Red meat consumption and risk of stroke in Swedish men

Susanna C Larsson, Jarmo Virtamo, and Alicja Wolk

ABSTRACT

Background: Red and processed meat consumption has been implicated in several diseases. However, data on meat consumption in relation to stroke incidence are sparse.

Objective: Our objective was to examine the associations of red meat and processed meat consumption with stroke incidence in men.

Design: We prospectively followed 40,291 men aged 45–79 y who had no history of cardiovascular disease or cancer at baseline. Meat consumption was assessed with a self-administered questionnaire in 1997.

Results: During a mean follow-up of 10.1 y, 2,409 incident cases of stroke (1,849 cerebral infarctions, 350 hemorrhagic strokes, and 210 unspecified strokes) were identified from the Swedish Hospital Discharge Registry. Consumption of processed meat, but not of fresh red meat, was positively associated with risk of stroke. The multivariable relative risks (RRs) of total stroke for the highest compared with the lowest quintiles of consumption were 1.23 (95% CI: 1.07, 1.40; P for trend = 0.004) for processed meat and 1.07 (95% CI: 0.93, 1.24; P for trend = 0.77) for fresh red meat. Processed meat consumption was also positively associated with risk of cerebral infarction in a comparison of the highest with the lowest quintile (RR: 1.18; 95% CI: 1.01, 1.38; P for trend = 0.03).

Conclusion: The findings from this prospective cohort of men indicate that processed meat consumption is positively associated with risk of stroke. The Cohort of Swedish Men is registered at clinicaltrials.gov as NCT01127711. Am J Clin Nutr 2011;94:417–21.

INTRODUCTION

Reduced consumption of red meat and avoidance of processed meat has been recommended as a way to lower the risk of cancer (1). Recent evidence has also indicated that high consumption of red meat, particularly processed meat, may be a risk factor for coronary heart disease (2–4) and type 2 diabetes (3). Red meat consumption has been positively associated with blood pressure (5), incidence of hypertension (6, 7), the metabolic syndrome (8), and inflammation (8). Although red meat consumption may be a risk factor for stroke, epidemiologic studies of red meat consumption in relation to stroke incidence or mortality are sparse and results are inconsistent (9–12). We recently reported on the associations of red and processed meat consumption with stroke incidence in the Swedish Mammography Cohort (12). In that cohort of women, a high processed meat consumption was associated with a statistically significant increased risk of stroke (12). To our knowledge, only 2 previous studies, 1 in the United States (10) and 1 in Japan (11), have examined the relation between red meat consumption and stroke incidence (10) or mortality (11) in men. For elucidating potential biological mechanisms and guiding policy priorities, it is important to assess fresh red meat and processed meat consumption separately in relation to stroke risk. The aim of this study was to investigate the associations of fresh red meat and processed meat consumption with stroke incidence in a large prospective cohort of Swedish men with 11 y of follow-up.

SUBJECTS AND METHODS

Study population

The Cohort of Swedish Men was initiated in the autumn of 1997, when all men who were aged 45–79 y and resided in the Västmanland and Örebro counties of central Sweden received a questionnaire that included ~350 items concerning diet and other lifestyle factors. Of the 48,850 men (49% of the source population) who returned a completed questionnaire, we excluded those with an erroneous or a missing national identification number and those with implausible values for total energy intake (ie, 3 SDs from the log-transformed mean energy intake). We further excluded men with a history of stroke, coronary heart disease, or cancer at baseline because these diseases might have caused a change in diet. After these exclusions, 40,291 men remained for analysis. The study was approved by the Regional Ethical Review Board at the Karolinska Institutet (Stockholm, Sweden).

Baseline data collection

Information on education, body weight, height, smoking status and history, physical activity, aspirin use, history of diabetes and hypertension, family history of myocardial infarction before age 60 y, alcohol consumption, and diet was obtained in 1997 by
using a self-administered questionnaire. Body mass index (BMI) was calculated by dividing the weight (in kg) by the square of height (in m). Pack-years of smoking history were calculated as the number of packs of cigarettes smoked per day multiplied by the number of years of smoking. Participants reported their level of activity at work, home/housework, walking/bicycling, and leisure-time exercise in the year before study enrollment. The questionnaire also included questions on inactivity (watching television and reading) and hours per day of sleeping and sitting/lying down. The time spent per day at each activity was multiplied by its typical energy expenditure requirements (expressed in metabolic equivalents (METs) and added together to create a MET-h/d (24-h) score (13).

