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Original article

Dietary patterns and the risk of esophageal squamous cell carcinoma: A population-based case–control study in a rural population

Xudong Liu^a, Xiaorong Wang^{a,b,*}, Sihao Lin^{a,b}, Xiangqian Lao^a, Jin Zhao^c, Qingkun Song^d, Xuefen Su^a, Ignatius Tak-Sun Yu^{a,b}

^a JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China

^b Hong Kong Occupational and Environmental Health Academy, Hong Kong, China

^c Shenzhen Center for Disease Control and Prevention, Shenzhen, China

^d Beijing Key Laboratory of Cancer Therapeutic Vaccine, Capital Medical University Cancer Center, Beijing Shijitan Hospital, Beijing, China

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SUMMARY

Background & aims: Few studies were available in exploring the roles of dietary patterns in the development of esophageal cancer, especially in China. This study aimed to investigate the roles of dietary patterns in the risk of esophageal squamous cell carcinoma (ESCC) in a Chinese rural population.

Methods: A population-based cases–control study was designed and conducted in Yanting County, Sichuan Province of China during two years (between June 2011 and May 2013). A total of 942 pairs of ESCC cases and controls were recruited. A food frequency questionnaire was adopted to collect information of dietary consumption. Dietary patterns were extracted by using principle component and factor analysis based on 24 dietary groups. Odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated by using logistic regression model, with adjustment for possible confounding variables.

Results: Four major dietary patterns were identified, which were labeled as “prudent”, “vegetable and fruits”, “processed food” and “alcohol drinking”. In comparison of the highest with the lowest quartiles of pattern scores, the processed food pattern (OR: 2.84, 95% CI: 2.13–3.80) and alcohol drinking pattern (OR: 2.69, 95% CI: 1.95–3.71) were significantly associated with an increased risk of ESCC, while the vegetable and fruit pattern (OR: 0.70, 95% CI: 0.53–0.92) was associated with reduced risk by 30%. The prudent pattern was associated with a reduced risk by 33% (OR: 0.67, 95% CI: 0.50–0.88) in a multivariate logistic regression model, but no statistical significance was reached in a composite model.

Conclusions: The results suggest an important role of dietary patterns in ESCC. Diets rich in vegetables and fruits may decrease the risk of ESCC, whereas diets rich in processed food and drinking alcohol may increase the risk.

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1. Introduction

Esophageal cancer (EC) is the one of the most common cancers and the most common causes of cancer death worldwide [1]. The overwhelming majority of EC cases and deaths occurred in the developing countries, including China [1]. There were 288,000 cases diagnosed annually in China [2], contributing to about 50% of

the world's total EC cases [1]. In China, EC was the third most common cancer in rural areas and the sixth in urban areas [3]. It was estimated that more than 90% of diagnosed EC cases in the country were esophageal squamous cell carcinoma (ESCC) [3].

Existing evidence has suggested some dietary components have pivotal roles in carcinogenic process of EC [4,5]. In practice, different foods and nutrients are often mixed together and consumed foods contain literally thousands of nutrients and chemicals. These foods and nutrients likely have interactive effects. Studies on individual nutrients or foods hardly assess synergistic or inhibitory effects. Therefore, observed associations between individual nutrient/food and health outcomes may be attenuated [6]. Dietary pattern, as a holistic and comprehensive approach, may better capture the effects of diets. Dietary patterns can more accurately assess actual dietary exposure, better control dietary

* Corresponding author. JC School of Public Health and Primary Care, The Chinese University of Hong Kong, 4/F School of Public Health, Prince of Wales Hospital, Shatin, N.T., Hong Kong, China. Tel.: +852 22528756; fax: +852 2606 3500.

E-mail addresses: liuxudong@cuhk.edu.hk (X. Liu), xrwang2000@yahoo.com (X. Wang), shlin@aliyun.com (S. Lin), xqlao@cuhk.edu.hk (X. Lao), szhaojin@gmail.com (J. Zhao), songqingkun@aliyun.com (Q. Song), xuefensu@cuhk.edu.hk (X. Su), iyu@hoeha.org.hk (I. Tak-Sun Yu).

confounders, deal with problems of conflicting results, and identify nutrients or foods that may have a relatively small effect. A recent literature review provided some suggestive evidence on the association between dietary patterns and ESCC risk [7]. Furthermore, dietary pattern might be a better method for appropriate intervention [8].

However, no study was available on the association between dietary pattern and ESCC risk in China, where there were high incidence and mortality rates of ESCC. Therefore, we designed and conducted the current study in Yanting County located in Sichuan Province, which is one of the areas with the highest incidence and mortality of ESCC in China [2]. The incidence of ESCC in Yanting was 100.11/100,000 for males and 57.10/100,000 for females according to 2009 data [3], much higher than the rates of Sichuan Province (10.38/100,000 for combined genders) [9], and rates of the country (24.42/100,000 for males, 9.60/100,000 for females) [2], and rural area as a whole (32.96/100,000 for males, 14.21/100,000 for females) [2]. Most of people in Yanting were farmers with low socio-economic status. The people had a special preference for cereals and tuber-crops, pickled and preserved vegetables, and salted meat [10–15]. Although there have been a great change in eating habits and lifestyle in Chinese population in recent decades, such changes have been relatively small and slow in Yanting area because of historically low economic status and geographically remote [16]. Some lab studies indicated that that Yanting diets could induce esophageal cancer in human cell lines [17,18]. Epidemiological studies conducted in Yanting also suggested possible roles of several individual foods or dietary habits in the development of ESCC [11–15]. The objective of the current study was to explore the associations of dietary patterns with the risk of ESCC.

