Even-Chain UFA Pattern, n-3 Long-Chain PUFA Pattern and Risk of Esophageal Squamous Cell Carcinoma in Southeast of China

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Research

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Abstract

Objective: To characterize and examine associations between dietary fatty acid intake patterns and the risk of esophageal squamous cell carcinoma (ESCC).

Methods: A total of 422 patients and 423 controls were recruited. Dietary fatty acids, as a percentage of total fat, were entered into a factor analysis. Multinomial logistic regression and restricted cubic spline were used to evaluate the risk of ESCC specific for different dietary fatty acid patterns (FAPs). A forest plot was applied to show the potential effect modification.

Results: The factor analysis generated 4 major fatty acid patterns: a long-chain SFA (LC-SFA) pattern; an even-chain unsaturated fatty acid (EC-UFA) pattern; a short and medium-chain SFA (SMC-SFA) pattern, and an n-3 long-chain polyunsaturated fatty acid (n-3 LC-PUFA) pattern. In the multivariate-adjusted model, the odds ratios (ORs) with 95% confidence interval (CI) of ESCC were 2.069(1.314,3.257), and 0.525 (0.340–0.811) for the highest versus the lowest tertile of EC-UFA pattern and n-3 LC-PUFA pattern, respectively. The LC-SFA, SMC-SFA patterns were not associated with ESCC. There existed a nonlinear positive association between the EC-UFA pattern and the risk of ESCC (p for nonlinearity <0.05), nevertheless, there was a nonlinear negative association between the n-3 LC-PUFA pattern and the risk of ESCC (p for nonlinearity <0.001). Multiplicative interaction between fried food, pickled food, hard food, tobacco smoking, alcohol drinking, and four FAPs was also observed.

Conclusions: Our study indicates that EC-UFA pattern, n-3 LC-PUFA pattern intake are associated with ESCC, which might provide a potential dietary intervention for ESCC prevention.

Introduction

Esophageal carcinoma has the 7th highest incident and constitutes the 6th leading cause of cancer deaths worldwide by GLOBOCAN 2018. Asia accounted for about 78% of all esophageal carcinoma cases, while 49% of cases occurred in China[1, 2]. As the fifth-most common and the fourth-most deadly cancer[3], the age-adjusted 5-year survival of esophageal carcinoma is relatively poor, in the range of 20–30%[4, 5]. More than 90% of esophageal cancer cases are ESCC in China[6].

The incidence and prognosis of ESCC are affected by many different factors. Tobacco smoking, alcohol drinking, environmental carcinogen exposure are the major recognized risk factors for ESCC[7, 8]. Remarkably, a growing body of research has highlighted the key role of nutrition in this cancer[9, 10]. Both theoretically and empirically, due to the limitations of a single nutrient or food approach, dietary pattern assessment has become an alternative method for measuring dietary exposure in nutritional epidemiology[11]. In the past several years, dietary guidelines for fat intake have been centered on reducing total fat or saturated fatty acid (SFA) intake. Whereas, recently fat quality has come into focus[12]. Combinations of multiple fatty acids may influence ESCC risk more than single fatty acids. A

direct association between total fat intake and ESCC outcomes is insufficient, so, it is important to consider the intake of fatty acid patterns.

At present, some studies have found that fatty acid patterns are closely related to the risk of certain diseases[13, 14]. However, as far as we know, the association of a combination of fatty acids with incident ESCC has not been evaluated. Therefore, the present study aimed to define specific dietary fatty acid patterns and then to investigate the relations between the generated fatty acid patterns and ESCC.

Methods

2.1 Study Design and Subjects

A hospital-based case-control study was conducted in Fujian province, China. Briefly, a total of 422 cases of ESCC were recruited from Fujian Provincial Cancer Hospital (FPCH) (176 cases), and the First Affiliated Hospital of Fujian Medical University (246 cases) in Fuzhou City during the period from June 2014 through December 2020 The inclusion criteria for cases were: (1) newly diagnosed primary patients who were histologically or cytologically diagnosed with ESCC (International Classification of Diseases 10th revision); (2) all cases were diagnosed with macroscopic type confirmed; (3) Chinese Han population who resided in Fujian Province at least past 10 years. Meanwhile, 423 controls were randomly chosen from community residents ordered health examination, with non-neoplastic conditions. This study was approved by the Institutional Review Board of Fujian Medical University (Fuzhou, China). Written informed consent was obtained from all participants before they participated in the study. All investigations performed in this study were conducted in accordance with the guidelines of the 1975 Declaration of Helsinki. A standard questionnaire was administered to cases and controls by specially trained interviewers. Questions covered demographic characteristics (e.g. gender, age, education level, job, marital status), dietary habits, lifestyle habits such as tobacco smoking and alcohol drinking, personal medical history, family history of cancer, and dietary factors(e.g. pickled food, fried food, hot food, hard food).

