factors in ovarian cancer etiology, apart from genetic and familial risk factors, which may lead to health promotion strategies for the primary prevention of the disease.

Soy food products are widely consumed in Asian countries, and soy is a primary source of isoflavones. Previous research has suggested soy consumption may prevent the development of ovarian cancer. A meta-analysis demonstrated the protective effect of soy, with odds ratio (OR) 0.52 (95% confidence interval (CI) 0.42 to 0.66) for the highest versus

Abbreviations: CI, confidence interval; MET, metabolic equivalent task; OR, odds ratio.

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the lowest level of intake [3]. Similarly, an Italian multicenter case–control study reported a 41% risk reduction for women with the highest intake of specific seed oils, such as soya [4]. For isoflavones, a large prospective cohort study in the USA observed a relative risk of 0.56 for daily intake of total isoflavones above 3 mg, when compared to below 1 mg per day [5]. Another case–control study undertaken in Hangzhou, China, found significant inverse associations between the ovarian cancer risk and intake of soy foods and specific isoflavones [6]. However, two population-based cohort studies conducted in the USA and Sweden found little association between the intake of phytoestrogens or phytoestrogen/flavonoid-rich foods and the ovarian cancer incidence [7,8], which could be attributed to the low consumption of soy products among adults in these countries. Given that soy food products are widely consumed in China and the biologically plausible cancer protective mechanisms of isoflavones, we hypothesized that soy and isoflavone intake is associated with a reduced risk of ovarian cancer in southern Chinese women.

Several types of soy foods are popular in southern China, including soybean, soy milk (produced by soaking and grinding dried soybeans) and tofu (fermented product of soy milk). In view of the conflicting epidemiological evidence, the present study aimed to assess the association between habitual soy food consumption, isoflavone intake and the risk of ovarian cancer among southern Chinese women.

2. Methods and materials

2.1. *Study design and participants*

A hospital-based 1:1 case–control study was conducted in Guangzhou, the capital city of Guangdong Province of southern China, between August 2006 and July 2008. Subjects were recruited from four public hospitals, namely, The Overseas Hospital (affiliated with Jinan University), Zhujiang Hospital, General Hospital of Guangzhou Military Command, and Second Affiliated Hospital of Zhongshan University. Cases were incident patients who had been histopathologically diagnosed with cancer of the ovary within the past 12 months and resided in the metropolitan Guangzhou area for at least the past ten years.

Potential cases were identified by searching the daily census of the hospitals. To ensure complete ascertainment of cases, all hospital medical records and laboratory pathology reports were reviewed during the recruitment period. Pathological diagnoses were based on the International Histological Classification of Ovarian Tumors [9]. Patients were excluded when ovarian cancer was histopathologically confirmed to be neither the primary nor final diagnosis, over 75 years of age, or if they confessed to have memory problems affecting their recall of past events. Of the total 504 cases consecutively recruited from the four hospitals, 500 patients with cancer of the ovary consented to participate and were capable of being interviewed.

During the same period, 512 eligible controls were recruited from inpatient wards of the Departments of ophthalmology, orthopedic, respiratory disease, gastroenterology and physiotherapy. These women were group matched to cases within 5 years of age. Exclusion criteria for controls were (i) previous diagnosis of ovarian cancer or other malignant diseases; (ii) a history of bilateral oophorectomy; (iii) having memory problems; (iv) on long-term modification of diet for medical reasons; in addition to non-Guangzhou resident and age over 75 years. Subjects to be approached for inclusion as controls were initially screened using the hospital daily census sheets. A selection of ward and patient ID was made using random numbers each day whenever more control subjects appeared to be available than could be interviewed. All eligible inpatients had their diagnosis subsequently confirmed by histopathological reports to avoid misclassification of the case–control status. This systematic selection process was adopted throughout the recruitment period. Twelve women who declined the interview or did not satisfy the eligibility conditions were later excluded, resulting in a final sample of 500 controls available for analysis. No statistically significant differences were found between the two groups in terms of age and main demographic variables.

2.2. *Interview*

An appointment for a face-to-face interview was then arranged with each participant in conjunction with the nursing staff to avoid interference with treatment at the ward and before being discharged from hospital. Whenever possible, subjects were interviewed in the presence of their next-of-kin to help the recall of dietary habits. All participants gave formal consent before the interview. They were also assured of confidentiality and their right to withdraw without prejudice. Each interview, conducted in either Mandarin or the Cantonese dialect, took about 45 minutes to complete. All participants were blinded to the study hypothesis. The project protocol was approved by the participating hospitals, the doctors-in-charge of the relevant wards, and the Human Research Ethics Committee of Curtin University (approval number HR 78/2006).

2.3. *Questionnaire and exposure measurements*

A structured questionnaire was administered to obtain demographic and lifestyle characteristics including age, weight (kg), height (m), education level, smoking status and alcohol consumption, as well as reproductive history, hormonal status and heredity. Self-reported data were cross-checked with medical records whenever available.

Participants were also requested to estimate their average time engaged in physical activities using validated questions [10]. Intensity was classified by the amount of energy or effort a person expends in performing the activity. Physical activity at each intensity level was quantified in terms of metabolic equivalent tasks (MET)-hours per week, with intensity codes 7.5, 6.0 and 4.5 MET assigned to strenuous sports, vigorous work and moderate activity, respectively. Total physical activity was then calculated by summing the product of MET score and activity duration over the three intensity levels.

Information on habitual food and beverage consumption was obtained using a 125-item semi-quantitative food frequency questionnaire developed and tested for the southern