Background—Reduction in dietary cholesterol is widely recommended for the prevention of cardiovascular disease. Although eggs are important sources of dietary cholesterol and other nutrients, little is known about the association between egg consumption and heart failure (HF) risk.

Methods and Results—In a prospective cohort study of 21 275 participants from the Physicians’ Health Study I, we examined the association between egg consumption and the risk of HF. Egg consumption was assessed with the use of a simple abbreviated food questionnaire, and we used Cox regression to estimate relative risks of HF. After an average follow-up of 20.4 years, a total of 1084 new HF cases occurred in this cohort. Although egg consumption up to 6 times per week was not associated with incident HF, egg consumption of ≥7 per week was associated with an increased risk of HF. Compared with subjects who reported egg consumption of <1 per week, hazard ratios (95% confidence intervals) for HF were 1.28 (1.02 to 1.61) and 1.64 (1.08 to 2.49) for egg consumption of 1 per day and ≥2 per day, respectively, after adjustment for age, body mass index, smoking, alcohol consumption, exercise, and history of atrial fibrillation, hypertension, valvular heart disease, and hypercholesterolemia. Similar results were obtained for HF without antecedent myocardial infarction.

Conclusions—Our data suggest that infrequent egg consumption is not associated with the risk of HF. However, egg consumption of ≥1 per day is related to an increased risk of HF among US male physicians. (Circulation. 2008;117:512-516.)

Key Words: diet ■ epidemiology ■ heart failure

Heart failure (HF) remains a major public health issue in the United States. The development of hypertension and myocardial infarction, 2 major risk factors for HF, is influenced by elevated plasma low-density lipoprotein (LDL) cholesterol. Hence, dietary guidelines to prevent the underlying atherosclerosis emphasize the reduction of dietary cholesterol.1,2 Although each egg contains on average 200 mg of cholesterol that can negatively influence the development of atherosclerosis, it is also known that eggs are rich in other important nutrients such as minerals, folate, B vitamins, proteins, and monounsaturated fatty acids that could reduce the risk of coronary heart disease (CHD).3,4 Current data on the effects of dietary cholesterol on serum cholesterol have been inconsistent, ranging from positive associations5–9 to no effects.7,10,11 The relation between dietary and serum cholesterol is complicated by the large variability in individual response to dietary cholesterol.11–13 Despite the fact that some studies have shown an association between egg consumption and CHD,14 no previous study has examined whether egg consumption is associated with the risk of HF in a community setting.

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Because eggs could serve as a good source for vitamins, proteins, and other nutrients in the United States, it is important to understand whether egg consumption as a whole food (as opposed to an individual component of eggs such as cholesterol) confers a lower or higher risk of HF. In the present project, we sought to prospectively assess whether egg consumption was associated with an increased risk of HF among US male physicians. In a secondary aim, we examined whether the relation between egg consumption and HF differs between HF with and without antecedent myocardial infarction.

Study Population

We used data from the Physicians’ Health Study (PHS) I, a randomized, double-blind, placebo-controlled trial designed to study the effects of low-dose aspirin and beta carotene on cardiovascular disease and cancer among US male physicians. A detailed description of the PHS I has been published previously.15 For the present analyses, we excluded 796 subjects with missing data on egg consumption.

Received August 13, 2007; accepted November 8, 2007.
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consumption was collected (24, 48, 72, 96, and 120 months after randomization), we classified each subject into 1 of the following categories of egg consumption: <1/wk, 1/wk, 2–4/wk, 5–6/wk, 1/d, and ≥2/d, respectively. High cholesterol was defined as total cholesterol of ≥240 mg/dL or reported current/past treatment for elevated cholesterol.

