

## RESEARCH ARTICLE

# Association between Dietary Behavior and Esophageal Squamous Cell Carcinoma in Yanting

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### Abstract

**Background:** Yanting is one of high risk areas for esophageal cancer and the screening program was therefore initiated there. This study was aimed to investigate the dietary behaviors on the risk of esophageal squamous cell carcinoma (ESCC), among the individuals with normal and abnormal esophagus mucosa. **Materials and Methods:** A frequency matched case-controls study was proposed to estimate the different distribution of dietary behavior between individuals of control, esophagitis and cancer groups. Cancer cases were selected from hospitals. Esophagitis cases and controls were selected from screening population for ESCC. Health workers collected data for 1 year prior to interview, in terms of length of finishing a meal, temperature of eaten food and interval between water boiling and drinking. Chi-square, Kruskal-Wallis tests and unconditional logistic regression model were used to estimate differences and associations between groups. **Results:** Compared with controls, length of finishing a meal  $\geq 15$ mins was related to a reduced OR for cancer (OR=0.46, 95% CI, 0.22-0.97) and even compared with cases of esophagitis, the OR of cancer was reduced to 0.30 (95% CI, 0.13-0.72). The OR for often eating food at a high temperature was 2.48 (95% CI 1.06, 5.82) for ESCC as compared with controls. Interval between water boiling and drinking of  $\geq 10$ mins was associated with lower risk of cancer: the OR was 0.18 compared with controls and 0.49 with esophagitis cases ( $p < 0.05$ ). **Conclusions:** Length of eating food  $\geq 15$ mins and interval between water boiling and drinking  $\geq 10$ mins are potentially related to reduced risk of esophageal SCC, compared with individuals with normal and abnormal esophageal mucosa. Recommendations to Yanting residents to change their dietary behaviors should be made in order to reduce cancer risk.

**Keywords:** Esophageal SCC - dietary behavior - risk reduction - Yanting, China

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### Introduction

Esophageal cancer is the eighth most common cancer worldwide, with 481 000 new cases and 406 000 deaths in 2008 (Ferlay et al., 2010). More than 50% of the cases and of the deaths occurred in China (Ferlay et al., 2010). Esophageal cancer encompasses both adenocarcinoma and squamous cell carcinoma (ESCC) types, the latter is the predominant type in China (Lambert and Hainaut, 2007). The national average incidence was 14.3/105, accounting for 16% cancer deaths in 2009 (He, Zhao and Chen, 2011).

Yanting is one of high risk areas for ESCC in China (He et al., 2011; Song et al., 2012), the incidence nearly 5-fold higher than national figures. In 2006, China government initiated ESCC screening in Yanting, by the detecting method of endoscope with iodine staining (Dong and Peng, 2011). Individuals with pre-cancer lesions (i.e. severe dysplasia, carcinoma in-situ, mucosal carcinoma) were assigned early therapies (Dong and Peng, 2011).

Some dietary behaviors, such as fast eating and hot drinking, were suspected to be related with high risk of ESCC (Sewram et al., 2003; Yang et al., 2005). Previously, we presented the adverse effects of preserved vegetable consumption on ESCC and esophagitis (Song et al., 2013), but no dietary behaviors were investigated. This study aimed to investigate the contributions from these behaviors to the occurrences of ESCC and esophagitis detected by screening program in the high risk area.

### Materials and Methods

This was a frequency-matched study. Individuals of control and esophagitis were matched with ESCC cases by 5-year age and sex. All of subjects were collected between April 2011 and October 2011.

Individuals all aged from 40 to 69. Patients of ESCC were from Yanting Cancer Hospital. The included cases were Yanting local people and aged between 40 and 69,

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with pathological diagnosis of primary ESCC. The interval between diagnosis and interview was less than 3 months. Individuals of control and esophagitis came from the people participating into the screening program of EC, without any cancer history. In 2006, China government implemented the screening program in Yanting. Local people aging 40 to 69 years could join in the program and received the exam of endoscopy with iodine staining to detect the pre-cancer lesions (Dong and Peng, 2011). "Controls" were the people diagnosed as normal status by endoscope; "esophagitis" was the individuals with abnormal status by endoscopy with iodine staining rather than carcinoma by biopsy (Dong and Peng, 2011).

