Egg consumption and risk of heart failure, myocardial infarction, and stroke: results from 2 prospective cohorts

Susanna C Larsson,* Agneta Åkesson, and Alicja Wolk

Unit of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

ABSTRACT

Background: Some studies have found that egg consumption is associated with a higher risk of ischemic heart disease in patients with diabetes. Epidemiologic studies of egg consumption in relation to risk of heart failure (HF) and stroke types are scarce.

Objective: The aim of this study was to examine whether egg consumption is associated with incidence of HF, myocardial infarction (MI), or stroke types.

Design: In prospective cohorts of 37,766 men (Cohort of Swedish Men) and 32,805 women (Swedish Mammography Cohort) who were free of cardiovascular disease (CVD), egg consumption was assessed at baseline with a food-frequency questionnaire. Incident CVD cases were identified through linkage with the Swedish National Patient and Cause of Death Registers. The data were analyzed with the use of a Cox proportional hazards regression model.

Results: During 13 y of follow-up, we ascertained 1628 HFs, 3262 MIs, 2039 ischemic strokes, and 405 hemorrhagic strokes in men and 1207 HFs, 1504 MIs, 1561 ischemic strokes, and 294 hemorrhagic strokes in women. There was no statistically significant association between egg consumption and risk of MI or any stroke type in either men or women or HF in women. In men, consumption of ≤6 eggs/wk was not associated with HF risk; however, daily egg consumption (≥1/d) was associated with a 30% higher risk of HF (RR: 1.30; 95% CI: 1.01, 1.67). Egg consumption was not associated with any CVD outcome in individuals with diabetes.

Conclusions: Daily egg consumption was not associated with risk of MI or any stroke type in either men or women or with HF in women. Consumption of eggs ≥1 time/d, but not less frequent consumption, was associated with an elevated risk of HF in men.

Methods

Study population

The study population for the current study included participants from the Cohort of Swedish Men and the Swedish Stroke Association.

INTRODUCTION

Eggs are a rich source of protein and an important part of many diets worldwide. Although rich in healthy food components such as phospholipids, the carotenoids lutein and zeaxanthin, and many vitamins, the high content of dietary cholesterol in eggs has garnered the most attention with respect to health. Meta-analyses of intervention trials have shown that an increased intake of dietary cholesterol increases serum total, LDL, and HDL cholesterol concentrations, as well as the ratio of total and LDL cholesterol to HDL cholesterol (1, 2). However, findings from trials of the effects of high egg consumption on lipid profile concentrations have not been consistent. For example, a recent trial involving 140 overweight or obese individuals with prediabetes or type 2 diabetes observed no adverse effect from a diet high in eggs (2 eggs/d for 6 d/wk) on lipid profiles (3). Thus, better understanding of whether egg consumption is associated with risk of cardiovascular disease (CVD) is of high public health relevance.

The limited epidemiologic data available on egg consumption in relation to risk of heart failure (HF) (4, 5) and stroke types (6, 7) suggest that a high consumption of eggs is associated with an increased risk of HF (4, 5), with a reduced risk of hemorrhagic stroke (6), but that it is not associated with ischemic stroke (6, 7). Egg consumption generally has not been associated with risk of ischemic heart disease (IHD) in healthy individuals (8, 9), but some studies have reported a positive association between egg consumption and risk of IHD or overall CVD in individuals with diabetes (8–10).

We sought to examine whether egg consumption is associated with risk of HF; myocardial infarction (MI), ischemic stroke, and hemorrhagic stroke in 2 population-based prospective cohort studies of Swedish middle-aged and older adults. Moreover, we evaluated whether the associations were modified by a history of diabetes.