2.2 Assessment of Dietary Intake

The usual diet was assessed by a food frequency questionnaire (FFQ). The contents of the questionnaire mainly included: 1) grain, 14 items;2) Beans and their products, 8 items;3) Vegetables, 52 items;4) Fruit, 30 items;5) Animal food, 49 items;6) Bacteria, algae, and nuts, 8 items;7) Beverages, drinks, and soups, 10 items. There are seven categories of food in total, and the total number of food items is 171. The dietary data during 1 year before the diagnosis for cases or the year before the interview for controls were selected. Food items from the FFQ are converted into dietary fatty acids. The content of fatty acids and energy reference to 2018 "China Food Composition Tables-Standard edition”. To make the data follow the normal distribution, the natural logarithm (LN) conversion was carried out for the total energy and the daily intake of various dietary fatty acids, and the residual method was used to correct the total energy

for the average daily intake of various dietary fatty acids[15]. Missing values in the fatty acid data were replaced by the variable mean.

2.3 Definition of Variables

Subjects who had smoked at least one cigarette per day, lasting 6 months, were considered tobacco smokers[16]. Subjects who had at least one drink per week for at least 6 months were alcohol drinkers[17]. Tea drinkers were defined as drank at least one cup of tea per week continuously for more than 6 months[18]. All participants were additionally informed that the temperature of the food was classified on a scale ranging from 0 to 10, and ≥ 7 was defined as hot food. And then participants were asked to estimate the frequency that they burn their mouths when consuming hot food. Hard food was defined as food that was mechanically irritating and unpleasant to swallow, such as nuts, dried fruit, or ultra-dried meat. As for dietary data, participants were asked how often intake each food item according to the following options: ≥5times per week, 3–4 times per week, 1–2 times per week, less than one time per week, or not at all.

2.4 Statistical Analyses

After the investigation of all case and control subjects, the data were recorded using Epidata software (v3.1), with double-entry verification. The distributions of demographic characteristics, substance uses (tobacco, alcohol, and tea) of ESCC, and controls were compared by Chi-square test. The Mann-Whitney U test was used to test whether there was any difference in dietary fatty acid content distribution between the case group and control group. For descriptive purposes, we generated a hierarchical cluster tree to visually evaluate the correlations between individual fatty acids[19]. Pearson correlation coefficients between fatty acids were also calculated.

A factor analysis[11] was carried out to derive dietary fatty acid patterns (FAPs). Oblique rotation was used to derive dietary FAPs to obtain a simpler structure with greater interpretability. For deriving FAPs, the percentages of energy from the 36 FAs were used as input variables to adjust for an individual's daily energy intake. Finally, four FAPs were extracted considering eigenvalue (> 1), scree plot, and variance contribution. Participants were grouped into tertiles (T) according to the factor score of each pattern. The lowest score groups of each FAP were used as the reference. Using the Spearman correlation analysis, the associations between each pattern score with the intakes of 4 food groups (cereals, meat, freshwater fish, deep-sea fish), 3 oils (peanut oil, animal oil, blend oil) were assessed.

Three multivariable logistic regression models were applied to further estimate the OR value and 95%CI between dietary fatty acid pattern score and ESCC risk. Model 1 adjusted for gender, age, education level, marital status, family tumor history, occupation, tobacco smoking, alcohol drinking, tea consumption. To further control the influence of dietary habits on outcomes, hot food, hard food, pickled food, and fried food were included in model-2 additionally. Model 3 adjusted for model 2 and the other three FA scores.

The fitting performance of the three models was evaluated by Akaike Information Criterion (AIC). The restricted cubic splines were used to visualize the trend of dietary fatty acid scores with the risk in ESCC.

Finally, we used the forest plot to demonstrate the interaction of latent exposure factors on the potential correlation. All analyses were performed using R 4.0.3 software, with $\alpha_{two-sided} = 0.05$.

Results

3.1 General situation and comparison of dietary fatty acids

Table 1 presents the distribution of demographic characteristics, lifestyle risk factors in patient groups, and controls. Cases and controls had similar distributions of sex, alcohol drinking, and family history of cancer ($P > 0.05$). However, age, education level, marital status, occupation, income, tobacco smoking, and tea consumption were significantly different between these two groups ($P < 0.05$). S1 Table shows the difference in fatty acid intake between the case group and the control group after adjustment for energy.

3.2 The fatty acid–factor loadings of the 4 major factors

The correlation matrix of 36 fatty acids is in Fig. 1. Factor analyses, including 36 major fatty acids, identified 4 factors that explained 60.8% of the variation in these variables in the study population. A similar pattern was identified in cluster analysis, as fatty acids adjacent in the tree had similar loading values (Fig. 1). Four FA factor scores were extracted to construct the FAP score of dietary fatty acids. Based on the major contributors to each pattern (Table 2), the most powerful factor comprised mainly positive loadings from 20:0, 16:0, 18:0, 17:0. This factor was called the “LC-SFA” factor. The second most powerful factor comprised positive loadings from EC-UFA such as 22:6, 24:1, 20:5, 20:1, and 20:3. We characterized the third FA pattern as an “SMC-SFA pattern”, with high factor loading for 6:0. 10:0, and 4:0. “The n-3 LC-PUFA pattern” was characterized by high positive loadings of LC-PUFA, such as 22:3 and 22:5.

