

TABLE 5

Relative risks and 95% CIs of outcomes by egg consumption category in Cox analyses of men with data in the NIPPON DATA80 database¹

	Egg consumption					P for trend
	≥2/d (n = 149)	1/d (n = 1364)	1/2 d (n = 1216)	1-2/wk (n = 1204)	Seldom (n = 144)	
Age adjusted						
All-cause death	0.87 (0.57, 1.34)	1	0.88 (0.73, 1.08)	0.92 (0.77, 1.11)	0.80 (0.53, 1.21)	0.84
Stroke death	0.28 (0.03, 1.66)	1	1.04 (0.66, 1.64)	0.98 (0.63, 1.52)	0.91 (0.36, 2.40)	0.15
IHD death	—	1	1.34 (0.58, 3.10)	1.80 (0.85, 3.85)	1.51 (0.33, 6.81)	0.03
P	—		0.49	0.13	0.59	
Cancer death	1.53 (0.80, 2.88)	1	1.17 (0.83, 1.65)	1.15 (0.82, 1.61)	0.62 (0.25, 1.53)	0.51
Multivariate adjusted ²						
All-cause death	0.89 (0.57, 1.38)	1	0.89 (0.72, 1.08)	0.94 (0.78, 1.13)	0.73 (0.48, 1.12)	0.75
Stroke death	0.25 (0.03, 1.81)	1	1.10 (0.68, 1.76)	1.09 (0.69, 1.72)	0.93 (0.36, 2.40)	0.11
IHD death	—	1	1.49 (0.63, 3.48)	1.71 (0.78, 3.76)	1.18 (0.26, 5.42)	0.08
Cancer death	1.42 (0.73, 2.76)	1	1.12 (0.79, 1.58)	1.11 (0.79, 1.57)	0.60 (0.24, 1.49)	0.57

¹ NIPPON DATA80, National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged, 1980; IHD, ischemic heart disease.

² Age, serum creatinine, total cholesterol, blood glucose, BMI, systolic and diastolic blood pressures, use of blood pressure-lowering drugs, cigarette smoking, and alcohol intake were entered as covariates for multivariate analyses.

Japan that used the food record method in rural and urban populations and that was conducted during a similar time as the present study reported that egg consumption in Japan accounts for ≈48% of total dietary cholesterol intake (15).

The present study found dose-response relations of egg consumption to total cholesterol and age-adjusted total cholesterol concentrations in women but not in men. On the basis of metabolic ward studies, Keys proposed an equation to predict serum cholesterol concentrations based on dietary intakes of cholesterol and saturated and polyunsaturated fatty acids (3). We surveyed essential nutritional components by the food-frequency method and therefore have no data on total calorie intake or total dietary intakes of cholesterol or saturated and polyunsaturated fatty acids. On the basis of previous studies that used the 24-h food-recall method or food record method in rural and urban populations in Japan and that had a study period similar to that of the present study (13–15), the representative daily total energy intake of female subjects can be estimated to be 1970 kcal, with 350 mg total dietary cholesterol. If egg consumption is reduced from 1/d (215 mg cholesterol/d) to 1.5/wk (46 mg cholesterol/d), total energy intake should decrease by 63 kcal (80 kcal/egg), polyunsaturated fatty acid intake should decrease from 7 to 6.4 g, and saturated fatty acid intake should decrease from 7.7 to 6.4 g. Under these conditions, the Keys equation predicts that total cholesterol concentrations should decrease by 6.5 mg/dL (0.17 mmol/L). The actual difference observed between age-adjusted total cholesterol concentrations in the 1-egg/d category and those in the 1-2-eggs/wk category was 5.8 mg/dL (0.15 mmol/L). In men, a similar calculation yields a predicted reduction in total cholesterol concentrations of 5.4 mg/dL (0.14 mmol/L) (assumed total energy and dietary cholesterol intakes of 2400 kcal and 400 mg, respectively), but the actual observed difference in age-adjusted total cholesterol was only 0.8 mg/dL (0.02 mmol/L). Thus, differences in age-adjusted total cholesterol concentration between categories conformed to the Keys equation in the women but not in the men. Why is the relation between egg consumption and total cholesterol different between women and men? Ueshima et al (13) observed a high-order relation in several groups of Japanese men, with large differences between groups in both dietary intake and total cholesterol. However, only a

weak, although significant, correlation was noted between the dietary lipid score and serum total cholesterol for subjects within a culturally homogeneous population in which intraindividual variability is large compared with interindividual variability. In the study by Dawber et al (11), the distribution of daily dietary cholesterol intake was examined by tertile of egg consumption, and significant differences in total daily cholesterol intake between subjects within each egg consumption tertile were found in both women and men. However, markedly greater variability was seen in men. Therefore, men appear to consume dietary cholesterol from a greater variety of sources (ie, sources other than eggs) than do women.

