Processed and unprocessed red meat consumption and hypertension in women[1–3]

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ABSTRACT

Background: High processed red meat consumption is associated with increased risk of cardiovascular disease. The high sodium content of processed red meat could increase blood pressure and explain the association with cardiovascular disease.

Objective: We evaluated the relation between the consumption of unprocessed and processed red meat and incident hypertension.

Design: In a prospective cohort of 44,616 disease-free French women who responded to a validated dietary questionnaire, we observed 10,256 incident cases of hypertension between 1993 and 2008. Cases were identified through self-reports of diagnosed or treated hypertension. Multivariate Cox regression models were adjusted for age, education, smoking, physical activity, body mass index, menopause, menopausal hormone therapy, and alcohol, bread, coffee, and fruit and vegetable consumption.

Results: Women who consumed ≥5 servings of processed red meat/wk (50 g = 1 serving) had a 17% higher rate of hypertension than that of women who consumed <1 serving/wk (HR: 1.17; 95% CI: 1.09, 1.26; *P*-trend = 0.0002). No association was observed between unprocessed red meat consumption and hypertension. When women who consumed ≥5 servings of unprocessed red meat/wk (100 g = 1 serving) were compared with women who consumed <1 serving unprocessed red meat/wk, the multivariate HR was 0.99 (95% CI: 0.91, 1.08; *P*-trend = 0.63).

Conclusions: In this large prospective cohort of French women, we observed an association between the consumption of processed red meat and hypertension. We observed no association for unprocessed red meat consumption and hypertension. *Am J Clin Nutr* 2014;100:948–52.

INTRODUCTION

Red meat consumption is commonly considered a risk factor for cardiovascular disease because of its saturated fat and cholesterol contents (1). Although, in a meta-analysis of observational studies, unprocessed red meat consumption was not associated with coronary artery disease, there was significant 42% higher risk of coronary artery disease per consumption of a 50-g serving processed red meat/d (2). On the basis in part of studies included in the meta-analysis, the American Heart Association's 2006 Dietary Recommendations (3) and 2020 Impact Goals (4) specifically advocated the reduction of processed red meat consumption. However, lean processed red meats are still considered good alternatives because of their low saturated fat content (5). Therefore, providing additional information on the potential effects of processed red meats on cardiovascular disease risk may be important to strengthen dietary recommendations that promote health.

Processed and unprocessed red meats differ most notably in their sodium and nitrite contents, which are commonly used as preservatives in processed meats (2). Because sodium consumption has important effects on blood pressure (6), the strong association observed between processed red meat and coronary artery disease could be mediated by its effects on blood pressure. However, there has been limited information on the relation between processed and unprocessed red meat consumption and incident hypertension (7). Therefore, we investigated the relation between unprocessed and processed red meat consumption and incidence of hypertension in a large prospective cohort of French women.

SUBJECTS AND METHODS

Study population

The Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale (E3N) prospective study is

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a French study that started in 1990 when 98,995 women born between 1925 and 1950 and affiliated with a health insurance plan that covers mostly teachers and their spouses responded to a mailed questionnaire (8). Participants returned mailed questionnaires on reproductive characteristics, lifestyles, and newly diagnosed diseases in 1992, 1993, 1994, 1997, 2000, 2002, 2005, and 2008. Loss to follow-up has been low (3%) with an average follow-up in each questionnaire cycle of 83%. The E3N is the French component of the European Prospective Investigation into Cancer and Nutrition (9). All women signed an informed consent in compliance with the French National Commission for Computerized Data and Individual Freedom.

In 1993, 74,154 women responded to a follow-up questionnaire and validated self-administered diet-history questionnaire (8). We excluded women with no follow-up after 1993 ($n = 935$), prevalent stroke, coronary artery disease or hypertension ($n = 27,684$), or an unrealistic energy consumption ($n = 919$) defined by the first and 99th percentile of the ratio of energy intake to the basal metabolic rate computed on the basis of age, height, and weight (10). The final study population was 44,616 women.