3.3 Correlation between dietary fatty acid scores and food groups

The correlations of the four FACP scores with intakes of food groups and oil groups are shown in the S2 Table. The LC-SFA pattern score was positively correlated to the intakes of “animal oil” ($r = 0.124$ $p = 0.002$). The EC-UFA pattern represented a diet relatively high in “peanut oil”($r = 0.189$, $p < 0.001$). The “n-3 LC-PUFA pattern” score was positively correlated to the intakes of “deep-sea fish” ($r = 0.099$ $p = 0.015$).

3.4 Association of the fatty acid pattern score with the incidence of ESCC.

The model fit performance was evaluated according to the AIC, model 3 had the lowest AIC and the best fitting effect. In multivariable analyses, the n-3 LC-PUFA pattern was associated with a lower likelihood of ESCC after adjustment for all covariates (OR: 0.525, 95% CI: 0.340,0.811, $P = 0.003$). After adjustment for potential confounding variables, the EC-UFA pattern was positively associated with ESCC (OR: 2.069, 95%

CI: 1.314,3.257, P = 0.002). The LC-SFA pattern and SMC-SFA pattern were not significantly associated with ESCC. (Table 3).

3.5 Linear trend of dietary fatty acid score and incidence of ESCC

The dose-response relationship between four FAPs intakes and the risk of ESCC is shown in Fig. 2. There existed a nonlinear positive association between the EC-UFA pattern and the risk of ESCC (p for nonlinearity < 0.05), nevertheless, there was a nonlinear negative association between the n-3 LC-PUFA pattern and the risk of ESCC (p for nonlinearity < 0.001) (Fig. 2).

3.6 Cross-stratified heterogeneity test between dietary fatty acid score and ESCC incidence

After adjusting for potential confounding factors, there was a multiplicative interaction between the LC-SFA pattern and the fried food ($P_{\text{inter action}}$ = 0.024). we discovered an increased ESCC associated with the EC-UFA pattern was detected in EC-UFA pattern interacted with hard food ($P_{\text{interaction}}$ =0.022), pickled food ($P_{\text{interaction}}$ = 0.122), and alcohol drinking ($P_{\text{interaction}}$ =0.002) on the development of ESCC at the multiplicative scale of the standard model. Multiplicative interaction between the n-3 LC-PUFA pattern and ESCC risk across alcohol drinking ($P_{\text{interaction}}$ = 0.001), pickled food($P_{\text{interaction}}$ 0.001), fried food($P_{\text{interaction}}$ 0.001) were obtained (Fig. 3).

Discussion

In this hospital-based case-control study, four main dietary patterns were identified, i.e. long-chain SFA (LC-SFA), even-chain unsaturated fatty acid (EC-UFA), short &medium-chain SFA (SMC-SFA), n-3 long-chain polyunsaturated fatty acid (n-3 LC-PUFA) patterns. The EC-UFA pattern was found to be associated with an increased risk of ESCC, whereas the n-3 LC-PUFA pattern was associated with a decreased risk. There was no significant association with the LC-SFA, SMC-SFA patterns observed in the study subjects, however.

Fatty acid is the main structural component of dietary fat. Different types and contents of FAPs have different effects on the occurrence and development of ESCC. Although nutrition has consistently been found to be an important determinant of the ESCC risk, the impact of fatty acid intakes in the etiology of ESCC has not been thoroughly investigated, especially in high-risk countries. Besides, only a few previous studies have evaluated the cumulative effect of fatty acids intakes on the ESCC risk using factor analysis (principal component)[20, 21], while factor analysis as a posteriori method allows the study of synergy among nutrients and consequence of the interactions between them[22].To our knowledge, there has been no attempt to assess the effect of dietary FAPs on ESCC risk, but some components in the dietary patterns of this study were similar to those of the patterns defined in some other studies, although not all components were identical. The “LC-SFA pattern” “SMC-SFA pattern”, and “n-3 LC-PUFA pattern”, were similar to the FAPs from Korea [13], Uppsala [23].

The “LC SFA pattern” and “SMC-SFA pattern” in this study—which was characterized by a high intake of SFA—were no significantly associated with the risk of ESCC. SFAs are major sources of energy[24], attenuate weight gain[25], and have strong antibacterial effects[26], but there is a lack of evidence for the effect of SFA on ESCC risk. In a case-control study with adults in Iran, higher levels of SFA were associated with a lower risk of ESCC[27]. However, In a study in Korea, the “short & medium-chain SFA pattern” was associated with an increased risk of hyper-LDL cholesterolemia in men [13]. Another study highlighted that Saturated fat intake was associated with higher cancer mortality (highest vs. lowest quintile [Q5 vs. Q1]: HR: 1.26, 95% CI 1.20–1.32) in a prospective cohort study of 521,120 participants, with 16 years of follow-up[28]. High intake of saturated fat (but not total, monounsaturated or polyunsaturated fat intake) was associated with increased risk of breast cancer (Q5 vs. Q1: HR 1.13, 95% CI 1.00–1.27) in a large European multicentre prospective study (519,978 participants)[29]. Then in this study, SMC-SFA and LC-SFA patterns were not found to be associated with ESCC risk.

