

VISUOMENĖS SVEIKATA

Salt-preserved foods and risk of gastric cancer

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Key words: gastric cancer; case-control study; salt; salt-preserved foods.

Summary. Gastric cancer is one of the main health issues in Lithuania. The risk factors of the disease are related to nutrition and environment. There were no epidemiological studies on this subject in the country. The aim of the study was to assess the relationship between risk of gastric cancer and consumption of salt and salt-preserved food.

Material and methods. A hospital based case-control study included 379 cases with newly histologically confirmed diagnosis of gastric cancer and 1,137 controls that were cancer and gastric diseases free. Cases and controls matched by gender and age (± 5 years). Ratio of cases and controls was 1:3. A questionnaire was used to collect information on possible risk factors of gastric cancer. The odds ratios (OR) and 95% confidence intervals (CI) for gastric cancer were calculated by a conditional logistic regression.

Results. Cases had significantly lower education level and mostly resided in villages. After adjustments for other dietary habits and smoking, alcohol consumption, family history on cancer, education level, and residence, higher risk of gastric cancer was found for those using salt additionally to prepared meal or those who liked salty food. After controlling for other food items that were associated with gastric cancer and smoking, alcohol consumption, family history on cancer, education level, and residence, body mass index at 20 years of age, and physical activity, intake of salted meat (OR=1.85, 95% CI=1.12–3.04, 1–3 times/month vs. almost never; OR=2.21, 95% CI=1.43–3.42, ≥ 1 –2 times/week vs. almost never), smoked meat (OR=1.79, 95% CI=1.23–2.60, ≥ 3 –4 times/week vs. ≤ 1 –2 times/week), smoked fish (OR=1.70, 95% CI=1.13–2.53, ≥ 1 –2 times/week vs. ≤ 1 –3 times/month) was significantly associated with an increased risk of gastric cancer. Consumption of salted mushrooms was found to increase the risk of gastric cancer, however, this increase was not statistically significant.

In conclusion, higher risk of gastric cancer is found for people that like salty food, salt-preserved meat as well as fish.

Introduction

Nutritional factors are widely believed to be critical in carcinogenesis (1). The estimated proportion of gastric cancer due to dietary factors is about 90% (2). The Intersalt study showed that the prevalence of gastric cancer tends to be higher in populations where salt intake is high (3). Several case-control studies have reported strong statistically significant increases in gastric cancer risk due to overall dietary salt or sodium intake (4, 5) or use of table salt (6).

A variety of salted foods have been associated with increased risk of gastric cancer. Some studies found varying degrees of increased risk with higher levels

of consumption of salty foods in general, salted vegetables (5, 7), higher intake of salted fish (8). A small significant or non-significant increase in the risk was observed at the highest consumption of cured or processed meat (range of relative risk from 1.0 to 1.7) (6, 9), although the results were not consistent (10, 11).

Gastric cancer is an important health issue in Lithuania and the second most frequent cause of cancer death. In spite of some international projects assessing health behavior among adults (12) and studies on *Helicobacter pylori* infection in pathogenesis of gastric cancer (13, 14), there were no epidemiological studies on gastric cancer in our country. There-

fore, a hospital-based case-control study was conducted at the main hospitals of Lithuania. We aim to assess the relationship between gastric cancer and salt-preserved food.

Materials and methods

A hospital-based case-control study has been carried out at four hospitals in Lithuania (Lithuanian Oncology Center, Kaunas University of Medicine Hospital and Oncology Hospital as well as Klaipėda hospital). The study included 379 patients aged 22–86 years who had histologically confirmed diagnosis of gastric cancer (C16.0–C16.9) between December 2002 and March 2004. Controls were individually matched to case-patients by gender and age (± 5 years). Ratio of cases and controls was 1:3. Totally, we had 1,137 controls that were cancer and gastric diseases free.

A structured questionnaire developed on the basis of Aichi Cancer Center Questionnaire was used in the study. It included questions on dietary habits, diet (56 items), lifetime smoking habits, lifetime consumption of all types of alcoholic beverages (i.e. vodka/brandy, beer, wine), physical activity. In addition, we asked detailed questions regarding lifetime occupational history, personal history on various non-malignant diseases, family history of cancer.

