

SYSTEMATIC REVIEW

The Effect of Salted Food on the Risk of Oral Cancer: A Systematic Review

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ABSTRACT

Introduction: Oral cancer is one of the most prevalent forms of cancer. Oral cancer can develop when genetic and environmental factors interact. Food is believed to contribute to the increased risk of oral cancer and is responsible for 30–35% of all cancers. High levels of salt and nitrite in salted foods are linked to an increased risk of oral cancer. There is an increase in the consumption of salted foods in the global community, which is in line with the rise in worldwide oral cancer incidence. This study seeks to determine whether salted foods affect the risk of developing oral cancer. **Methods:** The research was conducted using a systematic review method that refers to the PRISMA approach. This review was conducted on articles published from 1950 to 2023 from PubMed, Cochrane, and Scopus databases, in addition to manual searches based on inclusion and exclusion criteria. **Results:** The data extraction process revealed 27 articles discussing salted food and oral cancer, including 16 variables of salted food, such as salted meat, processed meat, bacon, sausage, salami, ham, nitrite-containing meats, miso soup, pickled food, pickled chili, pickled fruits, pickled vegetables, salty food, salted fish, Chinese salted fish, and salted egg. **Conclusion:** Salted foods have the effect of increasing the risk of oral cancer.

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Keywords: Oral cancer, Salted foods, Processed foods, N-nitroso, Carcinogens.

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INTRODUCTION

Oral cancer is the sixth most prevalent cancer in the world (1). According to the Global Cancer Observatory (GCO), the incidence of oral cancer in 2020 reached 377,713 cases; the highest incidence was in Asia (248,360 cases), followed by Europe (65,279) and North America (27,469) (2). According to the GCO, the incidence and mortality rate of oral cancer are expected to increase by 40% by 2040 (3).

Oral cancer is indirectly developed by the interaction between genetic factors and the environment (4). The main causes are tobacco usage, alcohol consumption, and betel quid chewing (1). Carcinogens in food play a role in causing cancer, as much as 30–35%, and several foods have been identified as being associated with the development of oral cancer (5).

Some dietary patterns in Malaysia and Indonesia are associated with an increased risk of oral cancer, one of which is consuming a lot of salted foods. Salted food has also been linked to the risk of oral cancer, according to a Shanghai study (6). People in developing countries tend to consume processed or salted foods (7). Research shows a rapid increase in the consumption of processed foods or salted food in both developed and developing countries, especially among young adults (8,9)

The increase in the prevalence of oral cancer in the world is in line with the increasing consumption of salted food in the global community. This study was conducted to determine whether there is an effect of salted food consumption on the risk of oral cancer based on the results of previous studies.

METHODS

This article is a systematic review compiled using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (10). The research questions were identified with the PICO framework (11)

as follows: (1) Population: Oral cancer; (2) Intervention: Salted food; (3) Comparison: Processed food; (4) Outcome: Risk of oral cancer.

Search strategy

The search method for articles related to research questions uses the "Boolean Operators" technique with the keywords "oral cancer" OR "oral potentially malignant disorder" OR "oral squamous cell carcinoma" AND "salted food" OR "pickled vegetable" OR "salted meat" OR " salted duck egg" OR " dried or salted fish" OR "salted fish roe" OR "chinese style salted fish" AND "effect" via Pubmed, Scopus, and Cochrane Library databases. Searching for additional articles is also carried out using the hand-searching or snowball method.

Eligibility criteria

The inclusion criteria in this study were articles published within the last 73 years (1950-2023), English articles, human subjects, articles discussing the effect of salted food on the risk of oral cancer, and articles available in full text. Exclusion criteria were articles that did not discuss the effect of salted food on the risk of oral cancer and review articles.

Data extraction and quality assessment

Data extraction was performed on all selected articles to obtain important findings from each article. The selected articles will be analyzed using thematic analysis, which is an analytical technique carried out to identify, classify, analyze, explain, and carry out a report on the themes found in a number of pieces of data (12).

Risk of bias and quality assessment

Assessment of article quality with a case-control study design was carried out using JBI's Critical Appraisal Tools (13).