Nevertheless, those adhering more to the “even-chain UFA pattern” were found to be at a higher risk of ESCC. The “even-chain UFA pattern” had a high factor loading of even-chain UFA such as DHA(C22:6), nervonic acid(C24:1), EPA(C20:5), eicosenoic acid(C20:1), eicosatrienoic acid(C20:3), AA(C20:4). Some studies have shown that dietary unsaturated fatty acids are associated with an increased risk of cancer[30]. Especially, AA in the even chain fatty acid pattern is a precursor to pro-inflammatory molecules[31]. In humans, the even-chain UFA was found to be correlated with composite inflammation measures and may thus influence the risk of cancer[32]. Inflammation is a crux of the development of many chronic diseases, including cancer[33]. An inflammatory microenvironment is an important part of the tumor microenvironment[34]. Chronic inflammation is the cause of tumor transformation[35]. More studies are essential for exploring their association.

The last pattern of n-3 LC-PUFA was characterized by higher intake of DPA(22:5), docosatrienoic acid(22:3). Many previous studies have proved that the n-3 series of unsaturated fatty acids are mainly derived from fish[36], and our study also found a positive correlation between the fourth FAP and the intake of deep-sea fish. N-3 LC-PUFA pattern, an important fatty acid that may play a role in preventing some cancers[22]. Furthermore, the n-3 LC-PUFA pattern, which has pleiotropic effects and enhances cancer cell apoptosis, modulates various eicosanoid pathways leading to reduced inflammation, such as suppressing cyclooxygenase-2 synthesis and the inhibition of arachidonic acid-derived eicosanoids[37]. Animal studies and human observational studies have demonstrated that the n-3 LC-PUFA pattern may reduce the risk of cancers such as breast, colon, and prostate[37–39]. In this study, the n-3 LC-PUFA pattern was also found to reduce the risk of ESCC.

When exploring the linear relationship between dietary fatty acid patterns and the risk of ESCC. As we can be seen from Fig. 2, with the increase of EC-UFAs intake, the risk of ESCC increases. However, as the intake of n-3 LC-PUFAs improved, the risk of ESCC decreased. They were associated with a dose-response risk of ESCC. N-3 polyunsaturated fatty acids (PUFAs) express anti-inflammatory properties and prevent tumor progression[40], which is similar to our result.

Stratified by demographic characteristics and life exposure factors, we found the association between dietary fatty acid pattern and ESCC risk could be modified by smoking, drinking, pickled food, hard food, and fried food. Pickled food is often preserved with the addition of nitrates or nitrites, which increases the formation of N-nitroso compounds (NOCs), which were considered to be animal carcinogens and possible human carcinogens[41]. In addition, high concentrations of salt may increase ESCC risk. Salt might directly damage the esophageal mucosa, leading to susceptibility to esophagitis and an increased risk of ESCC[42]. In this study, there was heterogeneity in the relationship between dietary FAP and the risk of ESCC with the use of preserved foods, and the protective effect of the n-3 LC-PUFA pattern was reduced with the use of preserved foods.

There have been reports that a significant dose-response relationship between the intake frequency of fried food and the risk of ESCC[43]. Cooking meat at high temperatures produces large amounts of polycyclic aromatic hydrocarbons, and also high levels of heterocyclic amines[44]. Both groups of chemicals have been suggested to increase the risk of ESCC[45, 46]. After stratification by fried foods, we found that the protective effect of the n-3 LC-PUFA pattern was weakened in those who regularly consumed fried foods and differed from those who did not regularly consume fried foods.

The role of alcohol use in the etiology of carcinoma of the esophagus is well established[47]. Lots of studies conducted in Kenyan [48], Japan[49], have provided further evidence of the close and independent role of alcohol in the etiology of ESCC. Many epidemiological studies have shown that alcohol is associated with tumor suppressor gene promoter hypermethylation and global DNA hypomethylation in several cancers, including esophageal[50]. In this study, there was heterogeneity in the association between the LC-UFA pattern and ESCC, as shown in the previous study, alcohol consumption would increase the risk of pattern 2, and the association was distinct.

To the best of our knowledge, this is the first study that factor analysis has been used to reveal a causal relationship between dietary FAPs and ESCC risk in the Chinese population. In our daily life, people eat a diet made up of a variety of fatty acids, not just one kind of fatty acid. Therefore, it is important to consider the FAP analysis because it can reflect the actual dietary quality and summarize the effects of various dietary FAs. As compared with the traditional approach of analyzing single FA, factor analysis allows investigating the relationship between dietary habits and cancer accounting for complex interactions between dietary components.

Whereas, several limitations should be acknowledged in our study. Selection bias may exist in any hospital-based case-control study. However, all subjects were recruited from two hospitals according to strict criteria, which may minimize the selection bias. The study data were obtained from interviews and might lead to recall bias which may limit the accuracy of our results. To alleviate this effect, we performed face-to-face interviews and given the definitions of variables. Notwithstanding these limitations, to our knowledge, this is the first study to examine the effects of FACPs on the risk of ESCC. (3144 words)

Conclusions

We found that higher dietary intake of even-chain UFA pattern was associated with a higher risk of developing ESCC. On the contrary, a combination of individual fatty acids, characterized by n-3 LC-PUFA pattern, was associated with a lower incidence of ESCC. Further prospective studies with larger sample sizes are needed to confirm this association.