All subjects were asked to fill out a questionnaire by themselves. If there were some reasons not to do that (bad general status, poor vision, pathology of upper extremities or personal wish for assistance of filling out a questionnaire), they were interviewed by interviewers. Four interviewers were trained and were not aware of the study hypothesis. Cancer patients were asked to refer about some lifestyle habits (diet and physical activity) a year before the disease was diagnosed.

Diet was assessed according to consumption frequency (almost never, 2–3 times per month, 1–2, 3–4 or 5–6 times per week, one, two or three times per day) of different food items. Cigarette smoking was measured in pack-years (number of cigarettes smoked per day/20 \times smoking time (in years)) (15); alcohol consumption was assessed by sum of products that were calculated by multiplying consumption frequency of beer, wine and strong alcohol (vodka, brandy and etc.) by standard alcohol units (SAU), where 1 SAU is 10 g of pure alcohol found in 250 ml of beer or 120 ml of wine or 32 ml of vodka (16); family history on cancer categorized into three categories: do not know, mother/father has/had cancer and no

cancer; physical activity at leisure time was estimated by answers (no, sometimes, and yes) to a question “Do you perform exercises (sport, running, cycling, working in a garden) at your leisure time?”; subjects according to body mass index (BMI; calculated as weight (kg)/height² (m)) at 20 years of age were grouped into two groups: ≤ 24.99 kg/m² and ≥ 25 kg/m²; education level was categorized into three categories: lower than secondary, secondary, and university; residence assessed by living in the cities, towns, and villages.

A conditional logistic regression was used to calculate odds ratios (OR), and corresponding 95% confidence intervals (CI) for gastric cancer in relation to exposures of interest. Tests for trend were computed by fitting conditional logistic regression model to ordinal values representing levels of exposure. All reported trend test significance levels (p-values) were two-sided (17). The χ^2 test was utilized to calculate the difference between proportions. The level of significance was set at 5%. All the calculations were performed with the STATA 7 software program.

Results

The distribution of socio-demographic variables and selected risk factors among cases and controls is shown in Table 1. Cases had significantly lower education level and mostly resided in villages. There were more controls without history on cancer as compared to cases. Therefore, education level, residence and family history on cancer were included into logistic regression model like smoking, alcohol consumption, physical activity and BMI at 20 years of age as variables to adjust for.

There was a statistically significant relationship between the risk of gastric cancer and use of salt additionally to prepared meal or relish of salty food in univariate logistic regression model. After controlling for smoking, alcohol consumption and family history on cancer, use of salt additionally to prepared meal or relish of salty food was significantly associated with increased risk of gastric cancer (Table 2). The ORs remained statistically significant and after adjustment for residence and education level. After controlling for other dietary habits such as speed of eating, a portion of food, regularity of breakfast, use of fatty, spicy, fried, barbecued, cooked in oil and hot food, use of vegetables in winter and in summer, that were associated with the disease as well as smoking, alcohol consumption, family history on cancer, residence and education level, the ORs for gastric cancer

Table 1. Distribution of cases and controls according to selected sociodemographic and risk factors

Variable	Category	Cases		Controls		p-value
		n	%	n	%	
Gender	Men	228	60.16	684	60.16	matched
	Women	151	39.84	453	39.84	
Age (years)	≤44	26	6.86	95	8.36	matched
	45–54	77	20.32	192	16.89	
	55–64	84	22.16	315	27.70	
	≥65	192	50.66	535	47.05	
Education	Lower than secondary	162	42.74	349	30.75	<0.001
	Secondary	166	43.80	487	42.91	
	University	51	13.46	299	26.34	
Residence	City	118	31.55	544	47.97	<0.001
	Town	88	23.53	231	20.37	
	Village	168	44.92	359	31.66	
Marital status	Single	12	3.17	27	2.37	NS
	Married	274	72.49	868	76.48	
	Separated/widow	92	24.34	240	21.15	
Parents history on cancer	No	200	52.77	685	60.25	0.038
	Yes	109	28.76	276	24.27	
	Do not know	70	18.47	176	15.48	

NS – non significant.