RESULT

From the results of the searches in the three databases and by hand, 27 articles were found. The first screening was carried out by selecting 33,201 articles based on human subjects, resulting in a total of 10,290 articles. For the second screening, look for duplicate articles. As a result, 88 articles were chosen for duplication, and a total of 10,202 articles were found. The third screening was carried out by reading the title and abstract of the article and then selecting articles that did not match the inclusion criteria, so that 10,173 articles did not match the inclusion criteria, and a total of 29 articles were obtained. The last screening was done by reading the entire content of the article to determine its suitability for the research question. Therefore, two review articles were excluded, and a total of 27 articles were obtained. The article search process based on the PRISMA method is shown in Figure 1.

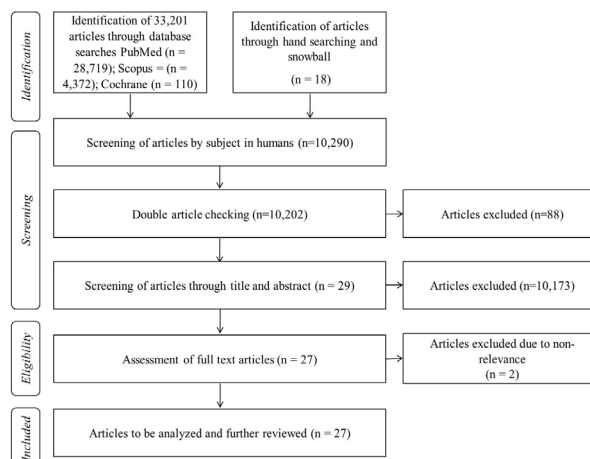


Figure 1: Prisma Flow

Study quality assessment

27 articles with a case-control study design were assessed for quality using indicators from JBI's Critical Appraisal Tools. The answers for each indicator are Yes, No, Unclear, and N/A (Not applicable) (13). Based on the results of the study, the risk assessment of bias using JBI's Critical Appraisal Tools showed 27 articles included in the low risk of bias category (Table I).

Table I. Study quality assessment

No	Study	JBI Critical Appraisal										Result
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	
1	De Stefani et al. 2009. [1]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
2	De Stefani et al. 2012. [2]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
3	Takezaki et al. 1996. [3]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
4	De Stefani et al. 1999. [4]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
5	Helen-Ng et al. 2012. [5]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
6	De Stefani et al. 1994. [6]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
7	Gridley et al. 1990. [7]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
8	De Stefani et al. 2005. [8]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
9	Zheng et al. 1993. [9]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
10	Amtha et al. 2009. [10]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
11	Franco et al. 1989. [11]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
12	Zheng et al. 1992. [12]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	90%
13	Chen et al. 2017. [13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
14	Levi et al. 2004. [14]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
15	Lissowska et al. 2003. [15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
16	Rajkumar et al. 2003. [16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
17	Sánchez et al. 2003. [17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
18	Garrote et al. 2001. [18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
19	Bravi et al. 2013. [19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
20	Petridou et al. 2002. [20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
21	Winn et al. 1984. [21]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	90%
22	Mclaughlin et al. 1988. [22]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	80%

CONTINUE

Table I. Study quality assessment(cont.)

No	Study	JBI Critical Appraisal										Result	
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10		
23	Franceschi et al. 1999. [23] Barra, Franceschi, and Talamini 1991. [24] Levi et al. 1998. [25]30 females Sapkota et al. 2008. [26] Toporcov, Antunes, and Tavares 2004. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
24	Franceschi et al. 1999. [23] Barra, Franceschi, and Talamini 1991. [24] Levi et al. 1998. [25]30 females Sapkota et al. 2008. [26] Toporcov, Antunes, and Tavares 2004. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90%
25	Franceschi et al. 1999. [23] Barra, Franceschi, and Talamini 1991. [24] Levi et al. 1998. [25]30 females Sapkota et al. 2008. [26] Toporcov, Antunes, and Tavares 2004. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
26	Franceschi et al. 1999. [23] Barra, Franceschi, and Talamini 1991. [24] Levi et al. 1998. [25]30 females Sapkota et al. 2008. [26] Toporcov, Antunes, and Tavares 2004. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
27	Franceschi et al. 1999. [23] Barra, Franceschi, and Talamini 1991. [24] Levi et al. 1998. [25]30 females Sapkota et al. 2008. [26] Toporcov, Antunes, and Tavares 2004. [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%