Abbreviations

AIC akaike information criterion

EC-UFA even-chain unsaturated fatty acid

ESCC esophageal squamous cell carcinoma

FAPs fatty acid patterns

FFQ food frequency questionnaire

LC-SFA long-chain saturated fatty acid

n-3 LC-PUFA n-3 long-chain polyunsaturated fatty acid

SFA saturated fatty acid

SMC-SFA short and medium-chain SFA

Declarations

Ethical Approval and Consent to participate

Informed consent was obtained from participants, and the study was approved by the Institutional Review Board of Fujian Medical University (number: 2015104)

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

All authors read and approved the final manuscript.

Competing interests

The authors state that there are no conflicts of interest to declare.

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Authors' contributions

The authors' responsibilities were as follows—HZJ and HCC: designed the study; LZ, LJB and CYM: supervised the data collection; TXW and SJY: analyzed the data; HCC, LZ and LZQ: contributed to the data interpretation and manuscript writing; HZJ: had primary responsibility for the final content.

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Tables

Table 1

Distribution of characteristics among cases and controls (n = 845)

Variable	controls n(%)	cases n(%)	χ2χ2	P
Age (years)			20.934	0.001
≤ 54	248(58.6%)	181(42.9%)		
54	175(41.4%)	241(57.1%)		
Gender			0.057	0.812
Male	240(56.7%)	236(55.9%)		
Female	183(43.3%)	186(44.1%)		
Education level			81.055	0.001
Low	161(38.1%)	291(69.0%)		
High	262(61.9%)	131(31.0%)		
Marital status			11.252	0.001
Married	392(92.7%)	412(97.6%)		
Other	31(7.3%)	10(2.4%)		
Occupation			113.326	0.001
Farmer and worker	145(34.3%)	299(70.9%)		
Other	278(65.7%)	123(29.1%)		
Income(RMB/monthly)			27.944	0.001
< 2000	302(71.4%)	364(86.3%)		
≥ 2000	121(28.6%)	58(13.7%)		
Tobacco smoking			31.699	0.001
No	291(68.8%)	210(49.8%)		
Yes	132(31.2%)	212(50.2%)		
Alcohol drinking			1.012	0.314
No	254(60.0%)	239(56.6%)		
Yes	169(40.0%)	183(43.4%)		
Tea consumption			9.279	0.002
No	148(35.0%)	191(45.3%)		

Variable	controls n(%)	cases n(%)	χ2χ2	P
Yes	275(65.0%)	231(54.7%)		
Family history of cancer			0.035	0.852
No	364(86.1%)	365(86.5%)		
Yes	59(13.9%)	57(13.5%)		

Table 2
The fatty acid–factor loadings of the 4 major patterns

Fatty acid	Pattern 1 LC-SFA	Pattern 2 EC-UFA	Pattern 3 SMC-SFA	Pattern 4 n-3 LC-PUFA
18:1	0.924	-0.001	-0.008	0.101
20:2	0.914	0.026	0.028	-0.136
20:0	0.898*	0.078	-0.058	-0.247
16:0	0.835*	0.115	0.075	0.199
11:0	0.82	-0.029	0.061	-0.386
12:0	0.816	-0.063	0.409	-0.226
8:0	0.723	-0.048	0.422	-0.375
18:0	0.701*	0.007	0.037	0.394
17:0	0.664*	0.005	0.117	0.316
16:1	0.656	0.425	-0.023	0.312
16:2	0.449	-0.053	-0.059	-0.032
18:2	0.435	0.017	-0.08	0.057
22:0	0.131	0.038	-0.129	-0.049
22:6	-0.084	0.993*	-0.028	-0.051
24:1	-0.075	0.990*	-0.026	-0.089
20:5	-0.092	0.988*	-0.033	0.028
24:0	-0.054	0.968	-0.03	-0.086
20:1	0.174	0.932*	-0.018	0.015
20:3	-0.078	0.928*	0.18	0.112
20:4	0.218	0.809*	-0.008	0.207
6:0	0.005	-0.063	0.961*	-0.004
10:0	0.081	-0.076	0.932*	-0.038
14:1	-0.018	0.188	0.916	0.024
4:0	-0.038	-0.055	0.714	-0.043

Fatty acid	Pattern 1 LC-SFA	Pattern 2 EC-UFA	Pattern 3 SMC-SFA	Pattern 4 n-3 LC-PUFA
13:0	-0.002	0.384	0.528	-0.036
14:0	0.383	0.209	0.526*	0.465
22:4	-0.025	0.106	-0.042	0.708
22:3	-0.069	0.122	-0.068	0.647*
22:5	-0.09	0.115	-0.067	0.566*
15:0	0.229	0.003	0.276	0.55
17:1	0.129	-0.072	0.031	0.47
19:0	0.264	-0.104	-0.015	0.265
18:3	0.196	-0.081	-0.127	0.239
15:1	0.128	0.068	0.144	0.207
22:1	-0.06	0.004	0.015	0.169
18:4	-0.057	-0.075	0.021	0.146
Eigen value	9.312	6.020	3.626	2.930
Total variance (%)	25.865	16.721	20.071	8.139

*Factor loadings that contribute to defining each factor.