Body mass index (BMI) was estimated by dividing weight in kilograms by current height in meters squared. Ever smoking was the smoking with more than 100 cigarettes or equivalent use of pipes in the lifetime (Pandeya et al., 2008). Ever alcohol drinkers were the individuals alcohol drinking at least once per month (Pandeya et al., 2009). Family EC history was EC occurrence among the first-degree genetic relatives (i.e. parents, siblings, offsprings). No fruit intake meant the intake frequency was less than once per month. Regular meal was the habit of taking meal regularly every day.

The workshop of data collection provided training to health workers at Yanting Cancer Hospital. Interviewers obtained written consent first and then interviewed individuals about the socio-economic, dietary and other lifestyle data 1-year ago by Modified Food frequency questionnaires.

SAS 9.0 was used to analyze the data. The difference of distributions of education level, smoking status, alcohol drinking status, family cancer history of EC and fruit intake was estimated by Chi-square test between the 3 groups. BMI difference was estimated by Kuskal-Wallis test. The frequencies of "Eating food at high temperature" and "Frequency of eating spicy food" were tested under Kuskal-Wallis test between the 3 groups and the other behaviors were analyzed by Chi-square test. The significant behaviors were further estimated odds ratio (OR) and 95% confidence interval in unconditional logistic regression, with adjustments of age, smoking, alcohol drinking, family history of EC, fruit intake, education level and BMI. Control and esophagitis individuals were both set as reference group in the analysis. All the tests were 2-tailed with the significant level of 0.05.

## Results

Among the 216 frequency-matched individuals by age and sex, education level, BMI, smoking and alcohol drinking status all distributed similarly ( $p>0.05$ ) (Table 1). Family history of EC had a positive trend with esophagus disease ( $p<0.05$ ) that ESCC cases had the highest occurrences, but fruit intake had a negative trend ( $p<0.05$ ) (Table 1).

The behaviors of taking regular meal, frequency of eating spicy food and temperature of drinking tea were statistically similar between individuals of controls, esophagitis and ESCC cases ( $p>0.05$ ) (Table 2). Length of finishing one meal was negatively related with esophageal

**Table 1. Characteristics between Individuals of Control, Esophagitis and ESCC\***

|                                     | Control<br>n (%) | Esophagitis<br>n (%) | ESCC<br>n (%) | p      |
|-------------------------------------|------------------|----------------------|---------------|--------|
| Age                                 |                  |                      |               |        |
| 45~                                 | 7 (9.7)          | 7 (9.7)              | 7 (9.7)       | -      |
| 50~                                 | 8 (11.1)         | 8 (11.1)             | 8 (11.1)      |        |
| 55~                                 | 19 (26.4)        | 19 (26.4)            | 19 (26.4)     |        |
| 60~                                 | 26 (36.1)        | 26 (36.1)            | 26 (36.1)     |        |
| 65~                                 | 12 (16.7)        | 12 (16.7)            | 12 (16.7)     |        |
| Sex                                 |                  |                      |               |        |
| Male                                | 51 (70.8)        | 51 (70.8)            | 51 (70.8)     |        |
| Female                              | 21 (29.2)        | 21 (29.2)            | 21 (29.2)     |        |
| Education level                     |                  |                      |               |        |
| ≤primary school                     | 50 (69.4)        | 48 (70.6)            | 51 (71.8)     | 0.9521 |
| >primary school                     | 22 (30.6)        | 20 (29.4)            | 20 (28.2)     |        |
| BMI*                                | 22.9±3.4         | 22.4±3.0             | 22.9±3.2      | 0.3514 |
| Smoking                             |                  |                      |               |        |
| Never                               | 32 (44.4)        | 36 (50.0)            | 27 (37.5)     | 0.3178 |
| Ever                                | 40 (55.6)        | 36 (50.0)            | 45 (62.5)     |        |
| Alcohol drinking                    |                  |                      |               |        |
| Never                               | 33 (45.8)        | 39 (54.2)            | 31 (43.1)     | 0.381  |
| Ever                                | 39 (54.2)        | 33 (45.8)            | 41 (56.9)     |        |
| Family history of esophageal cancer |                  |                      |               |        |
| No                                  | 63 (88.7)        | 59 (85.5)            | 45 (62.5)     |        |
| Yes                                 | 8 (11.3)         | 10 (14.5)            | 27 (37.5)     | 0.0002 |
| Fruit intake                        |                  |                      |               |        |
| No                                  | 27 (38.0)        | 31 (43.7)            | 47 (65.3)     | 0.0027 |
| Yes                                 | 44 (62.0)        | 40 (56.3)            | 25 (34.7)     |        |