Methods

Study population

The study population for the current study included participants from the Cohort of Swedish Men and the Swedish Stroke Association.
Mammography Cohort (SMC), which are population-based cohort studies of Swedish men and women, respectively, from 3 Swedish counties. The Cohort of Swedish Men was initiated in the autumn of 1997 with the aim to examine the associations between diet, lifestyle, and other modifiable factors and risk of CVD, cancer, and other noncommunicable diseases. All men in Västmanland and Örebro Counties who were born between 1918 and 1952 (n = 100,303) received an invitation to participate in the study, along with a 350-item questionnaire that elicited information on diet and other potential risk factors for non-communicable diseases. A total of 48,850 men responded to the questionnaire. The SMC was established in 1987–1990 with the aim of assessing the association between dietary and hormonal factors and risk of breast cancer; details have been reported elsewhere (11). In the autumn of 1997, all SMC participants who were still alive and living in the study area received a new questionnaire that was identical, except for some sex-specific questions, to the questionnaire sent to the Swedish men. We used 1997 as baseline for the SMC because the 1987–1990 questionnaire did not include major CVD risk factors.

For the present study, we excluded men and women with missing or erroneous personal identification numbers (n = 297 men and n = 243 women), those who died before the start of follow-up (n = 55 men and n = 26 women), those with cancer (n = 2592 men and n = 1811 women) or CVD (IHD, HF, or stroke; n = 5761 men and n = 4319 women) at baseline, and those with an implausible intake of total energy (i.e., 3 SDs from the loge-transformed mean energy intake; n = 441 men and n = 405 women) or missing data on egg consumption (n = 1938 men and n = 1455 women). This left 37,766 men 45–79 y of age and 32,805 women 49–83 y of age for the present analysis. The Regional Ethical Review Board at Karolinska Institutet in Stockholm, Sweden, approved the study.

**Diet assessment**

Diet was assessed at baseline with the use of a 96-item semi-quantitative food-frequency questionnaire (FFQ) designed to assess the Swedish diet. Participants were asked to indicate how often, on average, they had consumed eggs/omelets (hereafter referred to as eggs) during the past year. They could choose from 8 predefined frequency categories: never, 1–3/mo, 1–2/wk, 3–4/wk, 5–6/wk, 1/d, 2/d, or ≥3/d. The FFQ used in this study has been validated for nutrient intake; the Spearman correlation coefficients between FFQ-based estimates and the mean of fourteen 24-h recall interviews ranged from 0.44 (protein) to 0.81 (alcohol) for macronutrients, with a mean value of 0.65 (12).

**Assessment of covariates**

Information on education; weight; height; smoking; aspirin use; history of hypertension, high cholesterol concentrations, and diabetes; family history of MI before 60 y of age; and alcohol intake was obtained through a self-administered questionnaire. Participants were also asked to report how often they had walked/bicycled and exercised in the past year. Self-reported information whether diabetes may be an intermediate of the relation between egg consumption and CVD risk, we ran an analysis without adjustment for diabetes. We also examined whether the associations between egg consumption and the CVD outcomes were modified by history of diabetes through stratification. The stratified analyses

**Follow-up and case ascertainment**

Participants contributed person-time from 1 January 1998 until the date of diagnosis of each CVD event, date of death (information obtained from the Swedish Cause of Death Register), or censoring date (31 December 2010), whichever occurred first. Incident CVD cases were ascertained by linkage with the Swedish National Patient Register [includes inpatient and outpatient (non-primary care) data] and the Swedish Cause of Death Register (also includes nonhospitalized cases). CVD events were classified with the use of the following International Classification of Diseases, 10th Revision codes: I50 (includes acute or chronic HF and subtypes) and I11.0 (hypertensive heart disease with HF) for HF, I21 (acute MI) for MI, I63 (cerebral infarction) for ischemic stroke, and I60 (subarachnoid hemorrhage) and I61 (intracerebral hemorrhage) for hemorrhagic stroke. For each CVD outcome, only the first event for each individual and only the event listed as the primary diagnosis were defined as a case.