Table 2. Odds ratios (OR) and 95% confidence interval (CI) for gastric cancer in relation to dietary habit “to put salt to prepared meal” or “relish of salty food”

Variable	Cases		Controls		OR ¹ (95% CI) p for trend	OR ² (95% CI) p for trend	OR ³ (95% CI) p for trend
	n	%	n	%			
Do you put salt additionally to prepared meal?							
Never	101	26.93	606	53.53	1.00	1.00	1.00
When it is not enough or almost every time without tasting	274	73.07	526	46.47	3.10 (2.37–4.04) <0.001	3.00 (2.28–3.96) <0.001	2.98 (2.15–4.15) <0.001
Do you like salty food?							
No	35	9.31	208	18.34	1.00	1.00	1.00
Not very much	73	19.41	439	38.71	1.02 (0.64–1.62)	1.02 (0.63–1.65)	0.97 (0.58–1.62)
Like	222	59.04	440	38.80	2.98 (1.96–4.53)	2.90 (1.87–4.50)	2.37 (1.46–3.86)
Like very much	46	12.23	47	4.14	5.55 (3.13–9.87) <0.001	4.99 (2.75–9.06) <0.001	3.88 (1.98–7.60) <0.001

OR¹ – adjusted for smoking, alcohol consumption, family history on cancer;OR² – further adjustment for education level and residence;OR³ – adjusted for speed of eating, size of portion of food, regularity of breakfast, fatty, spicy, fried, barbequed cooked in oil and hot food, use of vegetables in winter and in summer, smoking, alcohol consumption, family history on cancer, education level and residence except for each independent variable.

Table 3. Odds ratios (OR) and 95% confidence interval (CI) for gastric cancer in relation to selected dietary variables

Variable	Category	Cases		Controls		OR ¹ (95% CI) p for trend	OR ² (95% CI) p for trend	OR ³ (95% CI) p for trend
		n	%	n	%			
Salted meat	Almost do not use 1–3 times/month	218 48	57.52 12.66	858 131	75.46 11.52	1.00 1.54 (1.06–2.24)	1.00 1.56 (1.06–2.28)	1.00 1.85 (1.12–3.04)
	≥1–2 times/week	118	29.82	148	13.02	2.95 (2.18–3.99) <0.001	2.71 (1.96–3.71) <0.001	2.21 (1.43–3.42) <0.001
Smoked meat	≤1–2 times/week	198	52.24	842	74.05	1.00 2.57 (2.00–3.32) <0.001	1.00 2.29 (1.76–2.99) <0.001	1.00 1.79 (1.23–2.60) 0.029
	≥3–4 times/week	181	47.46	295	25.95			
Salted fish	Almost do not use ≥1–3 times/month	163 216	43.01 56.99	399 738	35.09 64.91	1.00 0.67 (0.52–0.87) 0.002	1.00 0.64 (0.49–0.84) 0.001	1.00 0.69 (0.47–1.02) 0.051
	Smoked fish	≤1–3 times/month	270	71.24	884	77.75	1.00 1.37 (1.05–1.79) 0.021	1.00 1.49 (1.13–1.97) 0.006
≥1–2 times/week		109	28.76	253	22.25			
Pickled vegetables with salt and oil	Almost do not use 1–3 times/month	104 65	27.44 17.15	259 269	22.78 23.66	1.00 0.60 (0.42–0.86)	1.00 0.60 (0.41–0.87)	1.00 0.62 (0.32–1.21)
	≥1–2 times/week	210	55.41	601	53.56	0.82 (0.61–2.10) 0.371	0.79 (0.58–1.07) 0.276	1.01 (0.60–1.71) 0.908
Pickled vegetables with salt and vinegar	Almost do not use 1–3 times/month	110 78	29.02 20.58	272 268	23.92 23.57	1.00 0.74 (0.52–1.04)	1.00 0.75 (0.53–1.08)	1.00 1.34 (0.71–2.52)
	≥1–2 times/week	191	50.40	597	52.51	0.77 (0.58–1.03) 0.106	0.76 (0.56–1.02) 0.100	0.93 (0.55–1.57) 0.592
Salted mushrooms	≤1–3 times/month	334	88.13	1056	92.88	1.00 1.64 (1.11–2.41) 0.011	1.00 1.56 (1.04–2.34) 0.021	1.00 1.25 (0.73–2.15) 0.283
	≥1–2 times/week	45	11.87	81	7.12			

