CLINICAL RESEARCH STUDY

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Association Between Egg Consumption and Risk of Cardiovascular Outcomes: A Systematic Review and Meta-Analysis

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ABSTRACT

INTRODUCTION: Considerable controversy remains on the relationship between egg consumption and cardiovascular disease risk. The objective of this systematic review and meta-analysis was to explore the association between egg consumption and overall cardiovascular disease events.

METHODS: We systematically searched Ovid MEDLINE, Ovid Embase, Ovid Cochrane Database of Systematic Reviews, Scopus, and Web of Science from database inception in 1966 through January 2020 for observational studies that reported the association between egg consumption and cardiovascular disease events. Two investigators independently reviewed data. Conflicts were resolved through consensus. Random-effects meta-analyses were used. Sources of heterogeneity were analyzed.

RESULTS: We identified 23 prospective studies with a median follow-up of 12.28 years. A total of 1,415,839 individuals with a total of 123,660 cases and 157,324 cardiovascular disease events were included. Compared with the consumption of no or 1 egg/day, higher egg consumption (more than 1 egg/day) was not associated with significantly increased risk of overall cardiovascular disease events (pooled hazard ratios, 0.99; 95% confidence interval, 0.93-1.06; $P < .001$; $I^2 = 72.1\%$). Higher egg consumption (more than 1 egg/day) was associated with a significantly decreased risk of coronary artery disease (pooled hazard ratios, 0.89; 95% confidence interval, 0.86-0.93; $P < .001$; $I^2 = 0\%$), compared with consumption of no or 1 egg/day.

CONCLUSIONS: Our analysis suggests that higher consumption of eggs (more than 1 egg/day) was not associated with increased risk of cardiovascular disease, but was associated with a significant reduction in risk of coronary artery disease.

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KEYWORDS: Acute myocardial infarction; Cardiovascular disease; Egg consumption; Meta-analysis; Stroke; Systematic review

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INTRODUCTION

Eggs are a nutrient-dense (eg, minerals, folate, B vitamins, and fat-soluble vitamins), rich source of bioactive compounds (eg, lutein and zeaxanthin) and high-quality protein.[1] Nutrients and bioactive compounds in eggs may theoretically contribute to improving cardiovascular disease.[2] However, eggs are also high in cholesterol; for example, one large egg contains approximately 186 mg of cholesterol. Although there is no direct evidence that egg consumption can lead to elevated cholesterol levels, the American Heart Association Dietary Guidelines Revision 2000 recommended to the public that they consume <300 mg/day of cholesterol to minimize the elevation of blood cholesterol.[3] Interestingly, the more recent Dietary Guidelines for Americans 2015-2020[4] no longer provides limits on egg intake but recommends egg intake as part of healthy eating patterns. Previous studies have demonstrated inconsistent results of associations of egg consumption with cardiovascular disease, leading to considerable controversy.[5-8] To date, previous studies on egg consumption and cardiovascular disease risk have been inconclusive. The objective of this systematic review and meta-analysis was to explore the association between egg consumption and cardiovascular disease.

CLINICAL SIGNIFICANCE

- Consumption of more than one egg per day was not associated with an increased risk of cardiovascular disease.
- Consumption of more than one egg per day was associated with a reduction in the risk of coronary artery disease.
- Consumption of more than one egg per day was not associated with an increased risk of stroke.

METHODS

Search Strategy

We developed search strategies for Ovid MEDLINE, Ovid Embase, Ovid Cochrane Database of Systematic Reviews, Scopus, and Web of Science from database inception to January 2020. The search strategies were peer-reviewed by experienced librarians. The language or date of publication was not limited. The strategies included MeSH and Embase terms as well as keywords including egg, egg consumption, cardiovascular disease, cardiovascular events, coronary artery disease, acute myocardial infarct, acute coronary syndrome, stroke, or heart failure (see Supplementary Material, available online).

Study Selection

Studies were included in this analysis if they met the following criteria: the study design was either prospective or cross-sectional, the exposure of interest was egg consumption, the outcome was combined cardiovascular disease events, coronary artery disease, acute myocardial infarct, acute coronary syndrome, stroke or heart failure, and the investigators reported hazard ratios with 95% confidence intervals. Reviews, editorials, nonhuman studies, letters without sufficient data, and studies of other exposures and diseases were excluded.