Table 3
The association between dietary fatty acid patterns and esophageal cancer

model	Tertile of the fatty acid pattern score*			P_{trend}	AIC
	I	II	III		
PC1: LC-SFA					
case/control(n)	141/140	112/171	169/112		
model1	1.0(reference)	0.648(0.440,0.953)	1.278(0.867,1.833)	0.201	997.614
model2	1.0(reference)	0.716(0.481,1.064)	1.338(0.900,1.989)	0.147	962.2605
model3	1.0(reference)	0.681(0.448,1.033)	1.309(0.862,1.988)	0.159	953.3695
PC2: EC-UFA					
case/control(n)	114/167	150/133	158/123		
model1	1.0(reference)	1.849(1.256,2.723)	1.915(1.285,2.856)	0.001	995.8135
model2	1.0(reference)	1.887(1.264,2.817)	2.079(1.376,3.142)	0.001	956.6683
model3	1.0(reference)	1.694(1.104,2.600)	2.069(1.314,3.257)	0.002	952.2726
PC3: SMC-SFA					
case/control(n)	151/130	151/132	120/161		
model1	1.0(reference)	1.176(0.802,1.724)	0.754(0.513,1.108)	0.154	1013.972
model2	1.0(reference)	1.106(0.746,1.640)	0.720(0.484,1.070)	0.107	974.136
model3	1.0(reference)	0.978(0.655,1.459)	0.607(0.400,0.920)	0.021	950.7284
PC4: n-3 LC-PUFA					
case/control(n)	182/99	109/174	131/150		
model1	1.0(reference)	0.439(0.297,0.650)	0.517(0.348,0.769)	0.001	980.3383
model2	1.0(reference)	0.453(0.302,0.678)	0.608(0.401,0.921)	0.017	943.6093
model3	1.0(reference)	0.452(0.299,0.682)	0.525(0.340,0.811)	0.003	932.1294

*Three categories were obtained by tertile of the fatty acid pattern score. Each participant was assigned a fatty acid pattern score.

Multivariable-adjusted Logistic regression models.

Model 1 adjusted for demographic characteristics: gender, age, education level, marital status, family history of cancer, occupation, tobacco smoking, alcohol drinking, tea consumption

Model 2 adjusted for Model 1 and hard food□hot food□pickled food□fired food.

Model 3 adjusted for Model 2 and other three FA scores.

