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 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
Statistical Analysis

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 pâté, 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 1. Age-Standardized Characteristics of 34,670 Women in the Swedish Mammography Cohort by Red Meat Consumption in 1997

<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>
</tr>
</thead>
<tbody>
<tr>
<td>Red meat (g/d)</td>
<td>23.4</td>
<td>45.6</td>
<td>61.2</td>
<td>76.7</td>
<td>124.0</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.9</td>
<td>62.5</td>
<td>61.5</td>
<td>59.6</td>
<td>59.2</td>
</tr>
<tr>
<td>Education, university (%)</td>
<td>23.7</td>
<td>20.8</td>
<td>19.7</td>
<td>18.0</td>
<td>16.8</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>24.3</td>
<td>22.9</td>
<td>22.5</td>
<td>22.1</td>
<td>24.8</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.6</td>
<td>24.9</td>
<td>24.9</td>
<td>25.1</td>
<td>25.4</td>
</tr>
<tr>
<td>Total physical activity (MET h/d)</td>
<td>42.5</td>
<td>42.3</td>
<td>42.5</td>
<td>42.5</td>
<td>42.9</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>2.6</td>
<td>3.0</td>
<td>3.2</td>
<td>3.0</td>
<td>4.1</td>
</tr>
<tr>
<td>History of hypertension (%)</td>
<td>18.3</td>
<td>19.2</td>
<td>19.7</td>
<td>20.0</td>
<td>21.8</td>
</tr>
<tr>
<td>Aspirin use (%)</td>
<td>47.4</td>
<td>49.0</td>
<td>49.2</td>
<td>50.9</td>
<td>50.9</td>
</tr>
<tr>
<td>Family history of myocardial infarction (%)</td>
<td>17.0</td>
<td>16.1</td>
<td>16.2</td>
<td>16.4</td>
<td>17.3</td>
</tr>
<tr>
<td>Total energy (kcal/d)</td>
<td>1516</td>
<td>1614</td>
<td>1717</td>
<td>1820</td>
<td>2070</td>
</tr>
<tr>
<td>Alcohol intake (g/d)</td>
<td>3.8</td>
<td>4.2</td>
<td>4.3</td>
<td>4.4</td>
<td>4.4</td>
</tr>
<tr>
<td>Coffee (cups/d)</td>
<td>2.8</td>
<td>2.9</td>
<td>3.0</td>
<td>3.0</td>
<td>3.1</td>
</tr>
<tr>
<td>Fish intake (servings/week)</td>
<td>1.9</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Fruit intake (servings/d)</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Vegetable intake (servings/d)</td>
<td>3.1</td>
<td>3.1</td>
<td>3.2</td>
<td>3.3</td>
<td>3.8</td>
</tr>
</tbody>
</table>

*All values are means if not otherwise indicated. MET, indicates metabolic equivalent of energy expenditure (kcal/kg×h).
In this prospective cohort of Swedish women, consumption of red meat and processed meat was associated with an increased risk of cerebral infarction. However, there was no clear dose-response relationship compared with any other subtype. We found no significant associations between fresh 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. However, there was no clear dose-response relationship compared with any other subtype. We found no significant associations between fresh 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).
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 Study\(^10\) 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. Hyper-tension 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. Dietary cholesterol was not associated with risk of stroke in 2 prospective studies.

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. A low-sodium diet has also been found to decrease oxidative stress and to improve vascular function in salt-sensitive individuals, and a high sodium intake may promote vascular stiffness. Several prospective studies have observed a positive association between processed meat consumption and risk of type 2 diabetes, which is a risk factor for cerebral infarction.

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 meat were at increased risk of cerebral infarction because of other unhealthy habits and behaviors. However, our findings persisted after adjustment for a wide variety of potential confounders, including other dietary factors. Women with high red meat consumption reported higher consumption of fish, fruits, and vegetables, which have been inversely associated with risk of stroke. Thus, any residual confounding because of imprecise measurement of those food items would tend to attenuate rather than exaggerate the observed positive association between red meat consumption and stroke. Moreover, 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.

References


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