OR¹ – adjusted for smoking, alcohol consumption, family history on cancer, body mass index at 20 yr of age;

OR² – further adjustment for education level and residence;

OR³ – further adjustment for diet (salt preserved food items, bread, noodles, rice, different dairy products, mayonnaise, eggs, carrots, cabbage, broccoli, tomatoes, garlic, onion, paprika, bean, potatoes) and physical activity except for each independent variable.

in relation to use of salt additionally to prepared meal or relish of salty food decreased little, but remained statistically significant.

Higher consumption level of salted and smoked meat, salted and smoked fish, pickled vegetables with

salt and vinegar or oil and salted mushrooms was associated with risk of gastric cancer in univariate conditional logistic regression model. After controlling for smoking, alcohol consumption, family history on cancer, and BMI at 20 years of age, frequent intake of

salted and smoked meat, smoked fish and salted mushrooms was associated with an increased risk of the disease, while the use of salted fish or vegetables pickled with salt and oil was related to decreased risk of gastric cancer (Table 3). The dose-response relationships were statistically significant with p for trend varying from <0.001 for salted and smoked meat to 0.021 for smoked fish. The ORs and the dose-response relationships remained significant after further control for education level and residence.

Inasmuch as the risk of gastric cancer is related to many factors, finally, we used multivariate conditional logistic regression model that included all salt-preserved food items (salted and smoked meat, salted and smoked fish, vegetables pickled with salt and vinegar or oil, salted and pickled mushrooms) and other food items (bread, noodles, rice, different dairy products, mayonnaise, eggs, fresh vegetables, i.e. carrots, cabbage, broccoli, tomatoes, garlic, onion, paprika, beans, potatoes) that were associated with the disease, and smoking, alcohol consumption, family history on cancer, BMI at 20 years of age, educational level, residence and physical activity. A significant increase in the risk was observed at higher consumption level of salted and smoked meat as well as smoked fish (Table 3). The significant dose-response relationships were found between consumption of salt-preserved meat (salted and smoked) as well as smoked fish and risk of gastric cancer.

Discussion

The present study has demonstrated an increased risk of gastric cancer related to the consumption of salt and salt-preserved food. We found that people who liked to use salt additionally to prepared meal or liked salty food had an increased risk of gastric cancer. These findings are consistent with the data reported by other authors (6, 18). Epidemiological findings are supported by experiments on animals (19).

Our finding that frequent consumption of salted meat increased the OR for gastric cancer is in line with the established positive association between the consumption of salted meat and risk of gastric cancer (5, 20, 21). Elevated risk of the disease might be attributed to the potential carcinogens such as nitroso compounds contained in these foods, and may also involve the increased cell replication and susceptibi-

lity to carcinogenesis from the salt intake (22, 23).

We also found a significant increase in risk of gastric cancer for people with frequent consumption of smoked meat (ham, sausages). For those with higher intake of smoked fish an increase in the risk was also statistically significant. In most analytical studies smoked foods have been considered together with other preserved foods. The findings on smoked foods are not consistent in other surveys. Some studies have found a positive association between the risk of gastric cancer and consumption of ham (24), smoked fish (25) and smoked foods among blacks but not among whites in the USA (26). The others have found a non-significant increase in risk of the disease related to the consumption of sausage (24) or processed meat (smoked meats sausage, fried bacon and ham) (27, 28). Any hot flame leads to the production of nitrosyl compounds. Exposure of foods to these nitrosyl vapors essentially has the same effect as curing with nitrate or nitrite that role in carcinogenesis is still discussed (29).

Our data showed the increased, but not statistically significant, OR for gastric cancer with salted mushrooms. These findings are supported by G. S. Hamada *et al.* (30). However, most of the studies have found a significant increase in the risk of gastric cancer due to more frequent use of pickled vegetables (8, 21). Again, nitrosamine contamination has been reported to be present in pickled vegetables (31).

