Red Meat Consumption and Risk of Stroke in Swedish Women

Susanna C. Larsson, PhD; Jarmo Virtamo, MD; Alicja Wolk, DMSc

Background and Purpose—High red meat consumption has been associated with increased risk of some cancers and may also be a risk factor for cardiovascular diseases. However, epidemiological studies of red meat consumption in relation to risk of stroke are very limited. Our objective was to examine the association between red meat consumption and stroke incidence in the Swedish Mammography Cohort.

Methods—We prospectively followed 34 670 women without cardiovascular disease and cancer at baseline. Participants completed a self-administered questionnaire on diet and other risk factors for cardiovascular diseases in 1997. Cox proportional hazards models were used to estimate multivariable-adjusted relative risks (RR) and 95% CI.

Results—During a mean follow-up of 10.4 years, we ascertained 1680 incident cases of stroke, comprising 1310 cerebral infarction, 154 intracerebral hemorrhage, 79 subarachnoid hemorrhage, and 137 unspecified stroke. Total red meat and processed meat consumption was associated with a statistically significant increased risk of cerebral infarction, but not of total stroke, intracerebral hemorrhage, or subarachnoid hemorrhage. The multivariable RR of cerebral infarction for the highest versus the lowest quintile of consumption were 1.22 (95% CI, 1.01–1.46) for red meat and 1.24 (95% CI, 1.04–1.49) for processed meat. Fresh (unprocessed) meat consumption was not associated with total stroke or with any stroke subtype.

Conclusion—Findings from this study suggest that red and processed meat consumption may increase the risk of cerebral infarction in women. (Stroke. 2011;42:324-329.)

Key Words: epidemiology ■ meat ■ prospective studies ■ stroke

High consumption of red meat and/or processed meat has been associated with increased risk of some cancers1–3 and may also be a risk factor for cardiovascular diseases.3,4 Red meat is a source of saturated fat, cholesterol, and heme iron and has been positively associated with blood pressure5 and with incidence of hypertension,6,7 the metabolic syndrome, and inflammation.8 A recent meta-analysis found that processed meat consumption was associated with increased risk of coronary heart disease and type 2 diabetes.4 To date, only 3 studies have examined red meat consumption in relation to stroke incidence or mortality, with a positive association observed in 1 study,9 but not observed in the other 2 studies.10,11

Given the paucity of epidemiological data on red meat consumption in relation to incidence of stroke, we examined this association in the Swedish Mammography Cohort, a population-based prospective cohort of Swedish women.

Methods

Study Population

Details of the Swedish Mammography Cohort have been reported elsewhere.12 Briefly, the cohort was established between 1987 and 1990, when all women born between 1914 and 1948 who were living in central Sweden (Västmanland and Uppsala counties) were mailed questionnaire on diet. In the autumn of 1997, the 56 030 participants who were still alive and resided in the study area received a new expanded questionnaire that included ~350 items concerning diet and other lifestyle factors; 39 227 women (70%) completed the 1997 questionnaire. Because data on several potential confounders (eg, smoking, diabetes, hypertension, and physical activity) were obtained for the first time in 1997, only women who completed the 1997 questionnaire were included in the present study. We excluded women with an erroneous or missing national identification number; those with a history of stroke, coronary heart disease, or cancer before beginning of follow-up; and those with implausible values for total energy intake (ie, 3 SDs from the log-transformed mean energy intake in the cohort). This left 34 670 women age 49 to 83 years for analysis. The study was approved by the Regional Ethical Review Board at the Karolinska Institutet (Stockholm, Sweden).

Baseline Data Collection

The 1997 questionnaire included questions on education, weight, height, cigarette smoking, physical activity, aspirin use, medical history, family history of myocardial infarction before 60 years, alcohol consumption, and diet. Body mass index was calculated by dividing weight in kilograms by the square of height in meters.

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Pack-years of smoking history were calculated by number of packs of cigarettes smoked per day multiplied by number of years smoking. The participants reported their level of activity at work, home/housework, walking/bicycling, and exercise in the year before study enrollment. The questionnaire also included questions on inactivity (watching television/reading) and hours per day of sleeping and sitting/lying down. The reported time spent at each activity per day was multiplied by its typical energy expenditure requirements expressed in metabolic equivalents and added together to create a metabolic-equivalent hours per day (24-hour) 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 previous year, with 8 predefined frequency categories ranging from “never” to “3 or more times per day.” For this study, we grouped meats into red meat, fresh meat, and processed meat. Fresh meat intake was calculated using frequency of consumption and portion size information of all types of fresh and minced pork, beef, and veal. Processed meats included sausages, hot dog, salami, ham, processed meat cuts, liver paté, and blood sausage. Red meat was the sum of fresh meat and processed meat. Participants were also questioned about chicken/other poultry consumption.