Data Extraction

Two reviewers (CK and BN) performed data extraction using a standard extraction form and then additional review by other investigators (HH and HZ). Authors, year of publication, study name, study location, years of follow-up, sample size (number of participants and incident cases), participants' characteristics (age and sex), endpoints (eg, coronary artery disease, stroke), outcomes ascertainment, egg consumption categories, covariates adjusted in the multivariable analysis, and hazard ratios (95% confidence intervals) for all categories of egg consumption were extracted from included studies. Conflicts were resolved through consensus.

Quality Assessment

Two independent reviewers performed the quality assessment (BN and HJ) using the Newcastle-Ottawa quality assessment scale, a validated scale for nonrandomized studies in meta-analyses. Conflicts were resolved through consensus. We assigned scores of 0-3, 3.5-6, and 6.5-9 for low, moderate, and high quality of studies, respectively. We consulted dietitians and nutritionists for servings or nutritional units. We contacted the authors if the data of interest were not directly shown in the publications.

Statistical Analysis

In this meta-analysis, the hazard ratios (HRs) and 95% confidence intervals (CI) were considered as the effect size for all studies. Any results stratified by sex were separated as 2 cohorts. We used the DerSimonian & Laird random-effects method to pool HRs from the included studies. We also conducted subgroup analyses based on sex, study location, number of cases and participants, duration of follow-up, egg consumption measurements, study quality, and whether diet variables or cholesterol levels were controlled for in models. The difference between subgroups was evaluated using the interaction test proposed by Altman and Bland.[9] Heterogeneity between studies was measured by I^2. Substantial heterogeneity was defined as I^2 >50%. Stata version 11 (StataCorp LLC, College Station, Texas) and R version 3.6.1 were used for statistical analyses. A 2-sided P-value of < .05 was considered statistically significant.

Table Characteristics of Included Studies

Study	Year	Country	Study Design	Men %	Mean Age, Years	Follow-Up Term, Years	Subjects n	Cases n	Outcome Assessments	Outcome	Exposure Assessments	Adjusted Variables
Dehghan[32]	2020	21	Cohort	41.9	50.6 ± 9.9	4.6	146,011	3410	Self-reported questionnaire	Cardiovascular disease, all-cause mortality, major cardiovascular disease, lipid profile, blood pressure	FFQ	Age, sex, education, urban or rural location, smoking, physical activity, history of diabetes, fruit and vegetables, red meat, poultry, fish, dairy, percentage of energy from carbohydrates, and total energy intake
Djoussé[31]	2019	USA	Cohort	90.1	64.4	3.24	188,267	10,260	ICD codes	MI	FFQ	Age, sex, race, education, BMI, smoking, exercise, alcohol intake, DM
Zhong[30]	2019	United States	Cohort	44.9	51.6	17.5	29615	5400	Questionnaire	Cardiovascular disease	FFQ	Age, sex, race/ethnicity, education, total energy, smoking status, smoking pack-years, BMI, alcohol consumption, and use of hormone therapy
Xu[29]	2018	China	Cohort	28	62.1	9.8	28,024	2685	Medical records	Cardiovascular disease, Fasting sugar, BP, Lipid panel, BMI, all-cause mortality	FFQ	Age, sex, socioeconomic position (education, income, and occupation)
Qin[5]	2018	China	Cohort	41	50.7	8.9	461,213	83,977	ICD Codes	Cardiovascular disease, IHD, stroke, MCE	Diet Questionnaire	Age at recruitment and sex, education level, household income, marital status, alcohol consumption, tobacco smoking, physical activity in MET-hours/day, BMI, waist-to-hip ratio, prevalent hypertension, use of aspirin, family history of cardiovascular disease, intake of multivitamin supplementation and dietary pattern
Jang[28]	2018	Korea	Cohort	47.8	52	7.3	9248	570	Biennial questionnaire	Cardiovascular disease, T2DM	SQFFQ	Age, sex, educational level, residential area, monthly household income, alcohol drinking, smoking in pack-years, and physical activity level. dietary supplement use, history of hypertension and dyslipidemia, and the intake levels of total energy, total vegetables, total fruits, red meat, fiber, and vitamin E. BMI
Guo[27]	2017	UK	Cohort	100	61.6	22.8	1781	1863	Self-reported questionnaire	Cardiovascular disease, T2D, all-cause mortality	FFQ	Age, BMI, energy and alcohol intake, smoking, social class, energy expenditure, FH of MI or T2DM. Sugar, fruit, red meat and fiber intake
Espino[26]	2016	Mediterranean countries	Cohort	49.3	66.5	5.8	7216	342	Medical records	MI, stroke & death (CV causes)	FFQ	Age, Sex, BMI, DM, HTN, HLD, FH of premature coronary artery disease
Scrafford et al. (M)[25]	2011	USA	Cohort	100	42.1	8.8	6833	261	ICD codes I20-I25; I60-69	CHD mortality; stroke mortality;	Semiquantitative FFQ	Age, energy, marital status, race/ethnicity, smoking, BMI, WHR, DM, hypertension, dietary variables
Scrafford et al. (F)[25]	2011	USA	Cohort	0	42	8.9	8113	142	ICD codes I20-I25; I60-69	CHD mortality, stroke mortality;	Semiquantitative FFQ	Age, energy, marital status, race/ethnicity, smoking, BMI, WHR, DM, hypertension, dietary variables
Zazpe et al[24]	2011	Spain	Cohort	40.9	38.4	6.1	14,185	91	Medical record	Cardiovascular disease	Semiquantitative FFQ	Age, sex, energy, alcohol, smoking, BMI, DM, hypertension, physical activity, adherence to Mediterranean food pattern; hyperlipidemia, family history of cardiovascular disease