Dietary and covariate assessment

Between 1993 and 1995, dietary data were collected by using a validated 208-item self-administered diet-history questionnaire, with 11 categories of frequency of never or <1 time/mo, 1–3 times/mo, and 1–7 times/wk (8). Unprocessed red meat was defined as beef, pork, veal, horse, and sheep, whereas processed red meat was defined as sausage, salami, bacon, and ham. Energy intake was calculated by using a food-composition table derived from a French national database.

The validity and reproducibility of our dietary assessment questionnaire has been previously described (11). Briefly, in 1990, a sample of 119 females, similar to participants in the E3N study, were asked to complete 2 diet-history questionnaires at the beginning and end of the 1-y study period. Both questionnaires were compared with twelve 24-h dietary recalls carried out monthly throughout the study period (8). Correlation coefficients between the 1991 diet-history questionnaire, and 24-h recalls were 0.52 for unprocessed meat and 0.39 for processed meat.

Self-reported weight and height were used to calculate BMI (in kg/m^2), which was defined as weight divided by height squared (12). Individuals were classified as never, past, and current smokers. Treated hypercholesterolemia was based on self-reports. Menopausal status was determined by using information on the last menstruation, hot flushes, hysterectomy, ovariectomy and hormonal treatments. Regular moderate physical activity and vigorous physical activity were assessed by using a validated physical activity questionnaire, and responses were transformed to weekly metabolic equivalents (13). For alcohol, individuals were asked to specify the frequency of intake, glass size, and number of glasses of beer, cider, wine, port, and liquor, and this value was converted to grams per day.

Ascertainment of hypertension

At baseline in 1993 and in all subsequent questionnaires, participants reported hypertension diagnoses and treatments. We identified individuals who self-reported a diagnosis of hypertension or antihypertensive treatment. Most participants (68%) who reported a diagnosis of incident hypertension reported the month and year of diagnosis. For individuals who were missing the month of diagnosis, the date was imputed as June of the year of diagnosis. The median time between the date of diagnosis and date response to the questionnaire after the diagnosis was 12 mo; therefore, we assigned the date of diagnosis for individuals without one to be 12 mo before their report of hypertension. In 2004, a claims database became available for all participants. For cases identified after 2004, we used either the self-reported date of diagnosis or the first date of drug reimbursement for antihypertensive medications [diuretics, β-blockers, calcium, and angiotensin-converting enzyme inhibitors (Anatomical Therapeutic Chemical Classification System codes C02, C03, C07, C08, and C09)], with whatever happened first as the date of diagnosis. In addition, the claims database enabled us to evaluate the validity of self-reports. In women who were alive in January 2004 and up to their response to the last questionnaire in 2008, we observed a positive predictive value of 82% of self-reported hypertension when we compared the self-report to a drug reimbursement that corresponded to any of the previously specified codes.

Statistical analysis

Foods were energy-adjusted by using the residual method (14), and subsequently, the consumption of unprocessed and processed red meat was categorized (<1, 1–2.9, 3–4.9, and ≥5 servings/wk) and evaluated in indicator categories with the lowest category of intake as the referent. For unprocessed red meat, we considered one serving to be equal to 100 g. Conversely, 50 g were considered to represent one typical serving of processed red meat. The median value for each category was used as a continuous variable to test for a trend. Servings per day were also evaluated continuously. We calculated the person-time from the date of completion of the dietary questionnaire to the date of diagnosis, last follow-up available, or 25 June 2008, whichever occurred earliest.

HRs and 95% CIs were estimated from Cox regression models with age as the time scale (SAS 9.3; SAS Institute Inc). Final multivariable models were mutually adjusted for processed and unprocessed meat and adjusted for education (less than high school, high school, and college), smoking (never, past, and current), physical activity (metabolic equivalent tasks per week; quartiles), menopause or menopausal hormone therapy (premenopausal, menopausal hormone therapy current, past, or never use), BMI (<18.5, 18.5–22.4, 22.5–24.9, 25–29.9, and ≥30), and quartiles of intakes of energy, alcohol, fruit and vegetables, bread, and coffee. Because smoking is a major risk factor for hypertension, and smoking intensity was unavailable, we explored whether associations differed by smoking status (never, past, and current) in stratified analyses. We investigated the potential modifying effect of BMI in analyses stratified on BMI as <25 or ≥25. To test for heterogeneity, we included a cross-product term of the median value of intake for each category of meat consumption as a continuous variable and the 2 BMI categories and compared models with and without the cross-product term by using a log-likelihood test. All covariates had <5% of missing values; therefore, those values were replaced by modal (qualitative variables) or median (quantitative variables) values in subjects with complete data.