**Statistical analysis**

We classified participants into 4 groups according to their egg consumption: 0–3/mo (only 3.7% of the study population were nonconsumers), 1–2/wk, 3–6/wk, and ≥1/d. In a secondary analysis, we split the highest category into 1/d and ≥2/d to assess more extreme levels of egg consumption. Cox proportional hazards regression models stratified by age (mo) and sex (analyses of men and women combined) were used to compute HRs (hereafter referred to as RRs) and 95% CIs. In addition to age, all multivariable models were adjusted for education (less than high school, high school, or university); family history of MI before 60 y of age (yes or no); smoking (never; past <20 or ≥20 pack-years; or current <20 or ≥20 pack-years); aspirin use (never, 1–6 tablets/wk, or ≥7 tablets/wk); walking/bicycling (quintiles); exercise (quintiles); BMI (kg/m²; continuous); history of hypertension (yes or no), hypercholesterolemia (yes or no), and diabetes (yes or no); and intake of total energy (kcal/d; continuous), alcohol (quintiles), fruits and vegetables (quintiles), and processed meat (quintiles). Additional adjustment for other foods/food groups, including unprocessed red meat, fish, dairy products, sweetened beverages, coffee, and tea or dietary fiber and SPA, MUFA, and PUFA intake did not alter the results materially; thus, those variables were not included in the final multivariable model. The proportional hazards assumption, tested with the use of Schoenfeld residuals, was found to be satisfied.

We conducted tests for linear trend by creating a variable that assigned the median value for each category of egg consumption and then modeled this variable as a continuous variable. In addition, we used restricted cubic spline Cox proportional hazards regression with 4 knots to flexibly model egg consumption as a continuous variable in relation to the CVD outcomes. To assess whether diabetes may be an intermediate of the relation between egg consumption and CVD risk, we ran an analysis without adjustment for diabetes. We also examined whether the associations between egg consumption and the CVD outcomes were modified by history of diabetes through stratification. The stratified analyses
were performed for men and women combined because of few individuals with diabetes. Likelihood ratio tests that compared models with and without multiplicative interaction terms were used to assess the significance of interactions. Sensitivity analyses that excluded individuals with history of hypercholesterolemia or the first 2 y of follow-up were conducted. All probability values were 2-tailed ($\alpha = 0.05$). All analyses were performed with the use of SAS version 9.3 (SAS Institute).

RESULTS

Mean $\pm$ SD egg consumption was $1.4 \pm 1.6$/wk in men and $1.4 \pm 1.4$/wk in women. Only 2.7% of men and 2.1% of women consumed $\geq 1$ eggs/d. Compared with men and women who never or seldom consumed eggs, those with high consumption were somewhat older and were more likely to be current smokers (men), be overweight, have diabetes (men), and use aspirin frequently (women) (Table 1). Those with high egg consumption had a higher intake of energy, alcohol, and other foods and beverages. The prevalence of hypercholesterolemia decreased with increasing egg intake, probably reflecting a reduction in egg consumption in those with elevated cholesterol concentrations. The mean daily dietary cholesterol intake in those who consumed eggs daily was on average 200–240 mg (the amount of cholesterol in $\sim 1$ large egg) higher than in those who never or seldom consumed eggs.

During a follow-up of 13 y (January 1998–December 2010), we documented 1628 HFs, 3262 MIs, 2039 ischemic strokes, and 405 hemorrhagic strokes (327 intracerebral hemorrhages and 78 subarachnoid hemorrhages) in men. The corresponding numbers in women were 1207 HFs, 1504 MIs, 1561 ischemic strokes, and 294 hemorrhagic strokes (201 intracerebral hemorrhages and 93 subarachnoid hemorrhages).

The associations between egg consumption and CVD outcomes are presented in Table 2. Consumption of $\geq 6$ eggs/wk was not associated with risk of HF in either men or women. However, consumption of $\geq 1$ eggs/d was associated with a statistically significant higher risk of HF in men but not women. Egg consumption was not associated with risk of MI, ischemic stroke, or hemorrhagic stroke in either men or women. The reason for the disparate results for men and women is unclear. Potential explanations are that men are more sensitive to high consumption of eggs (or cholesterol) than women, or that egg consumption is associated with an uncontrolled risk factor other than diet that is not captured by our models.