Table (*Continued*)

Study	Year	Country	Study Design	Men %	Mean Age, Years	Follow-Up Term, Years	Subjects n	Cases n	Outcome Assessments	Outcome	Exposure Assessments	Adjusted Variables
Houston et al.[23]	2011	USA	Cohort	45.5	74.5	9	1941	203	Medical record	Cardiovascular disease	Interviewer administered questionnaire	Age, sex, race, energy, education, field center, smoking, alcohol, physical activity, BMI, multivitamin, aspirin, or statin, oral estrogen use, DM, hypertension, fiber, protein, or saturated fat intake
Djousse et al. (M)[22]	2010	USA	Cohort	42.8	73.2	11.3	1668	142	Medical record	DM	Picture-sort FFQ	Age, race, field center, BMI, physical activity, energy, smoking, alcohol, fiber intake
Djousse et al. (F)[22]	2010	USA	Cohort	57.2	72.1	11.3	2230	161	Medical record	DM	Picture-sort FFQ	Age, race, field center, BMI, physical activity, energy, smoking, alcohol, fiber intake
Djousse et al. (M)[21]	2009	USA	Cohort	100	53.5	20	20,703	1921	Self-report or medical record	DM	Semiquantitative FFQ	Age, BMI, smoking, alcohol consumption, exercise, red meat intake, quintiles of energy intake, fruits and vegetables, saturated fatty acids, trans fatty acids, polyunsaturated fatty acids, family history of diabetes, and history of hypercholesterolemia and hypertension.
Djousse et al. (F)[21]	2009	USA	Cohort	0	54.5	11.7	36,295	2112	Self-report or medical record	DM	Semiquantitative FFQ	Age, BMI, smoking, alcohol consumption, exercise, red meat intake, quintiles of energy intake, fruits and vegetables, saturated fatty acids, trans fatty acids, polyunsaturated fatty acids, family history of diabetes, and history of hypercholesterolemia and hypertension.
Djousse et al[2]	2008	USA	Cohort	100	53.7	20.4	21,275	1084	Medical record	HF	Semiquantitative FFQ	Age, BMI, smoking, alcohol consumption; DM, AF, hypertension, physical activity; history of valvular disease and treatment of cholesterol
Djousse et al[2]	2008	USA	Cohort	100	53.7	20.4	21,327	8071	The Endpoint Committee of the PHS	All-cause mortality; MI; stroke;	Semiquantitative FFQ	Age, BMI, smoking, alcohol consumption; DM, AF, hypertension, physical activity, history of valvular disease and treatment of cholesterol
Nettleton et al.[33]	2008	USA	Cohort	45.5	54.2	13.3	14,153	1140	ICD-9 (codes 428 and I50, ICD-10	HF	Interviewer-administered questionnaire	Age, race, education, BMI, physical activity, energy, smoking, alcohol, fiber, sodium, meat, fruit consumption, baseline history of disease
Qureshi et al.[34]	2007	USA	Cohort	38.7	49.2	20	9734	1239	ICD codes 9	IHD; stroke; all-cause mortality;	Diet questionnaire	Age, sex, serum cholesterol, hypertension, waist girth
Burke et al[35]	2007	Australia	Cross-sectional	50.8	NA	14	488	130	Medical records, ICD codes 9, 10, 410-414, 427, 428	CHD	Interviewer administered questionnaire	Age, sex, race, DM, serum cholesterol, smoking, hypertension, BMI, educational status