RESULTS

The mean (±SD) age at baseline was 51.9 ± 6.3 y. Mean unprocessed red meat consumption was 2.8 ± 0.9 servings/wk, whereas mean weekly processed red meat servings were 2.5 ± 1.0 servings/wk. Ham represented 55% of processed red meat intake, sausages represented 29% of processed red meat intake, salami represented 9% of processed red meat intake, and bacon represented 7% of processed red meat intake. Main contributors to unprocessed red meat were beef (33%), pork (24%), mutton (21%), and veal (18%). The highest proportion of current smokers was observed in the highest category of consumption of both processed and unprocessed red meats (**Table 1**). Consumptions of both types of red meat were positively associated with BMI and alcohol and coffee intakes. The mean caloric intake appeared to be the lowest for both the upper energy-adjusted quartiles of processed and unprocessed red meat consumption. Education was inversely associated with processed red meat consumption, whereas the association was in the opposite direction with unprocessed red meat. Physical activity and unprocessed red meat intake were inversely related.

After an average 13.8 y of follow-up and 536,997 person-years, we identified 10,256 cases of incident hypertension (19 cases/1000 person-years). The incidence of hypertension in participants in the highest category of processed red meat consumption was 20/1000 person-years, whereas it was 17/1000 person-years in those in the lowest category. The age-adjusted HR was 1.28 (95% CI: 1.20, 1.37; *P*-trend < 0.0001) for women who reported the consumption of ≥5 servings processed red meat/wk compared with women who consumed <1 serving processed red meat/wk. This estimate was somewhat attenuated after adjustment for BMI, which was a potential intermediate variable, but remained significant. Thus, the multivariable-adjusted HR for the comparison of women who consumed ≥5 servings processed red meat/wk with women who consumed <1 serving processed red meat/wk was 1.17 (95% CI: 1.09, 1.26; *P*-trend = 0.0002) (**Table 2**). When we evaluated processed red meat continuously, we observed a 2% increase in the rate of hypertension for an increase of a 50-g serving/wk (HR: 1.02; 95% CI: 1.01, 1.02). In multivariate analyses that considered individual types of processed red meat, ham, which was the most-consumed processed meat, was associated with hypertension (HR for extreme quartiles: 1.18; 95% CI: 1.12, 1.26; *P*-trend < 0.0001), whereas the other types were not.

For unprocessed red meat, incidence rates for highest and lowest intake categories were 19 and 21/1000 person-years, respectively. There was no association between unprocessed red meat consumption and incident hypertension [the HR for comparison of extreme categories was 0.99 (95% CI: 0.91, 1.08; *P*-trend = 0.63]. We observed no association when unprocessed red meat was included as a continuous variable [the HR for each 100-g serving/d was 1.00 (95% CI: 1.00, 1.01)].

In models stratified on smoking status, unprocessed red meat was not associated with hypertension. For processed red meat, associations tended to be strongest in never smokers, whereby women in the highest category of intake had a 25% higher rate of hypertension than that of women in the lowest category (HR: 1.25 95% CI: 1.13, 1.38; *P*-trend = 0.0002). There was no evidence of a difference in associations between processed meat and hypertension according to BMI. HRs for the comparison of extreme categories of processed red meat consumption were 1.19 (95% CI: 1.10, 1.29; *P*-trend = 0.0003) and 1.22 (95% CI: 1.04, 1.42; *P*-trend = 0.03) in women with BMI <25 and ≥25, respectively (*P*-heterogeneity = 0.85).

DISCUSSION

In this large prospective study, processed but not unprocessed red meat consumption was associated with the incidence of hypertension even after adjustment for main risk factors for hypertension. Conversely, we did not observe an association between unprocessed red meat and incident hypertension.

