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Processed meat and the risk of selected digestive tract and laryngeal neoplasms in Switzerland

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Background: Processed meat has been related to the risk of digestive tract neoplasms but the evidence remains inconclusive. We examined data from a network of case–control studies conducted between 1992 and 2002 in the Swiss Canton of Vaud.

Patients and methods: We studied 316 patients with incident, histologically confirmed oral and pharyngeal cancer, 138 patients with oesophageal cancer, 91 patients with laryngeal cancer and 323 patients with colorectal cancer. Controls were 1271 subjects admitted to the same hospital for a wide spectrum of acute non-neoplastic conditions, unrelated to long-term modification of diet.

Results: There were strong direct trends in risk between consumption of processed meat and the various neoplasms considered: the multivariate odds ratios for the highest quartile of intake compared to the lowest were 4.7 for oral and pharyngeal cancer, 4.5 for oesophageal cancer, 3.4 for laryngeal cancer and 2.5 for colorectal cancer. The association was stronger in younger subjects, in moderate drinkers and in non-smokers.

Conclusion: Processed meat represents a strong indicator of unfavourable diet for digestive tract and laryngeal cancer risk in this population.

Key words: cancer, case–control study, colorectum, diet, larynx, meat, oesophagus, oral cavity, pharynx, risk factors

Introduction

Ecological data had suggested that meat may have an unfavourable effect on the risk of several neoplasms, including in particular colorectal and pancreatic cancer [1–5].

Information is scanty and inconsistent with reference to various types of meat, including processed meat. Some processed meats are nitrite-cured and may give origin to nitrosamines, which are potential human carcinogens [6]. Elevated risk in subjects reporting high consumption of processed meats was reported for oral cancer in a case–control study from southern India, with a relative risk (RR) of 4.4 for regular consumers [7], for squamous cell oesophageal cancer [8], adenocarcinoma of the oesophagus and distal stomach [9] in case–control studies from the USA, and for colon cancer in cohort studies from The Netherlands [10] and Norway [11]. In a meta-analysis of published studies on colorectal cancer, however, the RR for the highest versus the lowest level of processed meat (RR = 1.31) was similar to that of red meat (RR = 1.35) [12]. Data are limited and inconclusive for other neoplasms [13, 14], although a series of studies of upper digestive tract and laryngeal cancers from Italy and Switzerland suggested that processed meat was an unfavourable indicator of risk. The RR, however, varied substantially in the two countries, with relatively limited associations for oral and pharyngeal cancer [15] and oesophageal [16] cancer in Italy, and appreciably stronger associations in Switzerland [17–19]. This may be due to chance or bias, but also to different composition or correlates of processed meats in various populations.

To provide further information on the role of processed meat on the risk of selected digestive tract and laryngeal neoplasms, we conducted a comprehensive analysis of data from a network of case–control studies conducted in Switzerland.

Patients and methods

Case–control studies of digestive tract and laryngeal neoplasms were conducted in the Canton of Vaud, Switzerland, between 1992 and 2002 [17–20]. Cases were subjects admitted to the University Hospital of Lausanne with incident, histologically confirmed cancer of the oral cavity and pharynx (316 patients; 251 men, 65 women), oesophagus (138 patients; 111 men, 27 women), larynx (91 patients; 85 men, six women), and colorectum (323 patients; 192 men, 131 women). Overall age range was 26–75 years (median age 61 years).

The control group comprised for oral cavity, pharynx, larynx and oesophagus, 660 subjects (564 men and 96 women) aged 23–75 years (median age 58 years) and, for colorectum, 611 subjects (330 men, 281 women) aged 27–75 years (median age 59 years). Controls were subjects admitted to the same hospital

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Table 1. Odds ratio (OR) and corresponding 95% confidence intervals (CI) among 316 cases of oral and pharyngeal cancer, 138 cases of oesophageal cancer, 91 cases of laryngeal cancer and 660 controls, and 323 cases of colorectal cancer and 611 controls, according to intake quartiles of processed meat (Vaud, Switzerland, 1992–2002)