Table *(Continued)*

Study	Year	Country	Study Design	Men %	Mean Age, Years	Follow-Up Term, Years	Subjects n	Cases n	Outcome Assessments	Outcome	Exposure Assessments	Adjusted Variables
Nakamura et al[39]	2006	Japan	Prospective	47.8		11	90,735	462	Medical record	CHD	Semiquantitative FFQ	Age, sex, BMI, hypertension, diabetes, use of cholesterol-lowering drugs, smoking (never, ex-, and current smoker), alcohol drinking (6 categories), whether or not intended to avoid cholesterol-rich diets, consumption frequencies of meat, fish, vegetables, fruits, and cohort effects
Montonen[38]	2005	Finland	Cohort	53	53.7	23	4304	383	Medical records	DM	FFQ	Age, sex, BMI, smoking, family history of diabetes, geographic area
Hu et al. (M)[37]	1999	USA	Cohort	100	53.3	8	37,851	866	Medical record	CHD, stroke,	Diet questionnaire	Age, sex, smoking, BMI, parental history of MI, multivitamin supplement, hypertension, physical activity, menopausal status
Hu et al. (F)[37]	1999	USA	Cohort	0	45.9	14	80,082	939	Medical record	CHD, stroke,	Diet questionnaire	Age, sex, smoking, BMI, parental history of MI, multivitamin supplement, hypertension, physical activity, menopausal status
Mann et al.[36]	1997	New Zealand	Cohort	38	33.4	13.3	10,802	525	ICD codes 410-414	All-cause mortality; IHD	Semiquantitative FFQ	Age, sex, smoking, social class

AF = atrial fibrillation; BMI = body mass index; BP = blood pressure; CHD = coronary heart disease; CV = cardiovascular; DM = diabetes mellitus; FFQ = food frequency questionnaire; FH = familial hypercholesterolemia; HLD = hyperlipidemia; HTN = hypertension; ICD = International Classification of Diseases; IHD = ischemic heart disease; MET = metabolic equivalent; MI = myocardial infarction; PHS = Physicians' Health Study; SQFFQ = semi-quantitative FFQ; T2DM = type 2 diabetes mellitus.

RESULTS

Figure 1 shows the results of literature research and selection. We identified 530 articles from PubMed, SCOPUS, and COCHRANE database from 1966 to January 31, 2020. We identified 23 prospective studies with a median follow-up of 12.28 years. A total of 1,415,839 individuals with a total of 123,660 cases and 157,324 cardiovascular disease events were included. We categorized cardiovascular disease as 94,175 coronary heart disease, 3,112 heart failure, 19,173 acute myocardial infarction, and 40,864 stroke cases. The study population included 565,385 individuals from China, 495,972 from the United States, 10,802 from New Zealand, 166,790 from Japan, 6,636 from Finland, 488 from Australia, 14,185 from Spain, 702 from Lithuania, 65,364 from France, 26,930 from Sweden, 9,248 from Korea, 1,781 from the UK, 7,216 from Mediterranean countries, 14,337 from the Middle East, 6,282 from Africa, and 23,721 from South America. (Table) We did not find a significant association between egg consumption and increased risk of overall cardiovascular disease events (HR 0.99; 95% CI, 0.93-1.06; I^2 = 72.1%) (Figure 2). Compared with the consumption of no or 1 egg/day, higher egg consumption (more than 1 egg/day) was associated with a significantly decreased risk of coronary artery disease (HR 0.89; 95% CI, 0.86-0.93; I^2 = 0%) (Figure 3); however, higher egg consumption (more than 1 egg/day) was not associated with the risk of stroke (HR 0.92; 95% CI, 0.84-1.02; I^2 = 60.1%) (Figure 4). In subgroup analyses using study type (prospective vs retrospective), geography, and follow-up year, we did not find any associations between egg consumption and risk of cardiovascular disease. There was no significant difference between the subgroups. After excluding studies with a moderate risk of bias, we did not find any associations between egg consumption and risk of cardiovascular disease.