A population with a low mean cholesterol concentration, such as the population in Japan, has a much lower IHD mortality rate than do Western populations (22). However, cholesterol has been shown to have predictive value for IHD mortality in Japan (18). Women in the 1-2-eggs/wk group had the lowest age-adjusted total cholesterol concentrations, and their relative risk of all-cause death was significantly lower than that of the women in the 1-egg/d group. The women in the 1-2-eggs/wk group also tended to have lower mortality due to stroke, IHD, and cancer than did the 1-egg/d group. Because of the relatively high participation rate in the present study (76.6%), generalization of the present results in Japan may be warranted.

Limitations of the study

We surveyed essential nutritional components by using the food-frequency method. Therefore, we have no data on total calorie intake or total dietary intakes of cholesterol or saturated and polyunsaturated fatty acids. To obtain this information, detailed food records or 24-h dietary recalls are needed. However, because of the large amount of effort required to collect and process multiple days of food records or recalls, these methods are impractical and seldom used as the primary method for estimating usual intakes in large-scale epidemiologic studies.

Another limitation is that we used mortality data as endpoints, which may have led to misclassification of the cause of death. However, the death-certificate diagnosis of stroke and cancer in Japan has been reported to be quite accurate (23, 24). However, it has also been reported that most cases of cardiac sudden death

tended to be described on Japanese death certificates as "coronary heart disease," "heart failure," or "unknown cause" (25, 26). Furthermore, mortality statistics for IHD may have been underestimated with the use of ICD9 by the end of 1994 because deaths coded as "heart failure" may have hidden some coronary events (25-28). Nevertheless, our results mainly focused on all-cause mortality, and thus the data were thought to be correct.

Finally, the consumption of only 1-2 eggs/wk by women may simply reflect a more health-conscious attitude that eventually results in a better outcome. We did not measure variables related to health consciousness, such as exercise or participation in sports; however, the percentage of women who smoked in the 1-2-eggs/wk category (10.6%) was not lower than that in the 1-egg/d category (7.5%) (Table 1). This suggests that the women in the 1-2-eggs/wk category did not have more health-conscious attitudes.

Conclusions

Dose-response relations of egg consumption to total cholesterol and age-adjusted total cholesterol concentrations were noted in the women, and all-cause mortality was affected by egg consumption. Among the women, tendencies for lower mortality due to stroke, IHD, and cancer in the 1-2-eggs/wk group than in the 1-egg/d group may have resulted in significantly fewer all-cause deaths. However, no such relations were noted in the men. Sources other than eggs may contribute to total cholesterol intake in men. These results suggest that limiting egg consumption may have some health benefits, at least in women in geographic areas where egg consumption makes a relatively large contribution to total dietary cholesterol intake.

For a list of the investigators and members of the NIPPON DATA80 Research Group, please see the appendix of reference 18.

YN participated in designing and conducting the study, analyzing and interpreting the data, and writing and preparing the manuscript. TO and AO participated in conducting the study and analyzing and interpreting the data. ST and TK participated in managing and interpreting the data. TH and YK participated in managing the data and conducting the study. HU was the principal investigator and participated in designing and conducting the study and analyzing and interpreting the data. None of the authors had any conflicts of interest.