**Case Ascertainment and Follow-Up**
Incident cases of first stroke that occurred between January 1, 1998 and December 31, 2008 were ascertained by linkage of the study cohort with the Swedish Hospital Discharge Registry, which provides virtually complete coverage of discharges. The International Classification of Diseases 10th revision (ICD-10) was used to identify stroke events. Strokes were classified as cerebral infarction (ICD-10 code I63), intracerebral hemorrhage (I61), subarachnoid hemorrhage (I60), and unspecified stroke (I64). Data on dates of death were obtained from the Swedish Death Registry.

**Statistical Analysis**
Each participant accrued follow-up time from January 1, 1998, until the date of the first stroke event: death or December 31, 2008, whichever came first. We used Cox proportional hazard models with age as the time scale to estimate relative risks (RR) with 95% CI of stroke by quintiles of red meat consumption. Entry time was defined as a subject’s age in months at start of follow-up, and exit time was defined as a subject’s age in months at stroke diagnosis or censoring. The proportional hazards assumption was tested and was met for all variables except diabetes. We adjusted for diabetes by stratification in the Cox model. The multivariable model included the following variables: smoking status and pack-years of smoking (never; past; <20, 20–39, or ≥40 pack-years; or current: <20, 20–39, or ≥40 pack-years), education (less than high school, high school, or university), body mass index (<20, 20–24.9, 25–29.9, or ≥30 kg/m²), total physical activity (by quartiles), self-reported history of hypertension (yes or no), aspirin use (yes or no), family history of myocardial infarction before 60 years of age (yes or no), and intakes of total energy (kcal/d, as a continuous variable), alcohol (nondrinkers, <3.4, 3.4–9.9, or ≥10.0 g/d), coffee (<1, 1–2, 3–4, or ≥5 cups/d), fish (5 categories), fruit (by quartiles), and vegetables (by quartiles). Tests for linear trends across quintiles were conducted by modeling red meat consumption as a continuous variable in the model with the median value of each quintile. We conducted analyses stratified by age (<70 or ≥70 years), history of hypertension (yes or no), smoking (never or ever), body mass index (<25 kg/m² or ≥25 kg/m²), and history of diabetes (yes or no) to assess possible effect modification by these variables. Tests for interaction were performed using the log likelihood ratio test. Statistical analyses were performed using SAS version 9.1 (SAS Institute Inc.). All probability values were 2 sided.

**Results**
During a mean follow-up of 10.4 years, we ascertained 1680 incident strokes, comprising 1310 cerebral infarction, 154 intracerebral hemorrhage, 79 subarachnoid hemorrhage, and 137 unspecified stroke. There was >5-fold difference in mean red meat consumption between the highest and lowest quintile (Table 1). In general, women in the highest quintile of red meat consumption were younger and less likely to have a university education, but were
Table 2. Relative Risks (95% CI) of Total Stroke and Stroke Subtypes by Red Meat Consumption in the Swedish Mammography Cohort, 1998 to 2008