\*(mean±SD, kg/m<sup>2</sup>) Kuskal-Wallis test

**Table 2. Distribution of Dietary Behaviors in Subjects**

|  | Control<br>n (%) | Esophagitis<br>n (%) | ESCC<br>n (%) | p      |
|--|------------------|----------------------|---------------|--------|
| Regular meal                           |                  |                      |               | 0.0623 |
| No                                     | 34 (47.2)        | 41 (56.9)            | 48 (66.7)     |        |
| Yes                                    | 38 (52.8)        | 31 (43.1)            | 24 (33.3)     |        |
| Length of finishing one meal           |                  |                      |               | 0.0168 |
| <15mins                                | 28 (38.9)        | 25 (34.7)            | 41 (56.9)     |        |
| ≥15mins                                | 44 (61.1)        | 47 (65.3)            | 31 (43.1)     |        |
| Eating food at high temperature        |                  |                      |               | 0.0306 |
| Never                                  | 44 (61.1)        | 36 (50.0)            | 29 (40.3)     |        |
| Sometimes                              | 11 (15.3)        | 15 (20.8)            | 13 (18.1)     |        |
| Often                                  | 17 (23.6)        | 21 (29.2)            | 30 (41.7)     |        |
| Frequency of eating spicy food*        |                  |                      |               | 0.2317 |
| Never                                  | 29 (40.3)        | 23 (31.9)            | 19 (26.4)     |        |
| Sometimes                              | 8 (11.1)         | 11 (15.3)            | 9 (12.5)      |        |
| Often                                  | 35 (48.6)        | 38 (52.8)            | 44 (61.1)     |        |
| Temperature of drinking tea*           |                  |                      |               | 0.1196 |
| Warm                                   | 40 (83.3)        | 36 (81.8)            | 28 (66.7)     |        |
| Hot                                    | 8 (16.7)         | 8 (18.2)             | 14 (33.3)     |        |
| Interval of water boiling and drinking |                  |                      |               | 0.0072 |
| <10mins                                | 13 (20.3)        | 21 (31.3)            | 30 (46.2)     |        |
| ≥10mins                                | 51 (79.7)        | 46 (68.7)            | 35 (53.8)     |        |

\* Kruskal-Wallis test

diseases, control individuals having the highest proportion of the length ≥15mins, followed by esophagitis and then ESCC cases (Table 2). Compared with controls, ORs of ≥15mins were 1.23 and 0.46 for esophagitis ( $p>0.05$ ) and ESCC ( $p<0.05$ ), respectively (Table 3). Frequency of eating food at high temperature had a positive trend with esophagus diseases that percentage of "often" was 23.6%, 29.2% and 41.7% in control, esophagitis and ESCC cases (Table 2), and compared with controls, often eating food at high temperature increased the ORs to 1.25 for esophagitis

**Table 3. Odds Ratio and 95% Confidence Interval of Dietary Behaviors with Esophagus Diseases\***

|   | Esophagitis vs control |           | ESCC vs control |            | ESCC vs Esophagitis |            |
|---|------------------------|-----------|-----------------|------------|---------------------|------------|
|   | OR                     | 95%CI     | OR              | 95%CI      | OR                  | 95%CI      |
| Length of finishing a meal                  |                        |           |                 |            |                     |            |
| <15mins                                     | 1                      |           | 1               |            |                     |            |
| ≥15mins                                     | 1.23                   | 0.56-2.68 | 0.46            | 0.22-0.97  | 0.3                 | 0.13- 0.72 |
| Eating food at high temperature             |                        |           |                 |            |                     |            |
| Never                                       | 1                      |           | 1               |            |                     |            |
| Sometimes                                   | 1.3                    | 0.48-3.58 | 1.82            | 0.64-5.14  | 1.33                | 0.47- 3.76 |
| Often                                       | 1.25                   | 0.53-2.96 | 2.48            | 1.06- 5.82 | 2.2                 | 0.87-5.53  |
| Interval between water boiling and drinking |                        |           |                 |            |                     |            |
| <10mins                                     | 1                      |           | 1               |            |                     |            |
| ≥10mins                                     | 0.42                   | 0.17-1.05 | 0.18            | 0.07-0.49  | 0.49                | 0.21-1.18  |

\*adjusting age, smoking, alcohol drinking, education level, BMI, family EC history and fruit consumption