REFERENCES

- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-9.
- Mattson FH, Erickson BA, Kligman AM. Effect of dietary cholesterol on serum cholesterol in man. *Am J Clin Nutr* 1972;25:589-94.
- Keys A. Serum cholesterol response to dietary cholesterol. *Am J Clin Nutr* 1984;40:351-9.
- Kummerow FA, Kim Y, Hull J, et al. The influence of egg consumption on the serum cholesterol level in human subjects. *Am J Clin Nutr* 1977;30:664-73.
- Porter MW, Yamanaka W, Carlson SD, Flynn MA. Effect of dietary egg on serum cholesterol and triglyceride of human males. *Am J Clin Nutr* 1977;30:490-5.
- Flynn MA, Nolph GB, Flynn TC, Kahrs R, Krause G. Effect of dietary egg on human serum cholesterol and triglycerides. *Am J Clin Nutr* 1979;32:1051-7.
- Oh SY, Miller LT. Effect of dietary egg on variability of plasma cholesterol levels and lipoprotein cholesterol. *Am J Clin Nutr* 1985;42:421-31.
- Nichols AB, Ravenscroft C, Lamphiear DE, Ostrander LD Jr. Independence of serum lipid concentrations and dietary habits. The Tecumseh study. *JAMA* 1976;236:1948-53.
- Nichols AB, Ravenscroft C, Lamphiear DE, Ostrander LD Jr. Daily nutritional intake and serum lipid concentrations. The Tecumseh study. *Am J Clin Nutr* 1976;29:1384-92.
- Frank GC, Berenson GS, Webber LS. Dietary studies and the relationship of diet to cardiovascular disease risk factor variables in 10-year-old children—The Bogalusa Heart Study. *Am J Clin Nutr* 1978;31:328-40.
- Dawber TR, Nickerson RJ, Brand FN, Pool J. Eggs, serum cholesterol, and coronary heart disease. *Am J Clin Nutr* 1982;36:617-25.
- Hu FB, Stampfer MJ, Rimm EB, et al. A prospective study of egg consumption and risk of cardiovascular disease in men and women. *JAMA* 1999;281:1387-94.
- Ueshima H, Iida M, Shimamoto T, et al. Dietary intake and serum total cholesterol level: their relationship to different lifestyles in several Japanese populations. *Circulation* 1982;66:519-26.
- Okayama A, Ueshima H, Marmot MG, Elliott P, Yamakawa M, Kita Y. Different trends in serum cholesterol levels among rural and urban populations aged 40-59 in Japan from 1960 to 1990. *J Clin Epidemiol* 1995;48:329-37.
- Yoshida Y, Okayama A, Makita K, et al. Dietary intake and its relationship to serum cholesterol concentrations among three Japanese populations in the early 1990s: INTERSALT II study in Japan. *J Shiga Univ Med Sci* 1998;13:63-79.
- Hayakawa T, Okayama A, Ueshima H, et al. Prevalence of impaired activities of daily living and impact of stroke and lower limb fracture on it in Japanese elderly people. *CVD Prev* 2000;3:187-94.
- Sakata K, Hashimoto T, Ueshima H, Okayama A, Group NDR. Absence of an association between serum uric acid and mortality from cardiovascular disease: NIPPON DATA 80, 1980-1994. National Integrated Projects for Prospective Observation of Non-communicable Diseases and its Trend in the Aged. *Eur J Epidemiol* 2001;17:461-8.
- Okamura T, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H. What cause of mortality can we predict by cholesterol screening in the Japanese general population? *J Intern Med* 2003;253:169-80.
- Japanese Ministry of Health and Welfare. National Survey on Circulatory Disorders. Tokyo: Japan Heart Foundation, 1982 (in Japanese).
- Myers GL, Kimberly MM, Waymack PP, Smith SJ, Cooper GR, Sampson EJ. A reference method laboratory network for cholesterol: a model for standardization and improvement of clinical laboratory measurements. *Clin Chem* 2000;46:1762-72.
- Bitner D, McCleary M. The cupric-phenanthroline chelate in the determination of monosaccharides in whole blood. *Am J Clin Pathol* 1963;40:423-4.
- Keys A, Menotti A, Aravanis C, et al. The seven countries study: 2,289 deaths in 15 years. *Prev Med* 1984;13:141-54.
- Hasuo Y, Ueda K, Kiyohara Y, et al. Accuracy of diagnosis on death certificates for underlying causes of death in a long-term autopsy-based population study in Hisayama, Japan; with special reference to cardiovascular diseases. *J Clin Epidemiol* 1989;42:577-84.
- Ron E, Carter R, Jablon S, Mabuchi K. Agreement between death certificate and autopsy diagnoses among atomic bomb survivors. *Epidemiology* 1994;5:48-56.
- Saito I, Folsom AR, Aono H, et al. Comparison of fatal coronary heart disease occurrence based on population surveys in Japan and the USA. *Int J Epidemiol* 2000;29:837-44.
- Saito I, Ozawa H, Aono H, et al. Change of the number of heart disease deaths according to the revision of the death certificates in Oita city. *Nippon Koshu Eisei Zasshi* 1997;44:874-9 (in Japanese).
- Tokashiki T, Muratani A, Kimura Y, et al. Sudden death in the general population in Okinawa: incidence and causes of death. *Jpn Circ J* 1999;63:37-42.
- Baba S, Ozawa H, Sakai Y, et al. Heart disease deaths in a Japanese urban area evaluated by clinical and police records. *Circulation* 1994;89:109-15.