Dietary assessment

Diet was assessed with a 96-item food-frequency questionnaire. Participants were asked to indicate how often, on average, they had consumed various foods over the past year, with 8 predefined frequency categories ranging from never to ≥3 times/d. We grouped meat into total red meat, fresh red meat, and processed meat. Fresh red meat consumption was calculated by using the frequency of consumption and age-specific portion size information of all types of fresh and minced pork, beef, and veal. Processed meats included sausages, hot dogs, salami, ham, processed meat cuts, liver paté, and blood sausage. Total red meat was the sum of fresh red meat and processed meat. The food-frequency questionnaire has been validated for nutrients (14), but not for food items, in 248 Swedish men aged 40–74 y; the mean Spearman correlation coefficients between estimates from the dietary questionnaire and the mean of fourteen 24-h recall interviews were 0.65 for macronutrients and 0.62 for micronutrients (14). The age-specific portion sizes (based on two 1-wk weighted dietary records) for fresh red meat ranged from 97 to 147 g per serving. For processed meat, the age-specific portion sizes ranged from 15 to 24 g (liver paté) to 133–150 g (blood sausage).

Case ascertainment and follow-up

Incident cases of first stroke that occurred between 1 January 1998 and 31 December 2008 were ascertained by linkage of the study cohort with the Swedish Hospital Discharge Registry, which provides virtually complete coverage of the discharges. The International Classification of Diseases 10th revision was used to identify stroke events. Strokes were classified as cerebral (ICD-10 code I60), subarachnoid hemorrhage (I61), intracerebral hemorrhage (I62), and unspecified stroke (I64). Compared with men in the lowest quintiles of red meat consumption, those in the highest quintiles were younger and were more likely to use aspirin (Table 1). High consumption of red meat, fresh red meat, and processed meat was associated with higher intakes of total energy, alcohol, monounsaturated fat, polyunsaturated fat, fish, fruit, vegetables, whole grains, and dairy foods. Men with a high consumption of total red meat and processed meat were less likely to have a university education and had a slightly higher BMI than did men with low consumption.

We observed no statistically significant dose-response association between total red meat consumption and risk of total stroke, cerebral infarction, or hemorrhagic stroke (Table 2). However, compared with men in the lowest quintile of red meat consumption, those in the highest quintile had a statistically significant increased risk of total stroke and hemorrhagic stroke.

Consumption of fresh red meat was not associated with total stroke or any stroke subtype (Table 3). Processed meat consumption was statistically significantly positively associated with risk of total stroke and cerebral infarction but not hemorrhagic stroke after adjustment for other risk factors (Table 3). The multivariable RR of total stroke for men in the highest quintile of processed meat consumption compared with those in the lowest quintile was 1.23 (95% CI: 1.07, 1.40). Additional adjustment for consumption of whole grains and dairy foods did not change the results materially. For example, the multivariable RR of total stroke for the highest compared with the lowest quintile of processed meat consumption was 1.23 (95% CI: 1.07, 1.41) after further adjustment for intakes of whole grains and dairy foods. The results were not altered appreciably when men with diabetes were excluded from the analysis. In men without diabetes, the multivariable RR of total stroke in a comparison of the highest with the lowest quintile of processed meat consumption was 1.19 (95% CI: 1.03, 1.39).
TABLE 1
Age-standardized characteristics of 40,291 men in the cohort of Swedish men by quintile (Q) of total red meat, fresh red meat, and processed meat consumption in 1997.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total red meat</th>
<th>Fresh red meat</th>
<th>Processed meat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1</td>
<td>Q5</td>
<td>P value(^2)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>63.2 ± 9.8</td>
<td>56.6 ± 8.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education, university (%)</td>
<td>18.4</td>
<td>16.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>26.3</td>
<td>26.9</td>
<td>0.36</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>25.7 ± 3.3</td>
<td>25.9 ± 3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total physical activity (MET-h/d)</td>
<td>41.8 ± 4.8</td>
<td>41.8 ± 4.9</td>
<td>0.56</td>
</tr>
<tr>
<td>History of diabetes (%)</td>
<td>5.2</td>
<td>6.6</td>
<td>0.11</td>
</tr>
<tr>
<td>Family history of myocardial infarction (%)</td>
<td>13.6</td>
<td>13.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily dietary intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>2286 ± 745</td>
<td>3199 ± 746</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol (g)</td>
<td>9.0 ± 8.4</td>
<td>11.8 ± 8.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>33.7 ± 9.4</td>
<td>35.9 ± 7.1</td>
<td>0.37</td>
</tr>
<tr>
<td>Monounsaturated fat (g)</td>
<td>23.4 ± 4.7</td>
<td>27.4 ± 3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Polyunsaturated fat (g)</td>
<td>9.5 ± 2.5</td>
<td>10.5 ± 1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fish (servings)</td>
<td>0.2 ± 0.3</td>
<td>0.4 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fruit (servings)</td>
<td>1.4 ± 1.2</td>
<td>1.7 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vegetables (servings)</td>
<td>2.2 ± 1.7</td>
<td>3.1 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Whole grains (servings)</td>
<td>4.2 ± 2.6</td>
<td>4.5 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dairy foods (servings)</td>
<td>5.3 ± 3.1</td>
<td>6.0 ± 3.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^1\) MET, metabolic equivalent of energy expenditure (kcal/kg × h).
\(^2\) P for trend across quintiles of meat consumption was calculated by using generalized linear models.
\(^3\) Mean ± SD (all such values).