<table>
<thead>
<tr>
<th>Red Meat Consumption (g/d)</th>
<th>&lt;36.5</th>
<th>36.5–53.6</th>
<th>53.7–68.3</th>
<th>68.4–85.9</th>
<th>≥86.0</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>72 371</td>
<td>71 532</td>
<td>71 407</td>
<td>72 228</td>
<td>71 475</td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>421</td>
<td>353</td>
<td>312</td>
<td>291</td>
<td>303</td>
<td></td>
</tr>
<tr>
<td>Age adjusted</td>
<td>1.00</td>
<td>0.97 (0.84–1.12)</td>
<td>0.95 (0.82–1.10)</td>
<td>1.06 (0.91–1.23)</td>
<td>1.14 (0.98–1.32)</td>
<td>0.06</td>
</tr>
<tr>
<td>Multivariable model*</td>
<td>1.00</td>
<td>0.99 (0.86–1.15)</td>
<td>0.97 (0.83–1.13)</td>
<td>1.08 (0.92–1.26)</td>
<td>1.12 (0.95–1.32)</td>
<td>0.12</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>321</td>
<td>284</td>
<td>238</td>
<td>223</td>
<td>244</td>
<td></td>
</tr>
<tr>
<td>Age adjusted</td>
<td>1.00</td>
<td>1.03 (0.88–1.21)</td>
<td>0.97 (0.82–1.14)</td>
<td>1.09 (0.92–1.30)</td>
<td>1.24 (1.05–1.46)</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivariable model*</td>
<td>1.00</td>
<td>1.06 (0.90–1.25)</td>
<td>0.99 (0.83–1.18)</td>
<td>1.12 (0.93–1.34)</td>
<td>1.22 (1.01–1.46)</td>
<td>0.04</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>49</td>
<td>28</td>
<td>31</td>
<td>25</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Age adjusted</td>
<td>1.00</td>
<td>0.64 (0.40–1.02)</td>
<td>0.78 (0.49–1.22)</td>
<td>0.72 (0.44–1.17)</td>
<td>0.62 (0.37–1.04)</td>
<td>0.09</td>
</tr>
<tr>
<td>Multivariable model*</td>
<td>1.00</td>
<td>0.62 (0.39–1.00)</td>
<td>0.74 (0.46–1.18)</td>
<td>0.68 (0.41–1.14)</td>
<td>0.59 (0.34–1.04)</td>
<td>0.09</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>16</td>
<td>9</td>
<td>17</td>
<td>20</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Age adjusted</td>
<td>1.00</td>
<td>0.58 (0.26–1.31)</td>
<td>1.11 (0.56–2.20)</td>
<td>1.35 (0.70–2.63)</td>
<td>1.17 (0.59–2.33)</td>
<td>0.24</td>
</tr>
<tr>
<td>Multivariable model*</td>
<td>1.00</td>
<td>0.56 (0.24–1.27)</td>
<td>1.10 (0.54–2.22)</td>
<td>1.25 (0.62–2.56)</td>
<td>1.02 (0.48–2.16)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

*Adjusted for age, smoking status and pack-years of smoking, education, body mass index, total physical activity, history of diabetes, history of hypertension, aspirin use, family history of myocardial infarction, and intake of total energy, alcohol, coffee, fish, fruits, and vegetables.

more likely to have diabetes and a history of hypertension compared with those in the lowest quintile. Women who reported high red meat consumption also had higher body mass index and higher intakes of energy, alcohol, coffee, fish, fruits, and vegetables.

Red meat consumption was positively associated with a statistically significant way with risk of cerebral infarction, but not with total stroke, intracerebral hemorrhage, or subarachnoid hemorrhage (Table 2). Compared with women in the lowest quintile of red meat consumption, the multivariable RR of cerebral infarction for women in the highest quintile was 1.22 (95% CI, 1.01–1.46). Additional adjustment for intakes of whole grains and dairy foods did not change results appreciably (highest versus lowest quintile: RR = 1.23; 95% CI 1.02–1.48). The association between red meat consumption and cerebral infarction was stronger when we excluded the first 3 years of follow-up (RR = 1.35; 95% CI, 1.10–1.66; P = 0.005).

When we stratified the analysis by smoking status, red meat consumption was positively associated with risk of cerebral infarction among never-smokers (highest versus lowest quintile: RR = 1.37; 95% CI, 1.08–1.79), but not among ever-smokers (corresponding RR = 1.07; 95% CI, 0.79–1.44); a test for interaction was not statistically significant (P = 0.16). Likewise, red meat consumption was positively associated with risk of cerebral infarction among women without diabetes (RR = 1.25; 95% CI, 1.03–1.52), but not among women with diabetes (RR = 0.88; 95% CI, 0.44–1.78), although a test for interaction was not statistically significant (P = 0.21). There was a clear dose-response relationship between red meat consumption and risk of cerebral infarction among never-smokers without diabetes (n = 17 659); the multivariable RRs across quintiles of red meat consumption were 1.00 (reference), 1.27 (95% CI, 1.02–1.57), 1.22 (95% CI, 0.97–1.53), 1.32 (95% CI, 1.03–1.69), and 1.43 (95% CI, 1.11–1.83) (P = 0.007). The association between red meat consumption and stroke was not modified by age or by hypertension.

To examine more extreme levels of red meat consumption, we categorized participants into deciles of red meat consumption. Compared with women in the lowest decile of red meat (<25 g/d, mean 15.7 g/d), the multivariable RR of cerebral infarction for those in the highest decile (≥102 g/d, mean 150.7 g/d) was 1.42 (95% CI, 1.11–1.81). Among never-smokers without diabetes, the corresponding RR was 1.68 (95% CI, 1.21–2.34).

Consumption of processed meat, but not of fresh meat, was associated with an increased risk of cerebral infarction; however, there was no dose-response relationship (Table 3). Risk of cerebral infarction was 10% to 28% higher among women in the highest 4 quintiles of processed meat consumption compared with those in the lowest quintile. We found no significant associations between fresh meat or processed meat consumption and risk of intracerebral hemorrhage or subarachnoid hemorrhage (Table 3). Poultry consumption was not associated with risk of total stroke or of any subtype, but consumption of poultry in this population was very low (median 0.5 servings/week).