DISCUSSION

The present meta-analysis, including studies from 1966 to 2020, identified no significant association between egg consumption and risk of cardiovascular disease events, but we found that egg consumption (>1 egg per day) is associated with a reduction in coronary artery disease risk. Similarly, the previous meta-analysis of 8 observational studies showed no significant association between egg intake and cardiovascular disease events.[10] However, there is substantial heterogeneity in that meta-analysis due to adjusted variables in included studies. A recent meta-analysis found that moderate egg consumption (≤1 egg per day) is not associated with cardiovascular disease risk overall.[11] These results are consistent with a subgroup analysis of our study. From evidence to date, either 1 egg or more than 1 egg consumption is not associated with cardiovascular disease. Another meta-analysis of overall dietary cholesterol, including eggs, found no significant either coronary artery disease or stroke risks.[12] However, those included studies

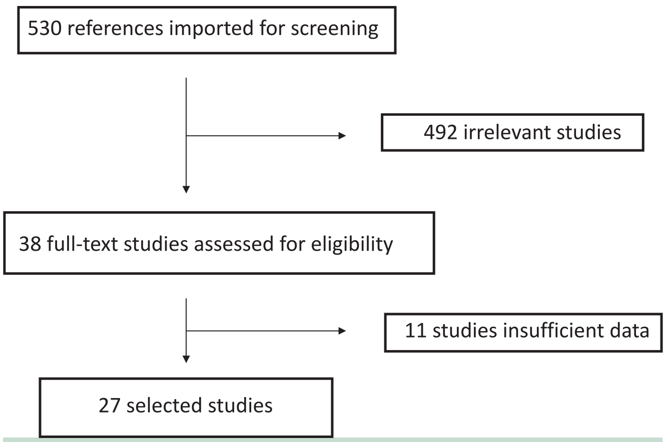

Figure 1 Study design. This flow chart illustrates the selection process for published reports.

in that meta-analysis were heterogeneous and lacked the methodologic rigor to draw any conclusions. To date, studies of egg consumption and coronary artery disease, including meta-analyses, have been inconsistent. The latest meta-analysis of intake of 12 major food groups, including eggs, suggested an optimal eggs consumption may lower risk of coronary artery disease.[13] A previous meta-analysis that included 7 prospective studies found no significant association with coronary artery disease by comparing high vs low egg consumption (summary relative risk estimates 0.97; 95% CI, 0.88-1.07).[14] However, the results may be confounded by the inclusion of diabetic patients who have higher cardiovascular disease risks due to dietary patterns than nondiabetic patients.[15] Another meta-analysis of 9 prospective studies reported that egg consumption was not associated with an increased risk of coronary artery disease but was associated with a significantly elevated risk of