### Egg Consumption

Information on egg consumption was self-reported with the use of a simple abbreviated semiquantitative food frequency questionnaire. Participants were asked to report how often, on average, they had eaten eggs during the past year. Possible response categories included “rarely/never,” “1 to 3/month,” “1/week,” “2 to 4/week,” “5 to 6/week,” “daily,” and “2+/day.” This information was obtained at baseline and 24, 48, 72, 96, and 120 months after randomization. We combined the first 2 categories to create a large and stable reference group.

### Ascertainment of HF in the PHS

End points in the PHS have been ascertained with the use of annual follow-up questionnaires. Specifically, a questionnaire was mailed to each participant every 6 months during the first year and has been mailed annually thereafter to obtain information on compliance with the intervention and the occurrence of new medical diagnoses, including HF. The validation of HF in the PHS has been reported previously.16

### Other Variables

Demographic data were collected at baseline. Information on comorbidity (ie, atrial fibrillation, hypertension, and diabetes mellitus) has been collected through annual follow-up questionnaires as described above. Data on selected foods such as fruits and vegetables; breakfast cereals; physical activity; smoking; alcohol consumption; and history of hypercholesterolemia (defined as total cholesterol ≥240 mg/dL or past/current treatment for elevated cholesterol) were obtained at baseline. Of the total subjects with reported egg consumption, total and high-density lipoprotein (HDL) cholesterol were measured at baseline on 4672 individuals by standard methods. We computed the ratio of total to HDL cholesterol.

### Statistical Analyses

At baseline and subsequent time points at which information on egg consumption was collected (24, 48, 72, 96, and 120 months after randomization), we repeated the main analysis using updated egg consumption at 24, 48, 72, 96, and 120 months in a time-dependent Cox model. To examine whether the relation between egg consumption and HF was mediated through cholesterol, we compared multivariable-adjusted mean total cholesterol, HDL cholesterol, and the ratio of the 2 variables using ANCOVA. All analyses were completed with the use of SAS.
Results

Among 21,275 participants in the PHS I, the mean age at randomization was 53.7 ± 9.5 years (range, 39.7 to 85.9 years). Approximately 64% reported egg consumption of 1 to 4 per week in this population, and only 8% reported consumption of ≥1 per day. Table 1 presents baseline characteristics of the study participants. Frequent consumption of eggs was associated with older age; higher body mass index; higher proportion of current smokers; alcohol consumption (>4 drinks per week); and history of diabetes mellitus, atrial fibrillation, and hypertension. During an average follow-up of 20.4 years, 1,084 cases of HF (4.7%) occurred in this cohort. Egg consumption declined over time, with 23.5% of subjects reporting no egg consumption at 10-year follow-up versus 6.9% at baseline. In addition, egg consumption of ≥1 per day decreased from 8.1% at baseline to 2.1% after 10 years of follow-up. In multivariable Cox regression models, egg consumption up to 6 per week was not related to HF, whereas consumption of 1 per day and ≥2 per day was associated with a 28% and 64% increased risk of HF, respectively (Table 2). Restricting the analysis to subjects with follow-up times beyond 2 years yielded similar results (P for trend = 0.004). Similar findings were obtained when egg consumption and interim myocardial infarction were updated with the use of a time-dependent Cox model (data not shown). There was no evidence for 2-way interaction between egg consumption and diabetes mellitus (P = 0.27), history of hypertension (P = 0.97), smoking (P = 0.70), or hypercholesterolemia (P = 0.85). Finally, we observed a similar association between egg consumption and HF without antecedent myocardial infarction (Table 3). We did not have enough cases of HF with antecedent myocardial infarction to obtain stable estimates. Using the subsample of individuals with data on cholesterol, we did not find an association between egg consumption and total cholesterol (P = 0.86), HDL cholesterol (P = 0.74), or ratio of total to HDL cholesterol (P = 0.97) in a model controlling for age, body mass index, smoking, alcohol consumption, exercise, and diabetes mellitus. Controlling for measured cholesterol