( $p>0.05$ ) and 2.48 for ESCC ( $p<0.05$ ) (Table 3). Trend of interval of water boiling and drinking was significant and negative from control to ESCC cases and proportion of  $\geq 10$ mins interval was 79.7%, 68.7% and 53.8% in control, esophagitis and ESCC individuals ( $p<0.05$ ) (Table 2). In contrast to controls, ORs of  $\geq 10$ mins interval of water boiling and drinking were 0.42 (95%CI 0.17, 1.05) for esophagitis and 0.18 (95%CI 0.07, 0.49) (Table 3)

## Discussion

This was a frequency-matched “case-control study”, which included 3 groups of individuals and presented the significant contributions from behaviors to high risk of esophagus diseases.

Fast eating speed was reported to increase ESCC from many studies. In Southern China, quick speed of eating was reported to be associated with a 5-fold high ESCC risk (Lin et al., 2011). Huai’an was another high risk area of esophageal cancer in China and a population-based case-control study presented a 3.34-fold risk for ESCC from fast eating (Wang et al., 2006). Yang et al. reported the OR of rapid eating speed was increased to 5.84 for ESCC (Yang et al., 2005). In Jiangsu Province, China, the significant association between eating speed and ESCC was observed in both high and low risk areas, and OR ranged from 3 to 4-fold high (Wu et al., 2006). Fast eating was possible to increase ESCC risk across China, because it was potential to cause physical injury to esophagus and lead to inflammatory reaction, which might result in cancer development. In our study, we showed that comparing with controls, the consuming length  $\geq 15$ mins was related with ESCC risk reduced to 0.46-fold; Comparing with esophagitis cases, OR decreased by 70% for ESCC. Fast eating not only introduced the high temperature of food but also the inadequate chewing, causing injuries to esophagus. It was significant to recommend Yanting population to slow down eating speed by increasing the consuming length at least 15 minutes; furthermore, the recommendation was also meaningful to the individuals with abnormal endoscope reports in screening.

Hot beverage drinking was another factor affecting ESCC risk, reported worldwide. In Uruguay and Paraguay, case-control studied reported that drinking very hot mate was associated with a 3.8 to 6.5-fold OR

for esophageal cancer (Rolon et al., 1995; De Stefani et al., 2003). Drinking very hot mate was related with a 2-fold high ESCC from another case-control study in Uruguay (Sewram et al., 2003). A pooled analysis in South America showed that heavy drinkers of very hot mate had the OR of esophageal cancer increasing to 4.14 fold high (Castellsague et al., 2000). In IARC monographs, mate is not classifiable as to its carcinogenicity to humans (Group 3), but hot mate drinking is probably carcinogenic to humans (Group 2A) (Sunyer and Basagaña, 2001). It suggested the high temperature drinking caused the injury to esophagus mucosa, which might lead to inflammatory reaction and initiated the possibility of carcinogen exposures. A population based case-control study in the high risk region, Iran, the amount of black tea drinking did not associated with the occurrence of ESCC, on the other side, drinking high temperature of black tea linked to a 7.42-fold higher risk of ESCC (Islami et al., 2009). In our study, the shorter interval between water boiling and drinking was a risk factor for ESCC. Though there was no significant difference between subjects about temperature of drinking tea, the higher frequency of drinking hot tea was observed in esophagitis and ESCC cases.

Yanting was one of high risk areas for ESCC in China and local residents suffered from cancer threats and poverty. Esophageal cancer had a 137.4/105 incidence and 80.0/105 mortality in Yanting (Zhang et al., 2006). Therefore, China government carried out esophageal cancer screening there, providing detection of endoscopy with iodine staining. Among the screening population, the rate of esophagitis (abnormal esophagus of endoscopy) was 45% and the cases were recommended biopsy detection and had a much higher risk to develop cancer (Wang et al., 2005). Our results showed that fast eating and hot beverage drinking were two risk factors for ESCC among esophagitis cases. It was meaningful to advise these people with abnormal esophagus mucosa altering their behaviors.

The small sample size was one of the potential limitations in this study, which was inadequate for some variable analyses. Esophagitis cases were not homogeneous and they were cases with abnormal esophagus mucosa, including mild dysplasia, moderate dysplasia, severe dysplasia and carcinoma in situ.

In conclusion, fast eating and hot beverage drinking were both related with high risk of ESCC, for cases with normal and abnormal esophagus mucosa. It was necessary to promote Yanting population to alter their behaviors, in order to reduce ESCC risk.

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