Cancer site	Intake quartile		OR[a]	OR[b]	χ^2_1 trend
	Frequency/week	Cases:controls	(95% CI)	(95% CI)	(*P* value)
Oral cavity and pharynx	<0.8	35:169	1[c]	1[c]	
	0.8–1.5	40:175	1.18 (0.70–1.97)	1.15 (0.59–2.24)	
	1.6–3.2	79:159	2.74 (1.70–4.42)	2.54 (1.36–4.74)	34.61
	>3.2	162:157	6.05 (3.82–9.56)	4.68 (2.54–8.62)	(<0.001)
Oesophagus	<0.8	15:169	1[c]	1[c]	
	0.8–1.5	22:175	1.54 (0.76–3.11)	1.58 (0.68–3.70)	
	1.6–3.2	34:159	2.62 (1.35–5.09)	2.33 (1.02–5.33)	17.87
	>3.2	67:157	6.16 (3.27–11.58)	4.48 (2.05–9.79)	(<0.001)
Larynx	<0.8	10:169	1[c]	1[c]	
	0.8–1.5	14:175	1.19 (0.51–2.78)	1.38 (0.52–3.68)	
	1.6–3.2	22:159	1.91 (0.86–4.23)	1.81 (0.70–4.67)	8.80
	>3.2	45:157	4.38 (2.09–9.20)	3.42 (1.38–8.46)	(<0.01)
Total	<0.8	60:169	1[c]	1[c]	
	0.8–1.5	76:175	1.28 (0.85–1.93)	1.18 (0.68–2.02)	
	1.6–3.2	135:159	2.55 (1.72–3.76)	2.06 (1.21–3.49)	26.52
	>3.2	274:157	5.78 (3.96–8.42)	3.39 (1.99–5.78)	(<0.001)
Colorectal	<0.8	36:136	1[c]	1[c]	
	0.8–4	46:139	1.23 (0.74–2.04)	1.03 (0.61–1.75)	
	1.6–3.9	111:182	2.28 (1.45–3.56)	1.82 (1.12–2.95)	16.32
	>4	130:154	3.37 (2.15–5.29)	2.53 (1.50–4.27)	(<0.001)

[a]Estimates from multiple logistic regression models adjusted for age and sex.

[b]Estimates further adjusted for education, tobacco smoking, alcohol drinking, total energy intake, and fruit and vegetable intake (for cancers of the upper digestive and respiratory tract); and education, tobacco smoking, alcohol drinking, total energy intake, fruit and vegetable intake, body mass index, and physical activity (for colorectal cancer).

[c]Reference category.

for a wide spectrum of acute, non-neoplastic conditions unrelated to smoking or alcohol consumption and long-term modification of diet. These included traumas (21%), other non-traumatic orthopaedic conditions (26%), acute surgical conditions (38%), and miscellaneous other diseases (15%). Participation rate was over 80% for both cases and controls.

Trained interviewers administered a structured questionnaire to cases and controls during their hospital stay. Information was collected on socio-demographic characteristics, lifestyle habits, including tobacco smoking and alcohol drinking. A food frequency questionnaire including 79 items was used in order to assess subjects' habitual diet, and estimate their total energy intake [17].

Odds ratios (OR) of various cancers and the corresponding 95% confidence intervals (CI) in subsequent quartiles of intake of processed meats (i.e. raw ham, boiled ham, salami and sausages) were estimated using unconditional multiple logistic regression models, including terms for age, sex, education, tobacco smoking, alcohol drinking, fruit and vegetable intake, total energy intake, plus body mass index, and physical activity for colorectal cancer.

Results

Table 1 gives the distribution of cases of upper digestive tract and laryngeal neoplasms, and of colorectal cancer with the corresponding controls according to approximate quartiles of consumption of processed meat, and the corresponding ORs. There were strong increasing trends in risk for oral and pharyngeal cancers (multivariate OR = 4.7 for the highest quartile of intake as compared to the lowest), oesophageal cancers (OR = 4.5) and laryngeal cancers (OR = 3.4). When all upper digestive and respiratory tract neoplasms were considered together, the ORs were 1.2, 2.1 and 3.4 for subsequent consumption quartiles of processed meat, with a highly significant trend in risk. For colorectal cancer, the ORs were 1.0, 1.8 and 2.5 for subsequent consumption quartiles, and the trend in risk was again significant. When single items included in the processed meats were considered (i.e. raw ham; boiled ham; salami, sausages, etc.), stronger risks were found for salami and sausages.