The median sodium content of a 50-g serving of processed red meat in the national nutrient database for France was 450 mg

TABLE 1
Age-standardized risk factors by processed and unprocessed red meat consumption in a cohort of 44,616 French women in 1993[1]

	Processed red meat (servings/wk)				Unprocessed red meat (servings/wk)			
	<1	1–2.9	3–4.9	≥5	<1	1–2.9	3–4.9	≥5
Persons (*n*)	6449	17,911	11,267	8989	3253	13,588	14,834	12,941
Median consumption (g/d)	4	16	26	39	7	31	56	87
Risk factors								
College education (%)	41.6	38.1	38.0	38.7	34.2	37.2	38.1	42.0
Current smoker (%)	12.7	13.4	14.8	17.0	13.9	13.4	13.5	16.5
Mean BMI (kg/m^2)	22.0	22.3	22.5	22.7	21.9	22.2	22.4	22.7
Physical activity (METs/wk)	55 ± 30[2]	55 ± 30	54 ± 30	52 ± 29	57 ± 31	57 ± 31	55 ± 30	51 ± 28
Current use of HRT (%)	23.0	21.7	21.3	22.9	19.7	22.1	22.2	22.3
Dietary intake								
Total energy (calories/d)	2179 ± 628	2265 ± 548	2087 ± 453	1862 ± 402	2103 ± 614	2243 ± 582	2155 ± 507	1978 ± 447
Alcohol (g/d)	9 ± 13	10 ± 14	13 ± 16	16 ± 20	9 ± 15	10 ± 14	12 ± 14	15 ± 19
Fruit and vegetables (g/d)	545 ± 253	483 ± 219	455 ± 204	451 ± 212	518 ± 264	479 ± 226	471 ± 211	477 ± 215
Coffee (cups/d)	2.2 ± 2.3	2.2 ± 2.1	2.4 ± 2.1	2.7 ± 2.4	2.2 ± 2.4	2.2 ± 2.2	2.3 ± 2.1	2.6 ± 2.3
Bread (g/d)	126 ± 90.9	114 ± 78	115 ± 75	115 ± 81	131 ± 104	115 ± 80.4	115 ± 75	115 ± 77

[1] HRT, hormone replacement therapy; MET, metabolic equivalent task.
[2] Mean ± SD (all such values).

TABLE 2
Age-adjusted and multivariable-adjusted HRs (95% CIs) of hypertension according to servings of processed and unprocessed red meat in the E3N cohort study (1993–2008)[1]

	Servings/wk				
	<1	1–2.9	3–4.9	≥5	*P*-trend[2]
Processed meat					
Cases	1348	4119	2617	2172	—
Persons	6449	17,911	11,267	8989	—
Person-years	78,678	217,058	135,180	106,081	—
Age adjusted	Reference	1.15 (1.08, 1.23)	1.20 (1.13, 1.29)	1.28 (1.20, 1.37)	<0.0001
Multivariate[3]	Reference	1.14 (1.08, 1.22)	1.19 (1.12, 1.27)	1.27 (1.18, 1.36)	<0.0001
Plus diet[4]	Reference	1.14 (1.07, 1.21)	1.18 (1.11, 1.26)	1.25 (1.16, 1.34)	<0.0001
Plus diet[5]	Reference	1.14 (1.07, 1.21)	1.18 (1.10, 1.26)	1.25 (1.16, 1.34)	<0.0001
Plus diet plus BMI[5]	Reference	1.11 (1.05, 1.19)	1.13 (0.19, 1.21)	1.17 (1.09, 1.26)	0.0002
Unprocessed meat					
Cases	735	3094	3403	3024	—
Persons	3253	13,588	14,834	12,941	—
Person-years	38,554	163,479	179,806	155,158	—
Age adjusted	Reference	1.00 (0.93, 1.09)	1.02 (0.94, 1.10)	1.07 (0.99, 1.16)	0.0098
Multivariate[3]	Reference	1.01 (0.93, 1.09)	1.03 (0.95, 1.11)	1.08 (1.00, 1.18)	0.004
Plus diet[4]	Reference	1.01 (0.93, 1.09)	1.02 (0.94, 1.10)	1.07 (0.99, 1.17)	0.009
Plus diet[5]	Reference	0.98 (0.91, 1.07)	0.99 (0.92, 1.08)	1.05 (0.96, 1.14)	0.02
Plus diet plus BMI[5]	Reference	0.97 (0.90, 1.06)	0.97 (0.90, 1.05)	0.99 (0.91, 1.08)	0.63