Notes: Q1 = Were the groups comparable other than the presence of disease in cases or the absence of disease in controls? Q2 = Were cases and controls matched appropriately? Q3 = Were the same criteria used for identification of cases and controls? Q4 = Was exposure measured in a standard, valid and reliable way? Q5 = Was exposure measured in the same way for cases and controls? Q6 = Were confounding factors identified? Q7 = Were strategies to deal with confounding factors stated? Q8 = Were outcomes assessed in a standard, valid and reliable way for cases and controls? Q9 = Was the exposure period of interest long enough to be meaningful? Q10 = Was appropriate statistical analysis used?

Table II Summary of the results of the analysis of the article

No	Author	Type of Study	Subject(n), age, gender	Food items	Result	Conclusion
1	De Stefani et al. 2009. [1]	Case control	Cases: 326 oral cancer patients; controls: 3,798 subjects; mean 62.6 years; male: 89.4%	Salted meat	OR 1.15, 95% CI 0.75-1.79	Salted meats were insignificantly associated with oral cancer
2	De Stefani et al. 2012. [2]	Case control	Cases: 283 oral/pharynx cancer patients, 274 males (age 60 years), 9 females (age 54.9 years), controls: 2,532 subjects	Processed meat (bacon, sausage, salami, ham mortadella, saucisson, hotdogs, air-dried and salted lamb)	OR 1.42, 95% CI 0.95-2.13 (pria)	Processed meat (mortadella, salami, hotdogs, ham, and salted meat) was found to be an insignificant risk for oral cancer, while bacon was found to be inversely related (preventive) and sausage was found to be unrelated to risk of oral cancer.
3	Takezaki et al. 1996. [3]	Case control	Cases (189 males, 77 females), references (9,858 males, 26,669 females), 20-79 years old	Miso soup	OR 1.3, 95% CI 0.98-1.7	Miso soup increases the risk of oral cancer, especially among women
				Pickles	OR 0.8, 95% CI 0.6-1.1	Oral cancer risk was reduced when pickles were consumed.
				Salty foods	OR 0.7, 95% CI 0.6-0.99	This research is difficult to prove an association between eating salty foods and risk of oral cancer because this study was conducted in patients with oral cancer who had changed their food preferences due to pain or damage of their taste buds.
4	De Stefani et al. 1999. [4]	Case control	Cases: 33 oral/pharynx patients, 393 controls, 30-89 years old.	Salted meat	OR 0.9, 95% CI 0.5-1.7	Salted and processed meat identified not to be associated to an increased risk of oral cancer due to limitations. The limited number of oral cancer patients caused it to be difficult to draw an accurate conclusion from the research.
				Processed meat (bacon, sausage, salami, mortadella, saucisson, ham)	OR 0.7, 95% CI 0.5-1.3	
				Nitrite-containing meats (canned beef, lunch meat, frankfurters, canned meat, bacon)	OR 1.1, 95% CI 0.7-1.9	

CONTINUE

Study characteristics

The general conclusions of the articles analyzed are shown in Table II. All of the articles were case-control studies, with data analyzed using an odd ratio (OR) and a 95% confidence interval (CI). The majority of the studies revealed an association between salted foods and an increased risk of oral cancer (14,15,24-33,16,34,35,17-23). A total of seven studies reported no association between salted foods and the risk of oral cancer (25,27,36-40).

DISCUSSION

Oral cancer is a type of cancer that develops in the mucosal layer of various anatomical areas, particularly the lips, tongue, and mouth (oral cavity) (1). Oral squamous cell carcinomas (OSCC) account for over 90% of all oral cancers (41). Eating foods preserved in salt has been associated with oral cancer, the mechanism might

Table II Summary of the results of the analysis of the article (cont.)