Figures

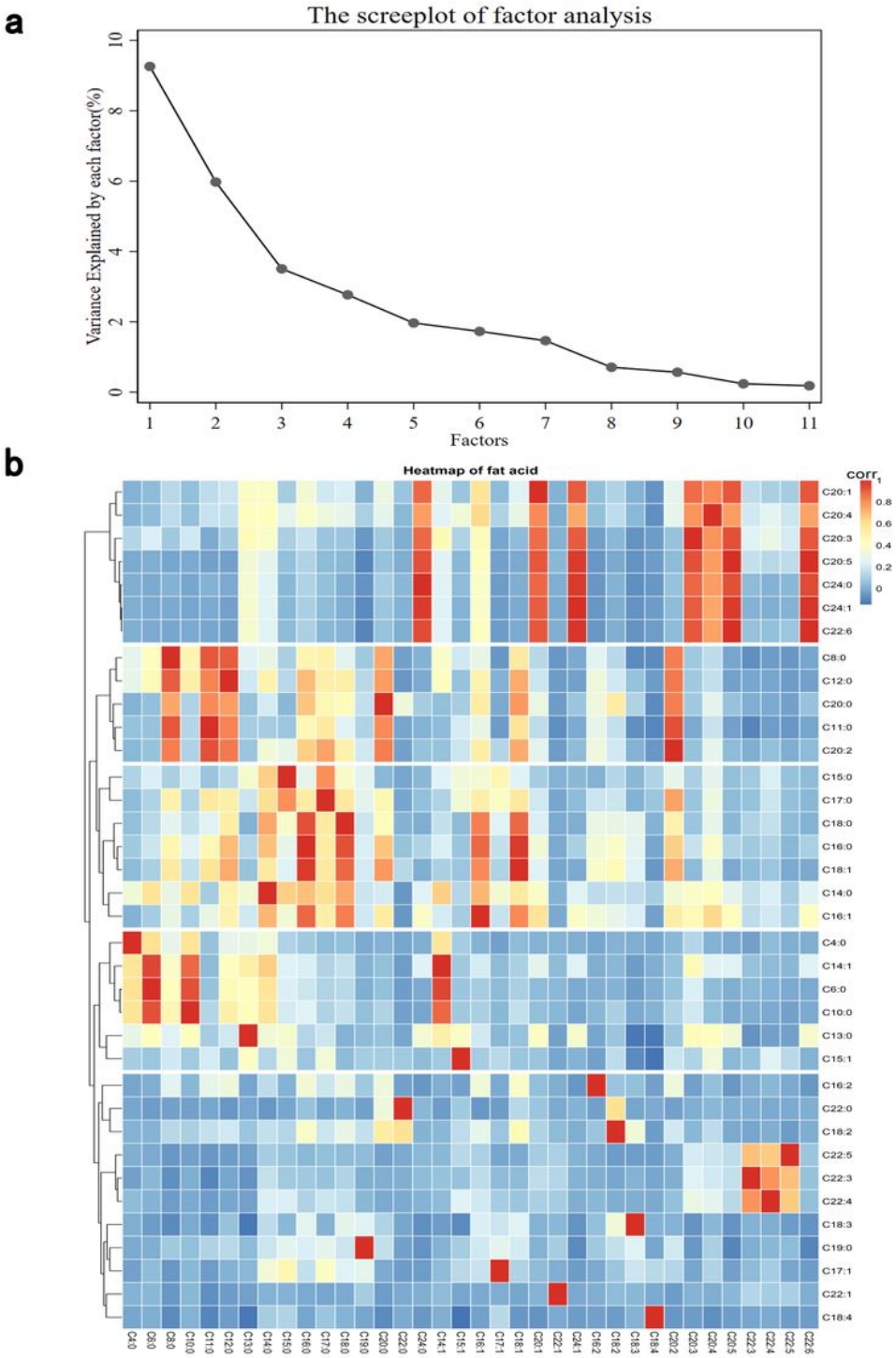

Figure 1

The correlation matrix of 36 fatty acids is in Fig 1. Factor analyses, including 36 major fatty acids, identified 4 factors that explained 60.8% of the variation in these variables in the study population. A similar pattern was identified in cluster analysis, as fatty acids adjacent in the tree had similar loading values (Fig 1).