When we analyzed total red meat consumption as a continuous variable, the multivariable RR of total stroke was 1.07 (95% CI: 1.00, 1.14) for a 100-g/d increment of total red meat consumption. The corresponding RRs were respectively 1.01 (95% CI: 0.96, 1.06) and 1.08 (95% CI: 1.01, 1.15) for a 50-g/d increase in fresh red meat and processed meat consumption.

Hypertension and diabetes may be intermediates of the association between red meat consumption and stroke. When we removed history of hypertension and diabetes variables from the multivariable model, the RRs of total stroke in a comparison of the highest with the lowest quintile of consumption were 1.06 (95% CI: 0.92, 1.23) for fresh red meat and 1.26 (95% CI: 1.10, 1.41) for processed meat.

TABLE 2
Relative risks (95% CIs) of total stroke and stroke subtypes by total red meat consumption in 40,291 men in the cohort of Swedish men, 1998–2008.

<table>
<thead>
<tr>
<th>Red meat consumption (g/d)</th>
<th>&lt;62.5</th>
<th>62.5–88.3</th>
<th>88.4–110.3</th>
<th>110.4–136.1</th>
<th>≥136.2</th>
<th>P for trend(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total stroke Person-years</td>
<td>80,842</td>
<td>79,858</td>
<td>82,414</td>
<td>82,086</td>
<td>82,441</td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>644</td>
<td>554</td>
<td>466</td>
<td>361</td>
<td>384</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>1.03 (0.92, 1.15)</td>
<td>1.03 (0.91, 1.16)</td>
<td>0.96 (0.84, 1.10)</td>
<td>1.10 (0.97, 1.25)</td>
<td>0.33</td>
</tr>
<tr>
<td>Multivariable(^3)</td>
<td>1.00</td>
<td>1.06 (0.94, 1.19)</td>
<td>1.08 (0.95, 1.22)</td>
<td>1.02 (0.89, 1.17)</td>
<td>1.15 (1.00, 1.33)</td>
<td>0.10</td>
</tr>
<tr>
<td>Cerebral infarction No. of cases</td>
<td>515</td>
<td>420</td>
<td>357</td>
<td>279</td>
<td>278</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>0.97 (0.85, 1.11)</td>
<td>0.99 (0.87, 1.14)</td>
<td>0.94 (0.81, 1.09)</td>
<td>1.01 (0.87, 1.17)</td>
<td>0.91</td>
</tr>
<tr>
<td>Multivariable(^3)</td>
<td>1.00</td>
<td>1.01 (0.88, 1.15)</td>
<td>1.04 (0.90, 1.20)</td>
<td>1.00 (0.85, 1.17)</td>
<td>1.06 (0.90, 1.25)</td>
<td>0.53</td>
</tr>
<tr>
<td>Hemorrhagic stroke No. of cases</td>
<td>75</td>
<td>89</td>
<td>56</td>
<td>56</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>1.36 (1.00, 1.84)</td>
<td>0.99 (0.70, 1.39)</td>
<td>1.09 (0.77, 1.55)</td>
<td>1.52 (1.10, 2.12)</td>
<td>0.06</td>
</tr>
<tr>
<td>Multivariable(^3)</td>
<td>1.00</td>
<td>1.38 (1.01, 1.88)</td>
<td>0.99 (0.69, 1.42)</td>
<td>1.14 (0.79, 1.65)</td>
<td>1.57 (1.09, 2.25)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

\(^1\) Relative risks and 95% CIs were estimated by using Cox proportional hazards regression models.
\(^2\) The test for trend was calculated by using the median red meat consumption in each quintile as a continuous variable.
\(^3\) The multivariable model was adjusted for age, smoking status, pack-years of smoking, education, BMI, total physical activity, histories of diabetes and hypertension, aspirin use, family history of myocardial infarction, and intakes of total energy, alcohol, fish, fruit, and vegetables.
DISCUSSION

In this prospective cohort of men, consumption of processed meat, but not of fresh red meat, was statistically significantly positively associated with risk of stroke. The risk of stroke increased by 8% for every 50-g/d increase of processed meat consumption.