### Table 2. Relative Risk (95% Confidence Interval) of HF According to Egg Consumption

<table>
<thead>
<tr>
<th>Egg Intake</th>
<th>Cases</th>
<th>Crude Hazard Ratio (95% CI)</th>
<th>Age-Adjusted Hazard Ratio (95% CI)</th>
<th>Model 1 Hazard Ratio (95% CI)</th>
<th>Model 2 Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1/wk</td>
<td>206</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1/wk</td>
<td>307</td>
<td>1.02 (0.85–1.22)</td>
<td>0.99 (0.83–1.18)</td>
<td>0.93 (0.80–1.16)</td>
<td>0.93 (0.78–1.12)</td>
</tr>
<tr>
<td>2–4/wk</td>
<td>359</td>
<td>1.15 (0.97–1.37)</td>
<td>1.10 (0.92–1.30)</td>
<td>1.02 (0.83–1.19)</td>
<td>1.03 (0.86–1.22)</td>
</tr>
<tr>
<td>5–6/wk</td>
<td>75</td>
<td>1.19 (0.91–1.55)</td>
<td>1.12 (0.86–1.45)</td>
<td>1.01 (0.78–1.32)</td>
<td>1.01 (0.78–1.32)</td>
</tr>
<tr>
<td>1/d</td>
<td>112</td>
<td>1.96 (1.56–2.46)</td>
<td>1.47 (1.17–1.85)</td>
<td>1.27 (1.01–1.60)</td>
<td>1.28 (1.02–1.61)</td>
</tr>
<tr>
<td>≥2/d</td>
<td>25</td>
<td>2.45 (1.62–3.71)</td>
<td>1.94 (1.28–2.95)</td>
<td>1.61 (1.06–2.44)</td>
<td>1.64 (1.08–2.49)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and ≥65 y), body mass index (<25, 25–29.9, ≥30 kg/m²), smoking (never, former, current smokers), alcohol consumption (<1, 1–4, 5–7, ≥8 drinks per week), and history of diabetes mellitus, atrial fibrillation, and hypertension.

†Additional adjustment for physical activity (<1/wk, ≥1/wk) and history of valvular heart disease and treatment for cholesterol.

### Table 3. Relative Risk (95% Confidence Interval) of HF Without Antecedent Myocardial Infarction According to Egg Consumption

<table>
<thead>
<tr>
<th>Egg Intake</th>
<th>Cases</th>
<th>Crude Hazard Ratio (95% CI)</th>
<th>Age-Adjusted Hazard Ratio (95% CI)</th>
<th>Model 1 Hazard Ratio (95% CI)</th>
<th>Model 2 Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1/wk</td>
<td>178</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1/wk</td>
<td>252</td>
<td>0.97 (0.80–1.17)</td>
<td>0.94 (0.77–1.14)</td>
<td>0.89 (0.73–1.08)</td>
<td>0.89 (0.73–1.07)</td>
</tr>
<tr>
<td>2–4/wk</td>
<td>294</td>
<td>1.09 (0.91–1.32)</td>
<td>1.04 (0.86–1.25)</td>
<td>0.97 (0.80–1.17)</td>
<td>0.97 (0.80–1.16)</td>
</tr>
<tr>
<td>5–6/wk</td>
<td>64</td>
<td>1.18 (0.88–1.57)</td>
<td>1.10 (0.83–1.46)</td>
<td>0.99 (0.75–1.32)</td>
<td>0.99 (0.74–1.31)</td>
</tr>
<tr>
<td>1/d</td>
<td>102</td>
<td>2.06 (1.62–2.63)</td>
<td>1.54 (1.21–1.97)</td>
<td>1.33 (1.04–1.69)</td>
<td>1.33 (1.04–1.70)</td>
</tr>
<tr>
<td>≥2/d</td>
<td>21</td>
<td>2.38 (1.51–3.74)</td>
<td>1.88 (1.20–2.95)</td>
<td>1.55 (0.99–2.44)</td>
<td>1.56 (0.99–2.46)</td>
</tr>
<tr>
<td>P for trend</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, and ≥65 y), body mass index (<25, 25–29.9, ≥30 kg/m²), smoking (never, former, current smokers), alcohol consumption (<1, 1–4, 5–7, ≥8 drinks per week), and history of diabetes mellitus, atrial fibrillation, and hypertension.