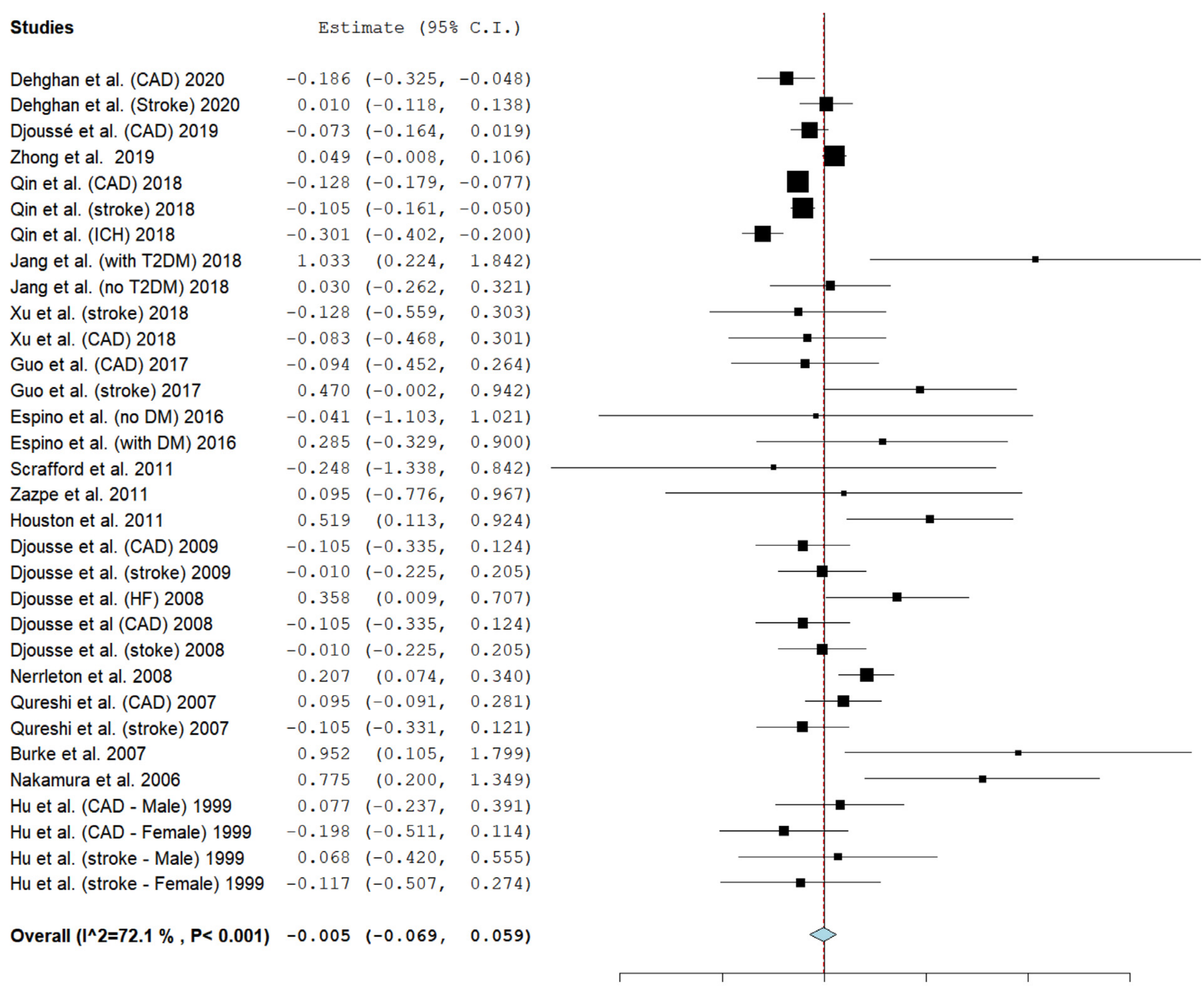

Figure 2 Hazard ratio of cardiovascular diseases associated with egg consumption (more than 1 egg/day vs. no/1 egg/day).

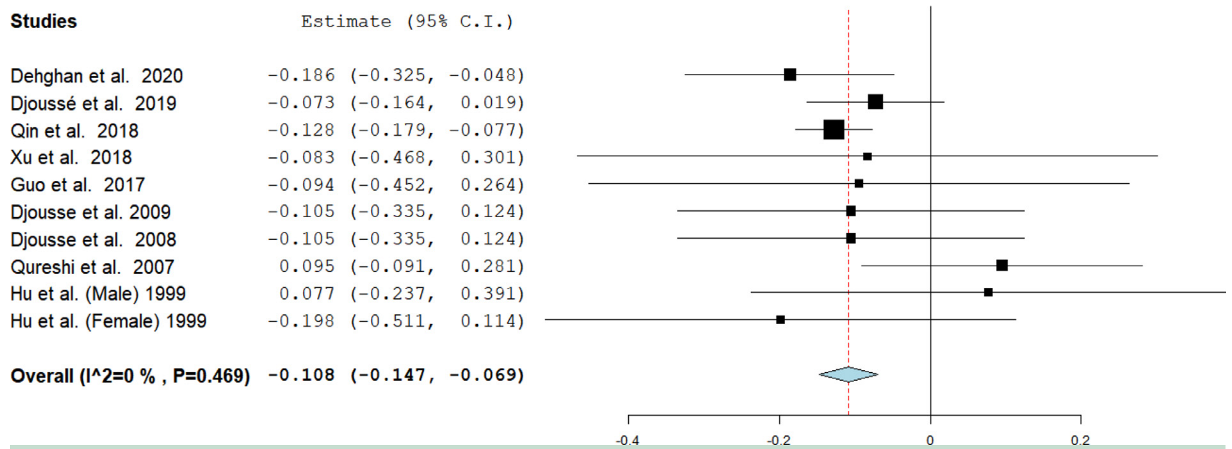

Figure 3 Hazard ratio of coronary artery disease associated with egg consumption (more than 1 egg/day vs. no/1 egg/day).