Discussion

In this prospective cohort of Swedish women, consumption of red meat and processed meat was associated with an increased risk of cerebral infarction but not of total stroke, intracerebral hemorrhage, or subarachnoid hemorrhage. Women who consumed 102 g or more of red meat per day (highest decile) had a 42% higher risk of cerebral infarction.
compared with those who consumed less than 25 g/d (lowest decile). Among never-smokers without diabetes, those in the highest decile of red meat consumption had 68% increased risk of cerebral infarction.

To our knowledge, only 3 previous studies have assessed the association between red meat consumption and stroke. In the Nurses’ Health Study, women who consumed 1 serving of red and processed meats per day had an RR of ischemic stroke of 1.86 (95% CI, 0.90–3.83; *P* = 0.005).9 Red meat consumption was not associated with incidence of ischemic or hemorrhagic stroke in the Health Professional Follow-up Study10 or with total stroke mortality in a cohort of Japanese men and women.11

There are several potential mechanisms whereby red meat consumption may increase the risk of stroke. Hypertension is the most important risk factor for stroke. In a prospective study of 28 766 US women, the risk of incident hypertension rose with increasing baseline total red meat consumption.7 Women who consumed 1.5 servings/d or more of red meat had a statistically significant, 35% higher risk of developing hypertension compared with those who consumed no red meat. Similarly, in a cohort of 4304 women and men, red and processed meat consumption was positively associated with risk of elevated blood pressure.6 Moreover, mean blood concentrations of total cholesterol, low-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, and triglycerides were decreased in persons who substituted red meat with fish.14,15

Red meat is a major source of bioavailable heme iron. Iron is a redox-active transitional metal that can catalyze the formation of hydroxyl radicals, which are powerful pro-oxidants. Vascular inflammation and monocyte recruitment are initiating events in atherosclerosis that have been suggested to be caused partly by iron-mediated oxidative stress. An experimental study showed that the intracellular iron chelator desferrioxamine inhibited inflammation and atherosclerosis in mice, suggesting that iron may play a role in atherogenesis.16 Elevated iron stores may impose oxidative injury and have been associated with inflammation,17,18 insulin resistance,19,20 the metabolic syndrome,21 and type 2 diabetes.22
also a source of saturated fat and cholesterol. Whether saturated fat affects markers of vascular function, insulin resistance, inflammation, or risk of stroke is unclear.\textsuperscript{23} Dietary cholesterol was not associated with risk of stroke in 2 prospective studies.\textsuperscript{24}

In this study, processed meat was positively associated more strongly with risk of cerebral infarction than was fresh meat. Sodium in processed meats could plausibly account, in part, for these findings. A reduction in dietary sodium intake has been shown to decrease significantly blood pressure in hypertensive individuals.\textsuperscript{25} A low-sodium diet has also been found to decrease oxidative stress and to improve vascular function in salt-sensitive individuals,\textsuperscript{26} and a high sodium intake may promote vascular stiffness.\textsuperscript{27} Several prospective studies have observed a positive association between processed meat consumption and risk of type 2 diabetes,\textsuperscript{4,28,29} which is a risk factor for stroke.\textsuperscript{30,31} Thus, any residual confounding because of wide variety of potential confounders, including other unhealthy habits and behaviors.

Strengths of this study include its prospective and population-based design and nearly complete follow-up of study participants by linkage with population-based Swedish registers. Although our study was much larger with regard to the number of incident stroke cases compared with previous studies, the number of cases of intracerebral infarction and subarachnoid hemorrhage was still relatively small; this leads to limited statistical power and unstable risk estimates. Because diet was assessed using a self-administered questionnaire, some measurement error in assessing meat consumption was inevitable. Given the prospective design, any measurement errors are likely to be nondifferential and would have tended to attenuate the association between red meat consumption and risk of cerebral infarction. Another limitation is that our assessment of medical history and other covariates was based on self-report. It is possible that women with high consumption of red meats may increase risk of cerebral infarction. These findings suggest that consumption of red and processed meats may increase risk of cerebral infarction. Furthermore, results persisted and were even stronger among never-smokers and women without diabetes.

In conclusion, results from this prospective study of women suggest that consumption of red and processed meats may increase risk of cerebral infarction. These findings merit confirmation in additional large prospective studies and in experimental studies on possible biological mechanisms.

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Disclosures
None.

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