2. Subjects and methods

The case–control study was carried out during two years, from June 2011 to May 2013. A detailed recruitment of cases and controls was described elsewhere [13]. Briefly, ESCC cases were selected from Yanting Tumor Hospital, a main institution to diagnose and treat ESCC in the area [14]. Inclusion criteria for cases were: 1) men or women who were aged 40–70 years, 2) newly diagnosed primary incident ESCC confirmed pathologically (ICD-10, code-C15), and 3) having lived in the Yanting area for at least 15 years. Those who had lived outside of Yanting area for six months or longer in the last 15 years were excluded. Among eligible ESCC cases, there were 942 (96%) cases who accepted an interview, accounting for more than 70% of incident cases during the period of the study. By comparing the recruited cases with non-recruited eligible cases, we did not find significant differences in age and gender.

The controls were selected by using a multi-stage sampling method from local residents. Inclusion criteria were: 1) no history of neoplasm at any site; 2) no digestive tract disease; and 3) having lived in the Yanting area for not less than 15 years. Those who had lived outside of the Yanting area for six months or longer in the past 15 years were also excluded. The procedures of sampling were described in detail in previous report [13]. In the end, 942 matched cases and controls (672 males and 270 females) were included in the study, with median age of 60 years. All participating subjects provided written consent following the Declaration of Helsinki. The study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee.

2.1. Data collection

Questionnaires were administered with a face-to-face interview. Interviewers and study subjects were all unaware of the

hypothesis and objectives of the study. Cases were interviewed at the hospital within a week once diagnosed with ESCC, and controls were interviewed at local health clinics. All questionnaires were checked once more each day after information was collected and any unclear responses were clarified by a contact with related subjects to reduce invalid information/data.

A structured questionnaire was used to collect information, including individual demographics (age, gender, education, marital status, occupation, monthly household income and history of residence), family cancer history, tobacco smoking and alcohol drinking history, and self-reported height and weight five years before ESCC diagnosed for the cases and prior to the interviews for the controls. An ever drinker was defined as consuming any alcoholic beverage, which included beer, wine or distilled spirits containing at least 20 g of ethanol, per week for minimum 6 months [19], while a never as one who had never been a regular or social drinker. An ever smoker was defined as smoking at least 10 cigarettes or equal amount of tobacco per week for minimal six months [19], while never smoker as individuals who had never smoked as many as one cigarette a day or equivalent for the duration of one year. The group of ever users could be further categorized into current users and former users. Current users were defined as one who had any of these habits within one year before the interview, while former users as had stopped any of these habits for at least one year before diagnoses or interviews. Body mass index (BMI) was obtained according to the formula: $\text{weight (kg)}/[\text{height (m)}]^2$.

A food frequency questionnaire (FFQ) with 76 items, which was proved to have moderate validity and reproducibility [20], was used to investigate usual dietary intake during the past five years before ESCC diagnosis for the cases or before the interviews for the controls. Three basic questions were asked to collect information on the consumption of each of the items. First, “Did you have ever consumed one certain dietary item” was asked. If the answer was “yes”, “how often the consumption was and how much consumed each time” were further asked. Average daily intake of each food or drink was estimated according to the formula: $\text{Average daily intake} = \text{Frequency of intake per day} \times \text{Amount of intake each time}$. The detailed calculation of average daily intake was described in previous reports [13,20].

2.2. Statistical analysis

t-Test or chi-square test was used to describe the difference of demographic variables and other factors between the case and controls. The association between possible risk factors and ESCC risk was examined by using logistic regression model (forward stepwise), expressed as odds ratios (OR) with 95% Confidence interval (95% CI). The individual and joint effects of smoking and alcohol drinking were deeply analyzed and the synergy index [21] was adopted to display the interaction of alcohol drinking and tobacco smoking on ESCC risk. However, in this study there were only 11 former drinkers and 14 former smokers in the cases and 0 former drinkers and 0 former smokers in the controls. Hence, it is not meaningful to divided ever smokers or drinkers into current and former subgroups.

The 76 dietary items were further grouped into 24 dietary groups, according to local eating habits, dietary guideline and balance diet pagoda for Chinese population [22] and whether or not the food was processed, so to derive dietary patterns. The 24 groups were used in all dietary assessment methods after similarities were tested, which ensured the consistency of groups entering into the factor analysis. The original absolute food intake was standardized before factor analysis was performed to avoid problems arisen from different measurement units and different intake amount.

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