No	Author	Type of Study	Subject(n), age, gender	Food items	Result	Conclusion
5	Hel-en-Ng et al. 2012. [5]	Case control	153 cases (ages 18-82 years, mean 52.4 years; 153 controls (17-81 years, mean 52.4 years)	Fermented/salted foods (salted fish, chinese salted fish, salted duck egg, fermented shrimp, shrimp paste, fermented durians, pickled chillies, pickled fruits, soy sauce, fish sauce)	OR 2.986, 95% CI 1.551–5.746	The combination of food groups (dairy, meat/products, and fermented/salted foods) is a significant risk factor for oral cancer. Consuming these diets regularly triples the risk of developing oral cancer.
				Processed food (bacon, processed meat (sausages/salami/hotdog), burger, pizza, sandwich, French fries, instant noodles, nuggets (fish/chicken), instant spices)	OR 0.790, 95% CI 0.418–1.490	The “modern” food groups (processed foods and snacks) were not considered relevant to the increased risk of oral cancer. This study’s reduced risk effect is probably due to dietary habits that combine high-risk foods (processed meats, smoked meats, and sausages) with low-risk foods (such as traditional Malay foods).
6	De Stefani et al. 1994. [6]	Case control	246 cases and 253 controls, 40-89 years old	Salted meat	OR 10.5, 95% CI 3.2-34.4	The risk of oral cancer increased by 40% (not significant) in people who did not regularly consume salted meat, while those who regularly consumed salted meat had a significantly increased risk of oral cancer..
7	Gridley et al. 1990. [7]	Case control	190 cases (142 males and 48 females), 201 controls (139 males and 62 females), mean age 57 years, range 22–79 years.	Nitrite-containing meats (liverwurst, cold cuts, bacon, sausage)	OR 3.1 (males), OR 0.9 (females)	Nitrite-containing meat intake is related to a significantly higher risk in men but not in women.
8	De Stefani et al. 2005. [8],	Case control	230 cases, 460 controls, 30-89 years old	Processed/preserved meat (bacon, sausage, blood pudding, mortadella, salami, saucisson, hotdogs, ham, salted meat)	OR 1.5, 95% CI 0.9–2.6	A high intake of processed meat is associated with a moderate but not significant increase in the risk of oral cancer.
9	Zheng et al. 1993. [9]	Case control	404 cases/controls, 18-80 years old	Salted meat	RR 1.22, 95% CI 0.43-3.44	Pickled vegetables were shown to be significantly correlated with an increased risk of oral cancer, while salted meat, bacon, and sausage were found to be unrelated to an increased risk of oral cancer.
				Salted egg	RR 0.69, 95% CI 0.24-1.79	
				Pickled vegetable	OR 1.73, 95% CI 0.79-3.77	
				Sausages	RR 0.55, 95% CI 0.26-1.17	
10	Amtha et al. 2009. [10]	Case control	81 cases (23–74 years) and 162 controls (22–79 years)	Fermented foods (salty eggs, salty fish, fermented prawns, soy ketchup, fermented fruit, pickles)	OR 2.17, 95% CI 1.05–4.50	The preferred category (fast food, cooked/raw vegetables, fermented food, seafood, canned food, and snacks high in fat and sugar) is considered to increase the risk of oral cancer by twofold.
				Processed foods (sausages, nuggets, meat/fish balls)	OR 2.85, 95% CI 1.34–6.05	The chemically related category (processed food and MSG) is considered to significantly triple the risk of oral cancer.
11	Franco et al. 1989. [11]	Case control	232 cases (201 males, 31 females), 464 controls, age (<40 years = 10; 40-49 years = 50; 50-59 years = 85; 60-69 years = 56; and >=70 years = 31 patients).	Pickled vegetable	RR 1.7, 95% CI 0.9-3.1	Consuming pickled vegetables was not associated with an increased risk of oral cancer because the RR estimate was ambiguous after adjusting for tobacco and alcohol use.

CONTINUE

Table II Summary of the results of the analysis of the article (cont.)