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In a secondary analysis, we examined the association between more extreme levels of egg consumption ($\geq 2$/d) and risk of CVD. In comparison with never or seldom egg consumption ($0–3$/mo), the multivariable RRs of HF associated with consumption of $\geq 2$ eggs/d were 1.99 (95% CI: 1.12, 3.53; n = 13 cases) in men and 0.95 (95% CI: 0.38, 2.35; n = 5 cases) in women. We observed no statistically significant association between consumption of $\geq 2$ eggs/d and risk of MI, ischemic stroke, or hemorrhagic stroke in either men or women. In restricted cubic spline analysis, egg consumption was positively associated with risk of HF in men but not women, and there was a borderline statistically significant positive association between egg consumption and ischemic stroke in men (Supplemental Figure 1); no relation between egg consumption and risk of MI or hemorrhagic stroke in either sex or ischemic stroke in women was observed.

DISCUSSION

In these 2 prospective cohort studies, egg consumption was not associated with risk of MI, ischemic stroke, or hemorrhagic stroke in either men or women or with HF risk in women. In men, consumption of $\leq 6$ eggs/wk was not associated with risk of HF; however, daily egg consumption was associated with a 30% elevated risk of HF, and consumption of $\geq 2$ eggs/d was associated with an almost 2-fold higher risk. The relation between egg consumption and CVD outcomes was not modified by diabetes.

Our findings for egg consumption and risk of HF in men is consistent with results from previous studies (4, 5). In the Physicians’ Health Study of 21,275 US men, consumption of $\leq 6$ eggs/wk was not associated with HF risk; however, men who consumed 1 egg/d and $\geq 2$ eggs/d had a 33% and 56% higher risk, respectively, of HF than did those who consumed <1 egg/wk (4). In the Atherosclerosis Risk in Communities study of 14,153 middle-aged US adults, every 1 serving/d increment in egg consumption was associated with a statistically significant 23% increase in risk of HF in men and women combined (5). In the current study, egg consumption was not associated with HF in women. The reason for the disparate results for men and women is unclear. Potential explanations are that men are more sensitive to high consumption of eggs (or cholesterol) than women, or that egg consumption is associated with an uncontrolled risk factor for HF in men but not in women. For example, we did not have information on consumption of bacon, specifically, which is a potential confounder of the association between egg consumption and HF risk. However, we adjusted for processed meat consumption (including sausages, hot dogs, salami, ham, processed meat cuts, and liver pâté), which is positively associated with HF risk in the Swedish cohorts (14, 15), and results did not change. Previous studies of egg consumption in relation to risk of HF did not control for consumption of bacon or other potential dietary confounders (4, 5). In our study, the number of HF cases was lower in women (only 37 cases in the highest category of egg consumption) than in men, and the lack of relation between egg consumption and HF in women, as well as the absence of interaction by sex, may be because of low statistical power. Because we conducted many analyses for different CVD outcomes in men and women separately, it is possible that the observed association between egg consumption and HF risk in men was a chance finding.

As in our cohorts, findings from meta-analyses of prospective studies of the association between egg consumption and risk of IHD and total stroke showed no overall association (8, 9). However, in subgroup analysis, high egg consumption has been associated with increased risk of IHD or overall CVD in diabetic patients (8–10). For example, in a meta-analysis by Shin et al.
### TABLE 1
Age-standardized baseline characteristics by categories of egg consumption in 37,766 men in the Cohort of Swedish Men and 32,805 women in the Swedish Mammography Cohort