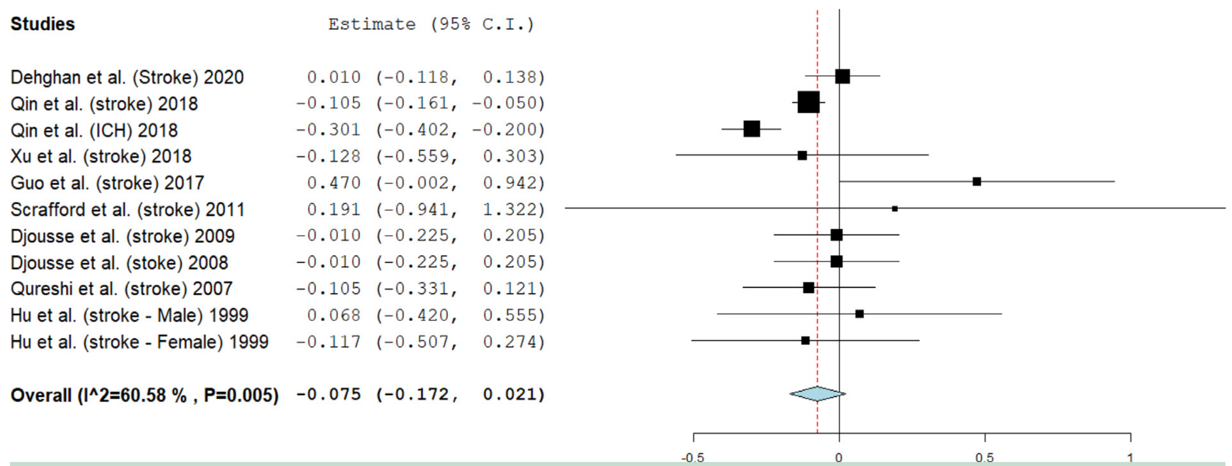

Figure 4 Hazard ratio of stroke associated with egg consumption (more than 1 egg/day vs. no/1 egg/day).

coronary artery disease in diabetic populations.[10] Interestingly, our study found no association between egg consumption and coronary artery disease in both diabetes groups and nondiabetes groups.

Egg consumption may reduce coronary artery disease via a mechanism of promoted carotenoid absorption,[16,17] enhanced high-density lipoprotein cholesterol function,[18,19] and increased bioactive compounds (eg, lutein and zeaxanthin), resulting in protecting against atherosclerosis.[20] The discrepancy of previous studies may be due to small sample sizes, a lack of adjustment for overall dietary pattern, ethnic difference, and only adjusting for blood glucose instead of excluding diabetic patients. For example, a recent meta-analysis found that egg consumption up to 1 egg per day is probably associated with a slightly lower cardiovascular disease risk among Asians.[11] Most importantly, individuals who consume egg may consume processed meats or bacon or high salt intake.

There are certain limitations to our meta-analysis. First, participants may have changed their dietary pattern during the long follow-up period, particularly in the United States (eg, the change in recommendation from the Dietary Guidelines for Americans 2015-2020).[4] Second, self-reported diet data could potentially lead to measurement errors. Third, the statistical power was limited in subgroup analyses of subtypes of stroke (ischemic vs hemorrhagic) or heart failure (heart failure with preserved ejection fraction vs heart failure with reduced ejection fraction). Fourth, dietary data collection with food frequency questionnaires inevitably leads to some measurement errors. Finally, the study findings are observational and cannot establish causality.

In conclusion, our analysis suggests that higher consumption of eggs (more than 1 egg/day) was not associated with increased risk of cardiovascular disease, but with a reduction in risk of coronary artery disease.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjmed.2020.05.046.

APPENDIX. SUPPLEMENTAL MATERIAL

Online Supplementary Table 1 Characteristics of Included Studies Using the Modified Newcastle—Ottawa Scale for Assessing the Quality of the Non-Randomized Studies