No	Author	Type of Study	Subject(n), age, gender	Food items	Result	Conclusion
12	Zheng et al. 1992. [12]	Case control	204 cases (115 males, 89 females) and 414 controls (269 males, 145 females), 20-75 years old	Salted vegetable Salted eggs Salted meat/fish	OR 1.2, 95% CI 0.61-2.33 (males), OR 1.09, 95% CI 0.48-2.48 (females) OR 1.25, 95% CI 0.49-3.21 (males), OR 1.25, 95% CI 0.35-4.48 (females) OR 2.47, 95% CI 1.10-5.52 (males), OR 3.37, 95% CI 1.05-13.03 (females)	After adjustment for alcohol consumption and smoking, consumption of salt-cured foods was associated with an increased risk of oral cancer. Among other salted foods, only salted meat/fish was specifically associated with oral cancer/pharyngeal cancer. Salted meat/fish may increase the risk of oral cancer more than pharyngeal cancer.
13	Chen et al. 2017. [13]	Case control	930 cases (588 men and 342 women), 2667 controls (1689 men and 978 women), age 20-80 years old	Pickled food Processed meat (sausage, bacon, ham)	OR 1.21, 95% CI: 1.02-1.43 OR 1.03, 95% CI 0.82-1.29	Consuming processed meat did not show a significant association with oral cancer risk, whereas consuming pickled food more than once per week made one more susceptible to oral cancer.
14	Levi et al. 2004. [14]	Case control	Cases 316 oral and pharynx cancer patients (251 men, 65 women, ages 26-75 years, median 61 years), controls 660 subjects (564 men, 96 women, ages 23-75, median 58 years)	Processed meat (raw ham, boiled ham, salami, sausages)	OR 4.68, 95% CI 2.54-8.63	Processed meats (raw ham, boiled ham, salami, and sausages) were assessed to be strongly and consistently associated with oral cancer risk. Salami and sausages were rated the riskiest compared to the others.
15	Lis-sowska et al. 2003. [15]	Case control	122 cases (44 women and 78 men) and 124 controls (72 men and 52 women), ages 23-80 years old	Ham, salami, sausages	OR 0.11, 95% CI 0.05-0.25	Consuming processed meat is considered to have a significant protective effect against oral cancer.
16	Raj-kumar et al. 2003. [16]	Case control	Cases: 309 males (median 56 years, range 22-85 years); cases: 282 females (median 58 years, range 18-87 years); controls: 292 males (median 55 years, range 20-76 years); controls: 290 females (median 52 years, range 18-80 years).	Ham and salami	OR 4.40, 95% CI 2.88-6.71	Ham and salami have a significant impact on the risk of oral cancer.
17	S6nchez et al. 2003. [17]	Case control	375 cases (304 men, 71 women, ages 20-91 years, median 60 years) and 375 controls (304 men, 71 women, ages 20-87 years, median 60 years).	Ham and salami	OR 0.79, 95% CI 0.52-1.21	There is no significant correlation between consuming ham and salami and the risk of oral cancer.
18	Garrote et al. 2001. [18]	Case control	200 cases (57 women, median 64 years) and 200 controls (64 women, median 62 years), ages 25-88 years	Ham and salami	OR 2.03, 95% CI 1.11-3.74	Consuming ham and salami was significantly associated with an increased risk of oral cancer.
19	Bravi et al. 2013. [19]	Case control	768 cases (593 men, 175 women, median 58 years, range 22-79 years) and 2,078 controls (1,368 men, 710 women, median 59 years, range 19-79 years).	Processed meat	OR 1.28, 95% CI 0.84-1.93	Processed meat is considered insignificant to the risk of oral cancer.

CONTINUE

Table II Summary of the results of the analysis of the article (cont.)