<table>
<thead>
<tr>
<th></th>
<th>Men (Cohort of Swedish Men)</th>
<th>Women (Swedish Mammography Cohort)</th>
<th>P-trend&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–3/mo (n = 17,635)</td>
<td>1–2/wk (n = 15,576)</td>
<td>3–6/wk (n = 3548)</td>
</tr>
<tr>
<td>Age, y</td>
<td>59 ± 9.4</td>
<td>59 ± 9.4</td>
<td>60 ± 9.2</td>
</tr>
<tr>
<td></td>
<td>61 ± 9.0</td>
<td>61 ± 8.9</td>
<td>62 ± 9.0</td>
</tr>
<tr>
<td>Postsecondary education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>19</td>
<td>24</td>
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<td>18</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>0.10</td>
<td>0.15</td>
<td>0.002</td>
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<tr>
<td>Family history of myocardial infarction</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Current smokers</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Aspirin use ≥7 tablets/wk</td>
<td>5.2</td>
<td>5.2</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>8.1</td>
<td>8.4</td>
<td>9.8</td>
</tr>
<tr>
<td></td>
<td>0.005</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Walk/bicycle ≥40 min/d</td>
<td>32</td>
<td>33</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>36</td>
<td>34</td>
</tr>
<tr>
<td>Exercise ≥2 h/wk</td>
<td>57</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>58</td>
<td>57</td>
</tr>
<tr>
<td>BMI ≥25 kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>54</td>
<td>55</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>14</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>9.2</td>
<td>6.5</td>
<td>5.1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7.3</td>
<td>7.0</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>3.6</td>
<td>3.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Total energy intake, kcal/d</td>
<td>2600 ± 790</td>
<td>2800 ± 790</td>
<td>2900 ± 860</td>
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<tr>
<td></td>
<td>1600 ± 480</td>
<td>1800 ± 500</td>
<td>2000 ± 540</td>
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<tr>
<td>Dietary cholesterol intake,&lt;sup&gt;4&lt;/sup&gt; mg/d</td>
<td>240 ± 54</td>
<td>280 ± 53</td>
<td>350 ± 67</td>
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<tr>
<td></td>
<td>250 ± 58</td>
<td>280 ± 54</td>
<td>340 ± 65</td>
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<tr>
<td>Alcohol intake, g/d</td>
<td>13 ± 19</td>
<td>15 ± 19</td>
<td>18 ± 25</td>
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<tr>
<td></td>
<td>5.1 ± 8.9</td>
<td>5.9 ± 8.2</td>
<td>7.1 ± 8.8</td>
</tr>
<tr>
<td>Daily food consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits and vegetables, servings</td>
<td>3.6 ± 2.2</td>
<td>4.0 ± 2.2</td>
<td>4.2 ± 2.3</td>
</tr>
<tr>
<td></td>
<td>4.7 ± 2.8</td>
<td>5.2 ± 2.7</td>
<td>5.6 ± 2.8</td>
</tr>
<tr>
<td>Processed meat, servings</td>
<td>0.7 ± 0.6</td>
<td>0.8 ± 0.6</td>
<td>0.9 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>0.5 ± 0.5</td>
<td>0.7 ± 0.5</td>
<td>0.7 ± 0.5</td>
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<tr>
<td>Unprocessed red meat, servings</td>
<td>0.5 ± 0.3</td>
<td>0.5 ± 0.3</td>
<td>0.6 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>0.4 ± 0.3</td>
<td>0.5 ± 0.3</td>
<td>0.5 ± 0.4</td>
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<tr>
<td>Fish, servings</td>
<td>0.2 ± 0.2</td>
<td>0.3 ± 0.2</td>
<td>0.3 ± 0.3</td>
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<tr>
<td></td>
<td>0.3 ± 0.2</td>
<td>0.3 ± 0.2</td>
<td>0.3 ± 0.3</td>
</tr>
<tr>
<td>Dairy products, servings</td>
<td>5.5 ± 3.1</td>
<td>59 ± 3.1</td>
<td>6.0 ± 3.3</td>
</tr>
<tr>
<td></td>
<td>4.9 ± 2.7</td>
<td>5.3 ± 2.8</td>
<td>5.7 ± 2.9</td>
</tr>
<tr>
<td>Sweetened beverages, glasses</td>
<td>1.1 ± 1.4</td>
<td>1.1 ± 1.4</td>
<td>1.3 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>0.7 ± 1.1</td>
<td>0.7 ± 1.1</td>
<td>0.8 ± 1.2</td>
</tr>
<tr>
<td>Coffee, cups</td>
<td>3.5 ± 2.1</td>
<td>3.5 ± 2.1</td>
<td>3.6 ± 2.2</td>
</tr>
<tr>
<td></td>
<td>3.1 ± 1.7</td>
<td>3.1 ± 1.8</td>
<td>3.2 ± 1.8</td>
</tr>
<tr>
<td>Tea, cups</td>
<td>1.1 ± 1.3</td>
<td>1.1 ± 1.3</td>
<td>1.2 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>1.1 ± 1.3</td>
<td>1.1 ± 1.3</td>
<td>1.1 ± 1.2</td>
</tr>
</tbody>
</table>