†Additional adjustment for physical activity (<1/wk, ≥1/wk) and history of valvular heart disease and treatment for cholesterol.
instead of prevalent hypercholesterolemia had no effect on the findings among subjects with blood lipids.

Discussion

In this prospective cohort, we demonstrated that infrequent consumption of eggs (up to 6 per week) was not associated with HF, whereas consumption of ≥7 eggs per week was associated with an increased risk of HF among male physicians. Furthermore, a similar association was observed for HF without antecedent myocardial infarction, and we did not find evidence for effect measure modification by hypercholesterolemia, diabetes mellitus, smoking, or hypertension on the observed associations.

Because eggs are rich in dietary cholesterol, researchers have been interested in the effects of egg consumption on serum cholesterol or other intermediate phenotypes. However, limited and inconsistent data have been reported on egg consumption and incident cardiovascular disease and mortality. Data from 514 Western Australian Aborigines showed a 2.6-fold increased risk of CHD comparing egg consumption of ≥2 versus <2 per week after ≈14 years of follow-up. Compared with egg consumption of <1 per week, the incidence rate ratio for total mortality was 1.23 and 2.68 among subjects consuming 1 to 5 and ≥6 eggs per week, respectively, after adjustment for age, sex, smoking, and social class. Qureshi et al. reported a 2-fold increased risk of CHD among people reporting an intake of ≥6 eggs per week compared with intakes of <1 per week. In addition, compared with egg intake of <1 per week, Hu et al. reported a 2-fold increased risk of CHD for egg consumption of ≥1 per day among 37,851 diabetic men from the Health Professionals Follow-up Study after adjustment for potential confounders; these data suggest that the observed increased risk of HF with egg consumption could be mediated through CHD. Unfortunately, we did not have enough cases of HF with antecedent myocardial infarction to examine this hypothesis further. The fact that we observed elevated risk of HF without antecedent myocardial infarction suggests that alternative physiological mechanisms could be responsible for the observed association. Alternatively, additional lifestyle/dietary factors associated with frequent egg consumption could be responsible for the observed relationship. Given the observational nature of our design, we cannot exclude chance or residual confounding by measured and unmeasured factors as a possible explanation of our findings. In particular, the lack of details on the dietary questionnaire prevented us from controlling for energy intake and other major nutrients. The hypothesis of chance finding or residual confounding is supported by the lack of association between egg consumption and CHD in other studies.

Changes in dietary patterns may lead to a spurious association between baseline exposure and incident outcome. In our data, we used time-dependent Cox regression models to update reported egg consumption at 24, 48, 72, 96, and 120 months after randomization. Such exposure update over time led to similar conclusions, suggesting that our findings are robust and not sensitive to possible changes in egg consumption over time. In addition, adjustment for interim cases of myocardial infarction had little effect on the results.

A wide variability in individual response to dietary cholesterol (hyperresponders versus hyporesponders) has been reported. It has been suggest that among hyperresponders, dietary cholesterol from eggs leads to a modest increase in serum LDL and HDL cholesterol and no effect on LDL/HDL ratio. Thus, it is possible that the observed increased risk of HF with egg consumption might be limited to hyperresponders. However, the fact that we did not observe an association between egg consumption and baseline cholesterol in our study does not lend support to this theory. The lack of a relationship between egg consumption and serum cholesterol is consistent with other reported findings showing no effect of egg consumption on the LDL subtraction.