Only a few previous studies have examined the association between red meat consumption and stroke incidence or mortality (9–12). Results from this study are consistent with those of the Swedish Mammography Cohort (12). In that cohort, women in the highest quintile of processed meat consumption had a statistically significant 24% increased risk of cerebral infarction compared with women in the lowest quintile (12). Results from the Nurses’ Health Study also showed a statistically significant positive association between red and processed meat consumption and risk of cerebral infarction (P for trend = 0.005) (9). No association between red meat consumption and incidence of cerebral infarction or hemorrhagic stroke was observed in the Health Professionals Follow-Up Study (10). In a cohort of Japanese men and women, no association was observed between consumption of fresh beef and pork or pork products (such as ham and sausage) and total stroke mortality (11).

Red meat is a major source of bioavailable heme iron. Elevated iron stores may cause oxidative injury and has been associated with inflammation (16, 17), insulin resistance (18, 19), the metabolic syndrome (20), and type 2 diabetes (21). In an experimental study, the intracellular iron chelator desferrioxamine inhibited inflammation and atherosclerosis in mice, which suggests a role of iron in atherogenesis (22). A high intake of cholesterol, which is found in red meat, has been shown to raise blood total and LDL-cholesterol concentrations (23, 24) and thus suggests a role of iron in atherogenesis (22).

Processed meat (g/d) was statistically significantly associated with risk of total stroke and cerebral infarction (P for trend = 0.044) for processed meat. The associations of fresh red meat and processed meat consumption (analyzed as continuous variables) were not modified by history of hypertension (9–12). Results from this study are consistent with those of the Swedish Mammography Cohort (12). In that cohort, women in the highest quintile of processed meat consumption had a statistically significant 24% increased risk of cerebral infarction compared with women in the lowest quintile (12). Results from the Nurses’ Health Study also showed a statistically significant positive association between red and processed meat consumption and risk of cerebral infarction (P for trend = 0.005) (9). No association between red meat consumption and incidence of cerebral infarction or hemorrhagic stroke was observed in the Health Professionals Follow-Up Study (10). In a cohort of Japanese men and women, no association was observed between consumption of fresh beef and pork or pork products (such as ham and sausage) and total stroke mortality (11).

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Sodium found in processed meats may explain the observed positive association between processed meat consumption and risk of total stroke and cerebral infarction. Reduced sodium intake has been found to significantly lower blood pressure in hypertensive patients (27).

The test for trend was calculated by using the median red meat consumption in each quintile as a continuous variable.

The multivariable model was adjusted for age, smoking status, pack-years of smoking, education, BMI, total physical activity, histories of diabetes and hypertension, aspirin use, family history of myocardial infarction, and intakes of total energy, alcohol, fish, fruit, and vegetables. Fresh red meat and processed meat were included in the same multivariable model.

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individuals (27). Hypertension is one of the most important risk factors for stroke. In a cohort study of 4304 men and women, high consumption of red and processed meat was associated with an increased risk of high blood pressure (6). Likewise, a cohort of 28,766 US women found a positive association between total red meat consumption and incidence of hypertension (7). A high sodium intake may also promote vascular stiffness (28). Furthermore, a low-sodium diet has been shown to reduce oxidative stress and improve vascular function in salt-sensitive individuals (29). Given that consumption of processed meat but not of fresh meat was positively associated with stroke risk, it is more likely that sodium and/or nitrite in processed meat rather than heme iron and cholesterol explain the observed association. These findings imply that meats that are currently considered healthier by the public and policymakers—such as low-fat deli turkey, ham, and bologna—may increase the risk of stroke.

The major strengths of this study included its prospective and population-based design and the virtually complete follow-up of study participants by linkage with population-based Swedish registers. Furthermore, this study included a large number of incident stroke cases, leading to high statistical power. This was the largest study to date on red and processed meat consumption in relation to risk of stroke. A limitation of this study was its observational design. Hence, we cannot entirely exclude the possibility that men with high consumption of red and processed meat were at increased risk of stroke as a result of other unhealthy habits and behaviors. However, our results persisted after adjustment for potential confounders, including other dietary factors. Residual confounding due to incomplete adjustment for other risk factors for stroke may have led to either attenuated or exaggerated risk estimates. Because diet was assessed with the use of a self-administered food-frequency questionnaire, and only once (at baseline), some measurement error in assessing meat consumption was inevitable. Nondifferential misclassification would most likely lead to an underestimation of the risk estimates for the associations between meat consumption and risk of stroke.

In conclusion, the results from this prospective cohort of men suggest that high consumption of processed meat may increase the risk of stroke. The associations of fresh red meat and processed meat consumption with stroke risk merit investigation in further prospective studies.

The authors’ responsibilities were as follows—SCL and AW: study concept and design; AW: data collection; SCL: statistical analyses and manuscript writing; and SCL, JV, and AW: interpretation of results and critical revision of manuscript. None of the authors had a personal or financial conflict of interest.

REFERENCES