<sup>1</sup>Values are means ± SDs or percentages.

<sup>2</sup>Mean ± SD egg consumption in this category is 1.2 ± 0.4 per day in men and 1.1 ± 0.4 per day in women.

<sup>3</sup>Assessed with the use of linear regression (continuous variables) or chi-square test (categorical variables).

<sup>4</sup>Energy-adjusted (to 2000 kcal/d) with the use of the residual method (13).
The pooled RR of overall CVD in patients with diabetes was 1.69 (95% CI: 1.09, 2.62) for ≥1/d vs. <1/wk or never consumption. We could not confirm a positive association in the Swedish cohorts. However, because of the low prevalence of diabetes in the study population, we had limited statistical power to detect an association in patients with diabetes.

Studies of egg consumption in relation to stroke types are sparse (6, 7). Results from the Nurses’ Health Study and the Swedish Mammography Cohort are presented in Table 2. The study includes 37,766 men in the Cohort of Swedish Men and 32,805 women in the Swedish Mammography Cohort, 1998–2010.

<table>
<thead>
<tr>
<th>Heart failure</th>
<th>Cases, n</th>
<th>0–3/mo</th>
<th>1–2/wk</th>
<th>3–6/wk</th>
<th>≥1/d</th>
<th>P-trend^1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00 (ref)</td>
<td>1.01 (0.91, 1.13)</td>
<td>1.03 (0.87, 1.22)</td>
<td>1.48 (1.15, 1.89)</td>
<td>0.01</td>
<td></td>
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<tr>
<td>Multivariable^2</td>
<td>1.00 (ref)</td>
<td>1.03 (0.93, 1.17)</td>
<td>0.99 (0.84, 1.19)</td>
<td>1.30 (1.01, 1.67)</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00 (ref)</td>
<td>0.91 (0.81, 1.03)</td>
<td>0.84 (0.68, 1.03)</td>
<td>1.20 (0.86, 1.69)</td>
<td>0.78</td>
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<tr>
<td>Multivariable^2</td>
<td>1.00 (ref)</td>
<td>0.92 (0.81, 1.04)</td>
<td>0.82 (0.66, 1.01)</td>
<td>1.06 (0.74, 1.52)</td>
<td>0.43</td>
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<td><strong>Men and women^3</strong></td>
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<tr>
<td>Multivariable^2</td>
<td>1.00 (ref)</td>
<td>0.98 (0.90, 1.06)</td>
<td>0.91 (0.79, 1.04)</td>
<td>1.20 (0.98, 1.47)</td>
<td>0.50</td>
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</table>