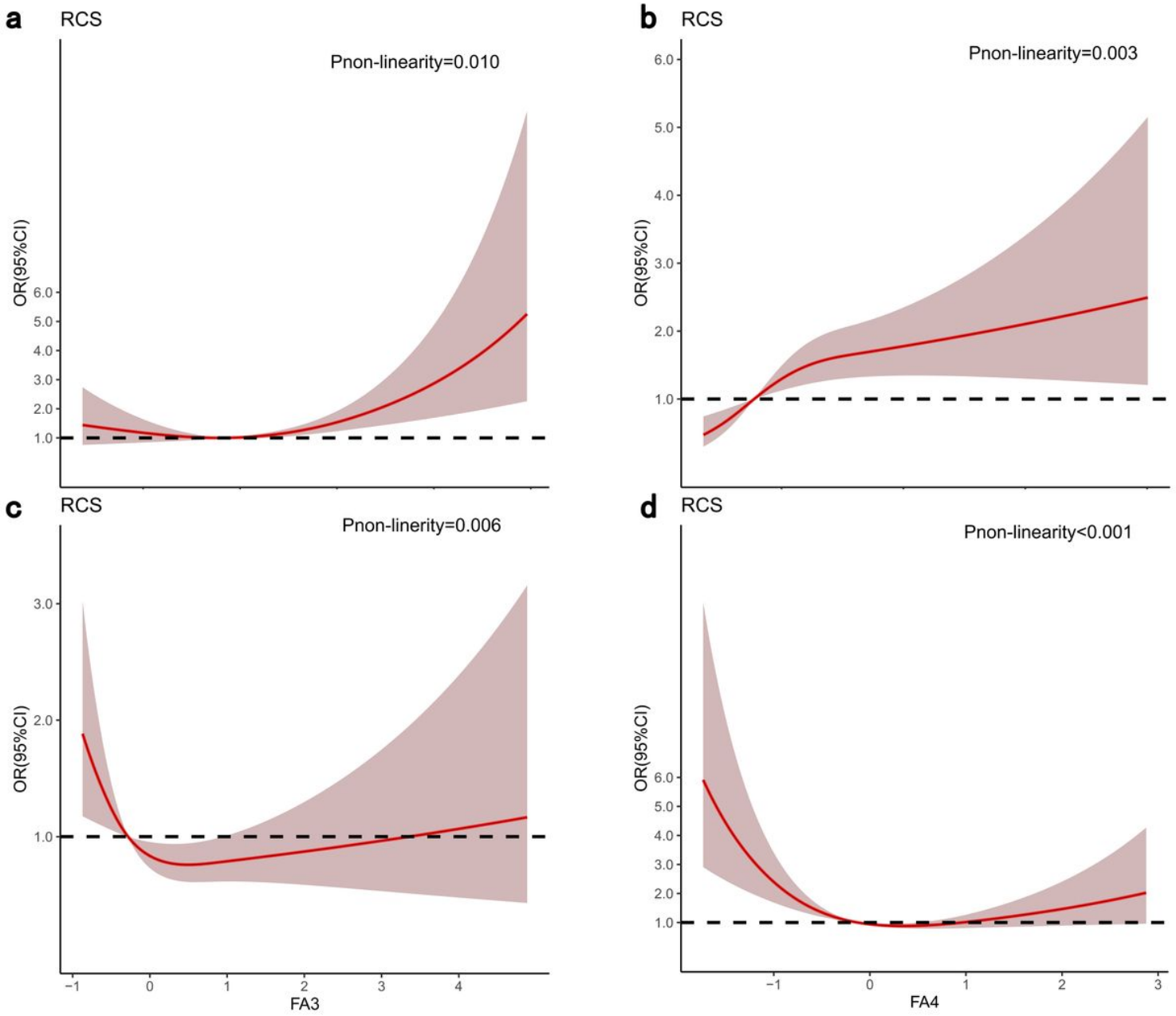

Figure 2

There existed a nonlinear positive association between the EC-UFA pattern and the risk of ESCC (p for nonlinearity <0.05), nevertheless, there was a nonlinear negative association between the n-3 LC-PUFA pattern and the risk of ESCC (p for nonlinearity <0.001) (Figure 2).

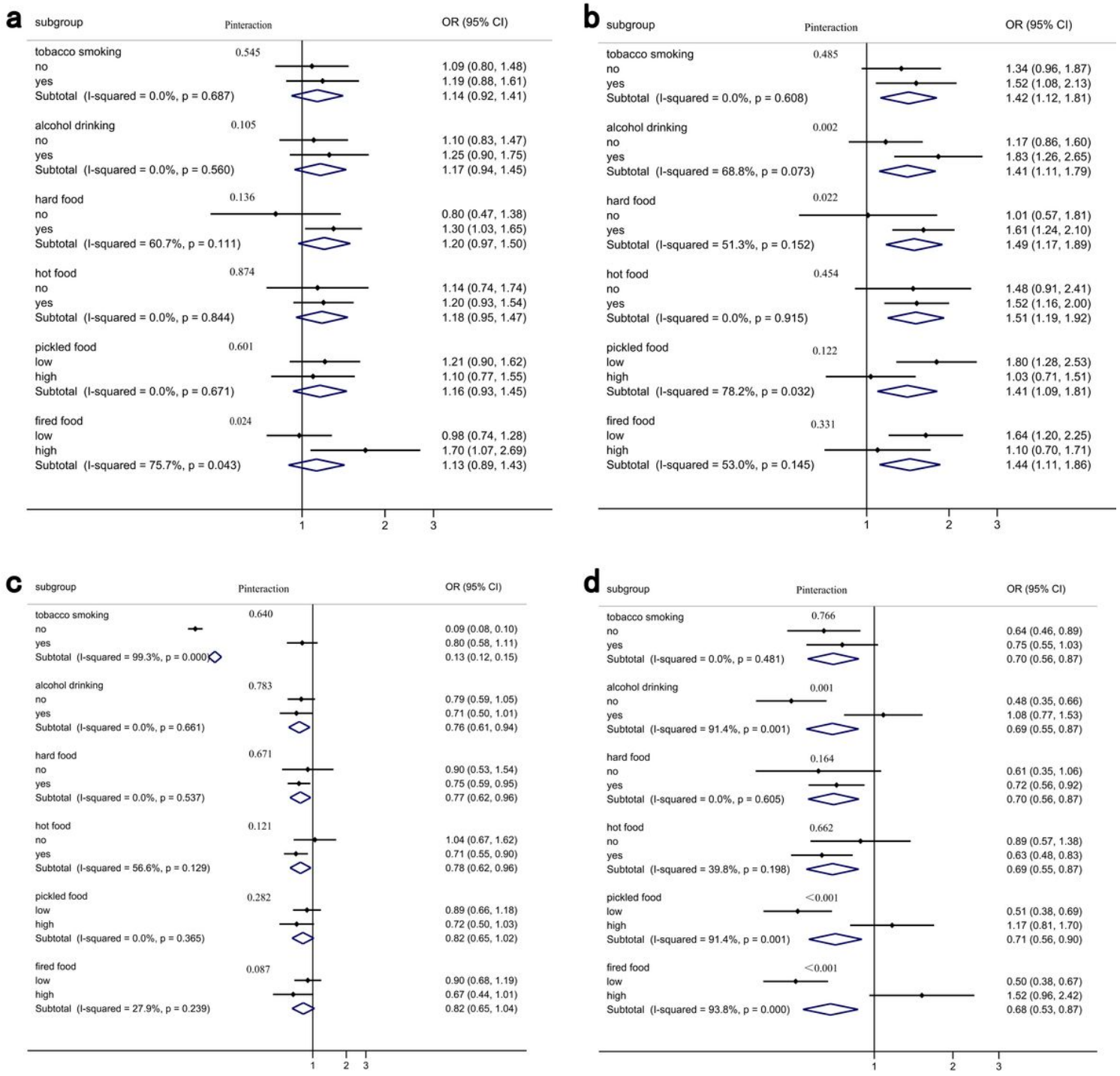

Figure 3

Multiplicative interaction between the n-3 LC-PUFA pattern and ESCC risk across alcohol drinking (Pinteraction = 0.001), pickled food(Pinteraction 0.001), fried food(Pinteraction 0.001) were obtained (Figure 3).

Supplementary Files

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- Supplementarydata.docx