The ORs for all cancers of the upper digestive and respiratory tract combined according to intake quartile of processed meat were further investigated in strata of selected covariates (Table 2). The risks were stronger in subjects <60 years (OR = 4.3 for the upper quartile of intake) than in those aged ≥60 years (OR = 2.9; *P* for interaction = 0.11), in subjects consuming less than three

Table 2. Odds ratio (OR) and corresponding 95% confidence intervals (CI) among 545 cases of cancers of the upper digestive and respiratory tract and 660 controls, according to intake quartiles of processed meat in strata of selected covariates (Vaud, Switzerland, 1992–2002)

Intake quartile	OR[a] (95% CI)					
	Age (years)		Alcohol (drinks/week)		Tobacco smoking	
	<60	≥60	<3	≥3	Non-smokers	Smokers and ex-smokers
I	1[b]	1[b]	1[b]	1[b]	1[b]	1[b]
II	1.67	0.89	1.47	1.03	0.98	1.38
	(0.79–3.55)	(0.39–2.01)	(0.49–4.43)	(0.48–2.22)	(0.21–4.53)	(0.76–2.51)
III	3.50	1.20	3.12	1.44	1.21	1.89
	(1.64–7.47)	(0.56–2.60)	(1.06–9.19)	(0.69–3.01)	(0.25–5.84)	(1.06–3.35)
IV	4.28	2.85	13.08	2.25	7.90	2.71
	(2.03–9.06)	(1.29–6.27)	(4.40–38.94)	(1.09–4.66)	(1.85–33.75)	(1.52–4.83)

[a]Estimates from multiple logistic regression models adjusted for age, sex, education, tobacco smoking, alcohol drinking, total energy intake, and fruit and vegetable intake.
[b]Reference category.

drinks of alcohol per week (OR = 13.1) than in those drinking ≥3 drinks per week (OR = 2.3; P for interaction <0.001), and in non-smokers (OR = 7.9) as compared to smokers and ex-smokers (OR = 2.7; P for interaction <0.001). For colorectal cancer, the OR was 2.7 (95% CI 1.2–5.9) in subjects <60 years, and 2.3 (95% CI 1.1–4.9) in those aged ≥60 years (data not shown).

Discussion

The present findings, from an integrated series of case–control studies conducted in an area where consumption of sausages and other processed meats is relatively high, show a strong association between measures of consumption of these foods and the risk of upper digestive and respiratory tract neoplasms. There was a significant association also for colorectal cancer, though somewhat less strong than for upper digestive and respiratory tract cancers.

As in most case–control studies, selection or information bias may have played some role, but it is in any case unlikely that any such bias can largely or totally account for such strong associations as those observed in this population, since cases and controls came from similar catchment areas, participation was high, and the questionnaire was satisfactorily reproducible and valid [21, 22].

Consumption of processed meat was directly but moderately correlated with tobacco ($r = 0.11$; $P = 0.06$), and alcohol ($r = 0.19$; $P < 0.001$) consumption, and inversely with vegetable ($r = –0.11$; $P = 0.07$) and fruit ($r = 0.10$; $P = 0.01$) intake, but accurate allowance for these covariates, as well as for total energy intake [23] was made in the analyses.

It appears, therefore, that processed meat is a consistent indicator of risk for the neoplasms considered. Processed meat may represent a more general indicator of unfavourable dietary patterns, but the excess risk is too strong to be only explained by any other dietary factor. The association was observed for various types of processed meats (ham, salami and sausages), and, for upper digestive and respiratory tract neoplasms, was apparently stronger in subjects at low baseline risk (i.e. younger age, as well as non- or moderate drinkers, and non-smokers), further suggesting that the confounding effect of these factors is unlikely to totally explain the association observed.

It is more difficult to understand whether the observation of such a strong and consistent relation between processed meat and the neoplasms considered implies causality. Processed meat is rich in saturated fats, which, as opposed to unsaturated ones, have been related to an increased risk of upper digestive and respiratory tract neoplasms [15, 17, 18] and of the large bowel [4]. Nitrates and other additives may also have played some role, although their impact on human carcinogenesis remains unclear [6]. These uncertainties notwithstanding, the strong unfavourable association between a single group of foods and the risk of the neoplasms considered remains remarkable in this population.

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