<table>
<thead>
<tr>
<th>Myocardial infarction</th>
<th>Cases, n</th>
<th>1531</th>
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<td>0.95 (0.89, 1.04)</td>
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^1Calculated by assigning the median value to each category and treating this variable as a continuous variable. ref, reference.
^2The Cox proportional hazards regression model is stratified by age (months) and includes education; family history of myocardial infarction before 60 y of age; smoking status and pack-years of smoking; aspirin use; walking/bicycling; exercise; BMI; history of hypertension, hypercholesterolemia, and diabetes; and intake of total energy, alcohol, fruit and vegetables, and processed meat. Multivariable RRs for men and women combined are further adjusted for sex through stratification.
^3P-interaction between egg consumption and sex = 0.41 for heart failure, 0.60 for myocardial infarction, 0.14 for ischemic stroke, and 0.74 for hemorrhagic stroke.
^4Intracerebral hemorrhage and subarachnoid hemorrhage combined.
Health Professionals Follow-Up Study showed no dose-response association or statistically significant results for the highest vs. lowest quintile of egg consumption and either ischemic or hemorrhagic stroke (6). However, when egg consumption was analyzed as a continuous variable, each 1 serving/d increment in egg consumption was associated with a statistically significant 44% lower risk of hemorrhagic stroke, but was not associated with ischemic stroke (6). In the first NHANES, there was no association between egg consumption and ischemic stroke (results for hemorrhagic stroke were not reported) (7). In the Swedish cohorts, we found no statistically significant association between egg consumption and any stroke types, but the spline analysis suggested a positive relation between very high egg consumption and ischemic stroke in men.

Eggs are a major source of dietary cholesterol. Although meta-analyses of intervention trials have found that increased dietary cholesterol intake modestly increases serum total and LDL cholesterol concentrations, as well as the LDL-to-HDL cholesterol ratio (1, 2), several prospective studies have observed no association between dietary cholesterol intake and risk of coronary artery disease, ischemic stroke, or hemorrhagic stroke (2). The effect of dietary cholesterol on blood cholesterol concentrations may be too modest to produce a statistically significant increase in CVD risk. In a meta-analysis of 17 trials, the addition of 100 mg dietary cholesterol/d increased total cholesterol concentrations by 0.056 mmol/L (2.2 mg/dL) and the ratio of total-to-HDL cholesterol by 0.020 units (1). Future investigations into underlying biological mechanisms by which frequent egg consumption might increase the risk of HF are warranted.

The strengths of our studies are the prospective design, large number of incident cases of CVD, and completeness of follow-up of participants through linkage with population-based Swedish

| TABLE 3 | RRs (95% CIs) of heart failure, myocardial infarction, ischemic stroke, and hemorrhagic stroke by egg consumption stratified by history of diabetes in 37,766 men in the Cohort of Swedish Men and 32,805 women in the Swedish Mammography Cohort, 1998–2010 |
|---------------------------------|-------------------------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                  | Egg consumption                                 | 0–3/mo | 1–2/wk | 3–6/wk | ≥1/d | P-trend |
|---------------------------------|-------------------------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Heart failure                   | Patients without diabetes                        |        |        |        |        |        |        |
| Cases, n                        | 1102                                            | 1006   | 224    | 94     |        | 0.74   |
| Multivariable                   | 1.00 (ref)                                      | 0.96 (0.88, 1.05)               | 0.85 (0.73, 0.99)               | 1.23 (0.98, 1.53)               |        |        |
| Patients with diabetes          | 182                                             | 160    | 52     | 15     |        | 0.24   |
| Cases, n                        | 1.00 (ref)                                      | 1.16 (0.88, 1.53)               | 1.36 (0.91, 2.04)               | 1.23 (0.63, 2.39)               |        |        |
| Myocardial infarction           | Patients without diabetes                        |        |        |        |        |        |        |
| Cases, n                        | 1953                                            | 1672   | 412    | 117    |        | 0.76   |
| Multivariable                   | 1.00 (ref)                                      | 0.96 (0.89, 1.02)               | 0.97 (0.87, 1.08)               | 1.01 (0.83, 1.22)               |        |        |
| Patients with diabetes          | 290                                             | 237    | 64     | 21     |        | 0.70   |
| Cases, n                        | 1.00 (ref)                                      | 0.98 (0.80, 1.21)               | 0.92 (0.66, 1.28)               | 0.95 (0.57, 1.60)               |        |        |
| Ischemic stroke                 | Patients without diabetes                        |        |        |        |        |        |        |
| Cases, n                        | 1432                                            | 1290   | 352    | 81     |        | 0.42   |
| Multivariable                   | 1.00 (ref)                                      | 0.98 (0.91, 1.06)               | 1.12 (0.99, 1.26)               | 0.98 (0.77, 1.23)               |        |        |
| Patients with diabetes          | 211                                             | 172    | 45     | 17     |        | 0.38   |
| Cases, n                        | 1.00 (ref)                                      | 1.03 (0.80, 1.33)               | 0.88 (0.60, 1.29)               | 0.83 (0.46, 1.48)               |        |        |
| Hemorrhagic stroke              | Patients without diabetes                        |        |        |        |        |        |        |
| Cases, n                        | 300                                             | 276    | 79     |        |        | 0.47   |
| Multivariable                   | 1.00 (ref)                                      | 0.99 (0.83, 1.17)               | 0.91 (0.70, 1.18)               | —                               |        |        |
| Patients with diabetes          | 20                                              | 13     | 11     |        |        | 0.58   |
| Cases, n                        | 1.00 (ref)                                      | 0.38 (0.11, 1.25)               | 1.63 (0.39, 6.74)               | —                               |        |        |