Salt is not directly acting carcinogen, but it is thought to increase the risk of gastric cancer through direct damage to the gastric mucosa, which results in gastritis, increased DNA synthesis, and cell proliferation (29). Superficial gastritis can lead to chronic atrophic gastritis, which is a precursor lesion in the development of gastric cancer (32). Salt not only enhances chemical gastric carcinogenesis, it also enhances *Helicobacter pylori* colonization, a gastric carcinogen, in both humans and animals (33, 34).

Conclusions

1. Higher risk of gastric cancer is found for people that put salt additionally to prepared meal or like salty food.
2. There is an association between increased risk of gastric cancer and frequent intake of salted or smoked meat as well as smoked fish.

Druska apdorotų maisto gaminių vartojimas ir skrandžio vėžio rizika

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Raktažodžiai: skrandžio vėžys, atvejo ir kontrolės tyrimas, druska, druska apdoroti maisto produktai.

Santrauka. Skrandžio vėžys – aktuali sveikatos problema Lietuvoje. Pagrindiniai šios ligos rizikos veiksniai susiję su mityba ir aplinka. Epidemiologinių tyrimų, kuriais nustatomas skrandžio vėžio priklausomumas nuo įvairių veiksnių, Lietuvoje neatlikta.

Darbo tikslas. Įvertinti ryšį tarp rizikos sirgti skrandžio vėžiu ir druskos bei druska apdorotų maisto gaminių vartojimo.

Tyrimo medžiaga ir metodai. Skrandžio vėžio atvejo ir kontrolės tyrimas atliktas Vilniaus, Kauno ir Klaipėdos ligoninėse. Atvejo grupę sudarė pacientai (n=379), kuriems pirmą kartą nustatyta ir histologiškai patvirtinta skrandžio vėžio diagnozė. Kiekvienam atvejui pagal lytį ir amžių (± 5 metai) parinkta kontrolinė grupė santykiu 1:3. Ją sudarė 1137 tiriamieji, nesirgę onkologinėmis bei virškinamojo trakto ligomis. Atlikta tiriamųjų anketinė apklausa. Šansų santykiai ir jų 95 proc. pasikliautinieji intervalai skaičiuoti taikant sąlyginę logistinę regresiją.

Rezultatai. Tyrimo duomenimis, sergantieji skrandžio vėžiu buvo mažesnio išsimokslinimo, dažniau gyveno kaime. Įvertinus kitus mitybos įpročius bei rūkymą, alkoholinių gėrimų vartojimą, paveldimumą, išsimokslinimą ir gyvenamąją vietą, didesnė skrandžio vėžio rizika nustatyta tiems, kurie papildomai deda druskos į paruoštą maistą arba mėgstantiems sūrų maistą. Įvertinus kitus maisto produktus, kurių vartojimas buvo reikšmingai susijęs su skrandžio vėžio rizika, bei rūkymą, alkoholinių gėrimų vartojimą, paveldimumą, išsimokslinimą, gyvenamąją vietą, kūno masės indeksą ir fizinį aktyvumą, nustatyta, kad sūdytos mėsos ($\text{ŠS}=1,85$, 95% PI=1,12–3,04, 1–3 kartai per mėnesį; $\text{ŠS}=2,21$, 95% PI=1,43–3,42, $\geq 1-2$ kartai per savaitę palyginus su tais, kurie beveik nevalgo sūdyto maisto), rūkytos mėsos gaminių ($\text{ŠS}=1,79$, 95% PI=1,23–2,60; $\geq 3-4$ kartai per savaitę palyginus su $\leq 1-2$ kartais per savaitę), rūkytos žuvies ($\text{ŠS}=1,70$, 95% PI=1,13–2,53; $\geq 1-2$ kartai per savaitę palyginus su $\leq 1-3$ kartais per mėnesį) vartojimas reikšmingai didino skrandžio vėžio riziką, o sūdytų grybų – nereikšmingai.

Išvada. Žmonėms, mėgstantiems sūrų maistą ir druska apdorotus mėsos bei žuvies gaminius, skrandžio vėžio rizika didesnė.

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