Study, year (reference)	Selection				Comparability	Outcome		
	Representativeness of the exposed cohort truly the general population in the community	Selection of the non exposed cohort from the same community as the exposed cohort (drawn from the same community as the exposed cohort)	Ascertainment of exposure (validated questionnaire or measurement tool)	Demonstration that outcome of interest was not present at start of study (no heart failure signs or/and symptoms at start of study)	Comparability of cohorts on the basis of the design or analysis (study controls for gender and cardiovascular risk factors)	Assessment of outcome (physician's diagnosis OR objective measurements)	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts (complated or loss follow up < 20%) or (The statistical test used to analyze the data is clearly described and appropriate)
Mann et al.	✓	✓		✓	✓	✓	✓	✓
Hu et al.		✓	✓	✓	✓	✓	✓	✓
Nakamura et al	✓	✓	✓	✓	✓	✓	✓	✓
Qureshi et al.	✓	✓	✓	✓	✓	✓	✓	✓
Burke et al.		✓	✓	✓	✓	✓	✓	
Djousse et al.		✓	✓	✓	✓	✓	✓	✓
Djousse et al.		✓	✓	✓	✓	✓	✓	✓
Nettleton et al.	✓	✓	✓	✓	✓	✓	✓	✓
Scrafford et al.	✓	✓	✓	✓	✓	✓	✓	✓
Zazpe et al.		✓	✓	✓	✓	✓	✓	✓
Houston et al.		✓	✓	✓	✓	✓	✓	
Djousse et al.		✓	✓	✓	✓	✓	✓	✓
Shi et al.	✓	✓	✓	✓	✓	✓		
Radzeviciene et al.	✓	✓	✓	✓	✓	✓		
Lajous et al.		✓	✓	✓	✓	✓		✓
Kurotani et al.	✓	✓	✓	✓	✓	✓	✓	
Virtanen et al.	✓	✓	✓	✓	✓	✓	✓	✓
Montonen et al.	✓	✓	✓	✓	✓	✓	✓	
Ericson et al.	✓	✓	✓	✓	✓	✓	✓	✓
Zhong et al.	✓	✓	✓	✓	✓	✓	✓	
Qin et al.	✓	✓	✓	✓	✓	✓	✓	✓
Jang et al.	✓	✓	✓	✓	✓	✓	✓	✓
Guo et al.	✓	✓	✓	✓	✓	✓	✓	✓
Espino et al.	✓	✓	✓	✓	✓	✓	✓	
Xu et al.	✓	✓	✓	✓	✓	✓	✓	✓
Dehghan et al.	✓	✓	✓	✓	✓	✓		✓
Djoussé et al.	✓	✓	✓	✓	✓	✓		✓

Online Supplementary Table 2 Summary of Critical Appraisal of Included Studies Using the Newcastle—Ottawa Scale for Assessing the Quality of Observational Studies

Study, year (reference)	Stars, n			total	Quality
	Selection	Comparability	Outcome		
Mann et al.	3	1	3	7	High
Hu et al.	3	1	3	7	High
Nakamura et al	4	1	3	8	High
Qureshi et al.	4	1	3	8	High
Burke et al.	3	1	2	6	Moderate
Djousse et al.	3	1	3	7	High
Djousse et al.	3	1	3	7	High
Nettleton et al.	4	1	3	8	High
Scrafford et al.	4	1	3	8	High
Zazpe et al.	3	1	3	7	High
Houston et al.	3	1	2	6	Moderate
Djousse et al.	3	1	3	7	High
Shi et al.	4	1	1	6	Moderate
Radzeviciene et al.	4	1	1	6	Moderate
Lajous et al.	3	1	2	6	Moderate
Kurotani et al.	4	1	2	7	High
Virtanen et al.	4	1	3	8	High
Montonen et al.	4	1	2	7	High
Ericson et al.	4	1	3	8	High
Zhong et al.	4	1	2	7	High
Qin et al.	4	1	3	8	High
Jang et al.	4	1	3	8	High
Guo et al.	4	1	3	8	High
Espino et al.	4	1	2	7	High
Xu et al.	4	1	3	8	High
Dehghan et al.	4	1	2	7	High
Djoussé et al.	4	1	2	7	High

Scores of 0-3, 3.5-6, and 6.5-9 for low-, moderate-, and high-quality prospective studies, respectively

a: maximum 4 stars

b: maximum 2 stars

c: maximum 3 stars

Search strategy

((((Egg*[title] AND (heart* OR cardiovasc* OR cardiac* OR stroke OR infarction*OR coronar*))) AND ((((cohort studies[mesh:noexp] OR longitudinal studies[mesh:noexp] OR follow-up studies[mesh:noexp] OR prospective studies[mesh:noexp] OR retrospective studies[mesh:noexp] OR cohort[TIAB] OR longitudinal[TIAB] OR prospective[TIAB] OR retrospective[TIAB])) AND Humans[Mesh])))) OR ((("Eggs"[Mesh]) AND ("Cardiovascular System"[Mesh] OR "Stroke"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Myocardial Infarction"[Mesh] OR "Heart Arrest"[Mesh] OR "Acute Coronary Syndrome"[Mesh])) AND (((cohort studies[mesh:noexp] OR longitudinal studies[mesh:noexp] OR follow-up studies[mesh:noexp] OR prospective studies[mesh:noexp] OR retrospective studies[mesh:noexp] OR cohort[TIAB] OR longitudinal[TIAB] OR prospective[TIAB] OR retrospective[TIAB])) AND Humans[Mesh]))