No	Author	Type of Study	Subject(n), age, gender	Food items	Result	Conclusion
20	Petridou et al. 2002. [20]	Case control	106 cases and controls, 65 men, 41 women, < 50 - ≥ 80 years old	Meats and meat products (pork, veal, beef, lamb, goat, chicken, turkey, ham, salami, and sausages; liver and other entrails; eggs; meat pies (1/2); mousaka (1/2); and pasticchio (1/2))	OR 1.28, 95% CI 0.94-1.76	Meats and meat products moderately increase the risk of oral cancer.
21	Winn et al. 1984. [21]	Case control	Cases: 227 female patients (96 patients aged <60 years, 131 aged 60 years), 405 controls (163 aged <60 years, 242 aged 60 years)	Pork products (ham or pork dried meats, bacon, sausage, brains, lunch meat, frankfurters, canned meats) Nitrite-containing meats (canned beef, lunch meat, frankfurters, canned meat, bacon)	OR 1.3, 95% CI 0.8-2.0 OR 1.1, 95% CI 0.7-1.9	Pork products and nitrite-containing meats may insignificantly increase the risk of oral cancer.
22	Mclaughlin et al. 1988.[22]	Case control	871 cases, 979 controls, ages 18-79, 77% male	Nitrite meats	OR 1.3 (male), OR 1.8 (female)	Nitrite-containing meat is associated with an increased risk of oral cancer in women but not in men.
23	Franceschi et al. 1999. [23]	Case control	271 cases of oral cancer (219 men, 52 women, median 58 years, range 22–77 years) and 1491 controls (1008 men, 483 women, median 57 years, range 20–78 years)	Processed meats	OR 1.6, 95% CI 1.1-2.4	High consumption of processed meat (especially in ham, salami, and sausage, except for prosciutto) can significantly increase the risk of oral cancer.
24	Barra, Franceschi, and Talamini 1991. [24]	Case control	302 oral cavity and pharyngeal cancer cases (266 men, 36 women, median 59 years) and 699 controls (549 men, 150 women, median 58 years)	Salami and sausages	OR 2.0	Consuming salami and sausage was found to be significantly associated with oral cancer risk.
25	Levi et al. 1998. [25]30 females	Case control	156 cases (126 men, 30 women, 26–72 years, median 55 years) and 284 controls (246 men, 38 women, 23–74 years, median 58 years.)	Pork and processed meat	OR 3.21, 95% CI 1.66–6.24	Higher consumption of pork and processed meat can significantly increase the risk of oral cancer.
26	Sapkota et al. 2008. [26]	Case control	Cases 378 oral/pharyngeal cancer patients (331 men and 47 women), 916 controls, 45-74 years old	Preserved (Pickled) vegetables Ham, salami, sausages	OR 1.92, 95% CI 1.23–2.99 OR 1.26, 95% CI 0.70–2.27	High consumption of pickle vegetables significantly increases the risk of oral/pharyngeal cancer. There is no significant association between oral cancer risk and meat consumption.
27	Toporcov, Antunes, and Tavares 2004. [27]	Case control	70 cases (20 women, 50 men, median 57.1 years, range 34-77 years) and 70 controls (20 women, 50 men, median 57.3 years, range 35-81 years)	Bacon	OR 2.667, 95% CI 1.197–6.159	Consuming bacon at least 2 times a week can significantly increase the risk of oral cancer.

Note:

R : Odd ratio, RR : Risk relative, CI : Convience interval

be through nitrosamine formation (42). The International Agency for Research on Cancer - European Prospective Investigation into Cancer and Nutrition (ARC-EPIC) categorizes several food processing methods such as pasteurization, fermentation, smoking, curing, and salting (43). Salting is a traditional practice used by many cultures to preserve food, particularly meat and fish (44). According to the classification of the International Food Information Council (IFIC), salted foods are processed foods (45). Based on the World Health Organization, salted foods are those that have been preserved through salting and have a high salt content (46). In this study, salted foods include salted meat, processed meat, bacon, sausage, salami, ham, nitrite-containing meats, salted fish, Chinese salted fish, salted egg or salted duck egg, miso soup, salty food, pickles or pickled food, pickled chili, pickled fruits, and pickled vegetables. (14,15,24–33,16,34–40,17–23)

According to WHO recommendations, daily salt intake should not exceed 5 g/day (47). Rust (48) states that salt intake from salted or processed foods may exceed the daily salt consumption limit. In addition to NaCl, nitrate and nitrite are used as preservatives and can give meat a red color; however, they can easily react due to nitrogen oxidation and form a number of derivatives (49). From the analysis of the article, we found that salted food contains a carcinogenic compound, namely N-nitroso, which is a strong electrophilic alkylating agent during metabolism and can alkylate biomolecules such as DNA (50). The most common carcinogenic N-nitroso compound in foods is N-nitrosodimethylamine (NDMA), which has been categorized by the International Agency for Research on Cancer as possibly carcinogenic to humans (category 2A) (51). NDMA is one of the derivatives of nitrosamines (52). N-nitrosamines are typically formed from natural foods, such as meat that has had its protein amines fermented or heated at high temperatures, and higher levels are produced in meat that has had nitrite added as a preservative (53). Nitrosamines have toxic, mutagenic, and teratogenic effects (54). Mutagenic effects can react directly with DNA, resulting in genetic mutations; even low concentrations can initiate tumor formation (55). Other studies have also shown increased cell death after exposure to NDMA compared to unexposed cells (56).