1Calculated by assigning the median value to each category and treating this variable as a continuous variable. ref, reference.
2The Cox proportional hazards regression model is stratified by age (mo) and sex and includes education; family history of myocardial infarction before 60 y of age; smoking status and pack-years of smoking; aspirin use; walking/bicycling; exercise; BMI, history of hypertension and hypercholesterolemia; and intake of total energy, alcohol, fruit and vegetables, and processed meat.
3P-interaction between egg consumption and diabetes = 0.27 for heart failure, 0.90 for myocardial infarction, 0.73 for ischemic stroke, and 0.20 for hemorrhagic stroke.
4Intracerebral hemorrhage and subarachnoid hemorrhage combined.
5Because of the small number of cases (n = 4) in the highest category of egg consumption in those with diabetes, the highest 2 categories were combined.
The main limitation is the observational design. Thus, we cannot rule out the possibility of residual confounding because of unmeasured or imprecise measurement of other risk factors for CVD. Another limitation is that diet was assessed with the use of a self-administered questionnaire and only at baseline. This will inevitably lead to some exposure measurement error. Because of the prospective design, any misclassification of egg consumption would most likely be unrelated to the outcome (CVD event) and most likely attenuate the results. Hence, we cannot exclude the possibility that the lack of observed association between egg consumption and risk of MI and stroke is due to imprecise measurement of egg consumption. Finally, because egg consumption was quite low, we had limited statistical power to assess the association between very high egg consumption (≥2/d) and the risk of CVD. Average egg consumption in the Swedish cohorts was similar to the intake in other cohorts (5, 6, 16).

In summary, we found no evidence that consumption of up to ≈1 egg daily was associated with risk of MI, ischemic stroke, or hemorrhagic stroke in either men or women, or with HF in women. Consumption of ≥1 eggs/d, but not less frequent consumption, was associated with an elevated risk of HF in men. However, given the absence of a positive association in women, the fact that we performed many analyses for several CVD outcomes (potentially resulting in false positives), and the lack of biological mechanisms, the association between high egg consumption and HF risk in men should be interpreted with caution.

The authors’ responsibilities were as follows—SCL, A and AW: designed the study and interpreted the data; AW: collected the data; SCL: performed the statistical analysis and drafted the manuscript; SCL and AW: handled funding; AA and AW: critically revised the manuscript for important intellectual content; and all authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

REFERENCES