Our study has additional limitations. Our participants are male physicians who may have different behaviors than the general population, thereby limiting the generalizability of our findings. Furthermore, we did not have data on protein intake, serum albumin, and creatinine to explore the influence of protein load on the observed association, especially in the presence of kidney dysfunction and/or type 2 diabetes mellitus. Egg consumption was assessed with the use of an abbreviated food questionnaire. This might have led to underreporting of usual egg consumption and a bias toward the null. However, if such a bias were present, we would anticipate the true effect measure to be even larger between frequent egg consumption and HF. In this study, we did not directly validate the abbreviated food questionnaire used to assess egg consumption. However, validation of full food frequency questionnaires (including the egg consumption questionnaire used in this study) has been published elsewhere. Finally, measured plasma total and HDL cholesterol were available at baseline only in a limited number of subjects. On the other hand, the large sample size, the longer duration of follow-up, and the robustness of our findings in sensitivity analyses are strengths of the present study.

In conclusion, our data suggest that egg consumption up to 6 per week is not associated with HF, whereas consumption of ≥7 eggs per week is related to an increased risk of HF. Confirmation of these findings is warranted along with exploration of underlying biological mechanisms.

Acknowledgments

We are indebted to the participants in the PHS for their outstanding commitment and cooperation and to the entire PHS staff for their expert and unfailing assistance.

Sources of Funding

The PHS is supported by grants CA-34944 and CA-40360 from the National Cancer Institute and grants HL-26490 and HL-34595 from the National Heart, Lung, and Blood Institute, Bethesda, Md. Dr. Djoussé is Principal Investigator on grant K01 HL-70444 from the National Heart, Lung, and Blood Institute, Bethesda, Md.

Disclosures

None.

References

Heart failure (HF) is a major cause of hospitalization and emergency department visits among older adults. Although previous studies have examined the influence of lifestyle and dietary factors on the risk of HF, it is not known whether egg consumption is associated with an increased risk of HF. An egg can contain as much as 200 mg of dietary cholesterol. In the present study, we followed 21,275 participants from the Physicians’ Health Study I for an average of 20 years to examine the association between egg consumption and the risk of HF. Egg consumption was assessed with the use of a simple abbreviated food questionnaire. During the follow-up, a total of 1084 new HF cases occurred in this cohort. Although egg consumption up to 6 times per week was not associated with incident HF, consumption of 1 egg per day was associated with a 28% increased risk of HF, whereas consumption of ≥2 eggs per day was associated with a 64% increased risk of HF after accounting for confounding factors. Similar results were obtained for HF without antecedent myocardial infarction. Overall, our data suggest that although infrequent egg consumption has no influence on the risk of HF, frequent consumption may increase the risk of HF among US male physicians.

**CLINICAL PERSPECTIVE**

Heart failure (HF) is a major cause of hospitalization and emergency department visits among older adults. Although previous studies have examined the influence of lifestyle and dietary factors on the risk of HF, it is not known whether egg consumption is associated with an increased risk of HF. An egg can contain as much as 200 mg of dietary cholesterol. In the present study, we followed 21,275 participants from the Physicians’ Health Study I for an average of ~20 years to examine the association between egg consumption and the risk of HF. Egg consumption was assessed with the use of a simple abbreviated food questionnaire. During the follow-up, a total of 1084 new HF cases occurred in this cohort. Although egg consumption up to 6 times per week was not associated with incident HF, consumption of 1 egg per day was associated with a 28% increased risk of HF, whereas consumption of ≥2 eggs per day was associated with a 64% increased risk of HF after accounting for confounding factors. Similar results were obtained for HF without antecedent myocardial infarction. Overall, our data suggest that although infrequent egg consumption has no influence on the risk of HF, frequent consumption may increase the risk of HF among US male physicians.
Egg Consumption and Risk of Heart Failure in the Physicians' Health Study
Luc Djoussé and J. Michael Gaziano

Circulation. 2008;117:512-516; originally published online January 14, 2008;
doi: 10.1161/CIRCULATIONAHA.107.734210
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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World Wide Web at:
http://circ.ahajournals.org/content/117/4/512

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