[1] E3N, Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale.
[2] Wald's test.
[3] Adjusted for education, smoking (never, past, and current), physical activity metabolic equivalent tasks per week (quartiles), hormone replacement therapy (premenopausal, current, past, and never), and energy (quartiles).
[4] Additional adjustment for alcohol (quartiles), fruit and vegetables (quartiles), bread (quartiles), and coffee (quartiles).
[5] Additional mutual adjustment.

in 1995. In contrast, an equivalent serving of unprocessed red meats contained 35 mg Na (15). In a nationally representative survey in France in 1998–1999, the sodium content of cooked pork meats was 5 times higher than that of unprocessed meats (16). High sodium intake triggers a physiologic response that results in increased intravascular volume and blood pressure (17). A recent meta-analysis that used information from 36 studies showed that a sodium reduction results in a reduction of blood pressure (18). Therefore, it is possible that the observed relation resulted from increased salt intake. Four recent prospective studies in the United States and Europe evaluated the relation between red meat consumption and coronary artery disease and mortality, and results supported strong associations for processed red meat intake and smaller or no associations with unprocessed red meat (19–21). Fewer studies have evaluated the association of meat consumption with blood pressure and hypertension (7, 22–26), and results have widely varied according to definitions of red meat and the differentiation of processed and unprocessed red meat. Two prospective Dutch studies that evaluated meat and hypertension risk provided null results, but the studies included poultry in the meat group (22, 23). A cross-sectional study on 17 population samples reported an association between meat intake and blood pressure (25). In this cross-sectional analysis, the relation was attenuated when the exposure was restricted to beef, which suggested that the association could have been driven by other meats including processed meats. In the Coronary Artery Risk Development in Young Adults study after 15 y of follow-up, a 39% higher rate of hypertension was observed for highest compared with lowest categories of intake; unfortunately, no distinction was made between unprocessed and processed red meat (24). The only study that made an explicit distinction between processed and unprocessed red meat was the Women's Health Study (7). Compared with the referent category, the rate of hypertension was ∼30% higher in women in the highest category for both processed and unprocessed red meat. However, in that study, women in the reference category were nonmeat eaters. Nonconsumption of red meat may be a marker of several health-seeking behaviors, and thus, the referent group may be one at particularly low risk of hypertension. In contrast, in our analysis, the referent category included individuals who consumed some red meat, which minimized the possibility that the referent group included individuals who differed drastically in other health-related behaviors from the rest of participants.

The current analysis had important strengths, including a prospective design, limited loss to follow-up, large number of cases, and the use of a validated dietary questionnaire. Nevertheless, there were some limitations to consider. Confounding by unmeasured factors such as dietary factors before baseline, genetic susceptibility, or determinants of behavior can never be ruled out. We were able to adjust for all well-known risk factors for hypertension with the exception of smoking intensity. However, we conducted analyses in nonsmokers to rule out the possibility that the observed association was attributable to residual confounding and showed that the association remained present. Measurement error is an important concern in studies that use a self-reported diet. In addition, we were only able to assess diet at baseline, and we could not exclude the possibility that participants may have changed their diets during follow-up. A reduction of red meat consumption is regarded as a healthy behavior, and if individuals reduced red meat consumption over time, our results may have been attenuated by an exposure

misclassification. We used self-reported information to identify cases of hypertension, and we may have misclassified individuals. The 82% positive predictive value for self-reported hypertension compared with that in a drug-claims database lent support to the validity of our outcome assessment. However, because some individuals may have received nonmedical treatment, it is possible that the use of the claims database may have underestimated the validity of the self-report. However, even in the presence of misclassification, self-reported hypertension is unlikely to be related to exposure status, and thus, this nondifferential misclassification would have also resulted in an attenuation of observed associations.

In conclusion, our results suggest that processed red meat consumption is associated with hypertension, whereas unprocessed red meat consumption is not. These observations support increased blood pressure through sodium intake as the underlying mechanism for the somewhat different association observed between unprocessed and processed red meat and cardiovascular disease. Dietary recommendations should focus on the avoidance of preservatives such as the ones shown in processed red meats and other highly processed foods.

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