Salted foods (rich in N-nitroso compounds) are associated with a higher risk of cancer (14). This statement is in line with the articles obtained; the chemical component involved in cancer initiation is the interaction of nitrite or nitrous oxide, which is commonly found in processed meat and salted fish (28). Other active substances mentioned as having an effect are N-nitroso (14,19,26,29,30,35), nitrites (20,22,23,25,28,32), nitrosamines (24,25,37), salt (22,24,25), high fat (33), saturated fat (20,22), animal fat, and cholesterol (17,30). Another possible carcinogenic mechanism is the mutagenic role of heterocyclic amines

and polycyclic aromatic hydrocarbons developed during cooking (25,30). Food preparation methods, food ingredients, the amount of spices used in cooking, and temperature, such as eating miso soup while it is still hot, can increase the risk of oral cancer (27,36). There are articles that claim salted meat does not induce oral cancer, but this finding is considered weak because of the limited number of cases studied (37).

The results show that there is a relationship between smoking, alcohol, salted food, and the risk of oral cancer. A total of 15 studies showed the effects of consuming salted food, alcohol, and cigarettes, which simultaneously significantly increased the risk of oral cancer (14,15,26–28,33,35,16–23). Toxic components of nicotine and alcohol may amplify the carcinogenicity of N-nitroso compounds found in pickled foods and have a synergistic effect on the risk of oral cancer (29). This is in line with research that states that ethanol can change the carcinogenic effectiveness of nitrosamines by changing their pharmacokinetics by reducing the ability of the liver to metabolize nitrosamines (57). Ethanol in alcohol can affect nitrosamine metabolism, which can increase DNA alkylation several times (58). This effect is synergistic with consuming salted meat, cigarettes, and alcohol (26).

The results of our study indicate that consumption of salted food types, including salted meat, salted fish, pickled vegetables, processed meat, ham, salami, sausage, and bacon, on a frequent basis may increase the risk of oral cancer (17–21,33). According to Zheng et al. 1992 (19), consuming salted meat or fish every week/day causes the risk of oral cancer to double in men and as much as three times in women. The research of Levi et al. (17,20) states that processed meat (ham, salami, and sausage) consumed more than three times a week can increase the risk of oral cancer up to four times. The research of Rajkumar et al. (21) indicates that consumption of ham and salami twice a week or more may result in a fourfold increase in the risk of developing oral cancer. The research of Sapkota et al. (18) suggests that consumption of pickled vegetables once or more in a week can cause a double risk of oral cancer. The research of Toporcov et al. (33) stated that consumption of bacon twice a week or more can lead to a double risk of developing oral cancer, while bacon consumed two or more times a week and accompanied by fried food at least four times in a week can increase the risk of oral cancer by up to 22-fold.

The limitations of this study include that the articles that were obtained were too general because there were no articles that specifically discussed salted food or a certain type of salted food on the risk of oral cancer, nor were there any articles that specifically explained the mechanism of the effect of salted food or one type of salted food against oral cancer. The results of other studies state that there is a possibility of the effect of

other carcinogenic agents apart from N-nitroso, but no one has studied them specifically, so further research is needed to investigate the effect of other carcinogenic agents found in salted food on the risk of oral cancer.

CONCLUSION

According to the results, salted foods have the effect of increasing the risk of oral cancer. Consuming salted foods such as salted meat, processed meat (bacon, ham, salami, sausage, and nitrite meats), pickled food (pickled vegetables, pickled chili, and pickled fruits), salted fish, Chinese salted fish, salted eggs, and salted duck eggs can increase the risk of oral cancer. This is due to the presence of N-nitroso in salted foods, which is a carcinogen and can induce DNA alkylation. Consuming salted foods, such as miso soup, in the heat is harmful as they may damage the mucous membranes. Furthermore, consumption of salted foods, in addition to drinking and smoking, can increase the risk of oral cancer.

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