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Egg Consumption and Carotid Atherosclerosis in the Northern Manhattan Study

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Abstract

Background—The evidence supporting recommendations to limit intake of cholesterol rich foods is inconclusive. We aimed to examine the association between egg consumption and carotid atherosclerosis phenotypes, and the association with clinical vascular events in a prospective, urban, multi-ethnic population.

Methods and Results—The Northern Manhattan Study is a population based cohort to determine stroke incidence, risk factors and prognosis. A sub-cohort of 1,429 NOMAS participants with both carotid ultrasounds and comprehensive dietary information was evaluated (mean±SD age of participants 65.80±8.80, 40% male, 18% white, 20% black, 60% Hispanic). The association between egg consumption and carotid intima media thickness (cIMT) was assessed with linear regression. Logistic and quantile regression was used to examine the association between egg consumption and carotid plaque presence, thickness, and area. The relation between egg consumption and clinical vascular events (N=2669) was examined with Cox models. The mean total cIMT was 0.91±0.08 mm and 58% had carotid plaque present. Increasing egg

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consumption was inversely associated with cIMT, plaque presence, thickness, and area, in models adjusted for demographics, vascular risk factors and diet. For every additional egg consumed per week, the risk of plaque decreased by 11% (95% CI 3%-18%). No association was detected between egg consumption and risk of clinical vascular outcomes, over a mean follow up of 11 years and after adjustment for covariates.

Conclusions—Frequency of egg consumption in the low to moderate range was inversely related to several markers of carotid atherosclerosis. No association with clinical vascular events, including stroke, was detected. Our findings do not support current vascular health guidelines suggesting the extreme limitation or avoidance of egg consumption due to its cholesterol content.

Keywords

atherosclerosis; cholesterol; egg consumption; myocardial infarction; stroke

Introduction

Diet is a complex and irrefutable risk factor for cardiovascular disease (CVD). In keeping with the diet-heart hypothesis which invoked dietary cholesterol as a major CVD risk factor, dietary guidelines have advised limiting the intake of cholesterol rich foods. Egg is a significant source of cholesterol, containing an average of 213 mg per egg. Since the 1970's, egg consumption in the United States has been particularly discouraged by health stakeholders in the absence of empirical data. The American Heart Association guidelines no longer restrict egg consumption, but the allotted cholesterol allowance of <200 mg/day for individuals at high risk of CVD, and <300 mg/day for otherwise healthy individuals, precludes significant egg intake when guidelines are followed in the context of an omnivorous western diet. European and Canadian guidelines, in contrast, do not restrict cholesterol, as the literature suggests that saturated and trans-fat restriction is a more effective means of CVD risk reduction.[1, 2]

Egg is a low glycemic index, whole-food that has been part of the human diet since early mankind. It is an inexpensive source of protein, essential fatty acids, antioxidants, vitamins, and minerals, and is one of the few dietary sources of choline, a potent anti-oxidant. Benefits of egg consumption are well described in the literature, including: the formation of larger, less atherogenic LDL and HDL particles,[3, 4] increased HDL-C formation,[5, 6] and protection against macular degeneration and cataracts.[7, 8]

A growing body of evidence supports the claim that egg consumption ≤1/day in healthy individuals is not associated with increased risk of CVD, yet inconsistent data remains. A recent study by Spence *et al.* described increased carotid plaque area, an imaging biomarker of atherosclerosis, in high risk individuals for CVD, consuming 3 or more eggs per week.[7] The study concluded that regular consumption of egg yolk should be avoided by individuals at high risk for CVD. This study contrasts starkly with the findings of other large, well-controlled, population based cohort studies which concluded that consumption of up to one egg per day does not increase CVD risk.[8-10]

Because of conflicting evidence, guidelines, and the declining overall health and nutritional status of North Americans, it is important to understand the effect of egg consumption in a healthy, ethnically diverse population. The relationship between egg consumption and atherosclerosis in particular requires further study. Stroke and other vascular events are etiologically heterogeneous and atherosclerosis is likely an important pathway linking diet with clinical vascular events. Therefore, in this cross sectional study we examined the association between egg consumption with carotid atherosclerosis phenotypes, including carotid plaque cIMT, and with clinical vascular events in an urban, multi-ethnic population-based cohort.

Methods

Study population

NOMAS is a prospective cohort study designed to determine stroke incidence, risk factors, and prognosis in a multi-ethnic urban population. Study details have been published previously.[11]

Eligible subjects: a) had never been diagnosed with ischemic stroke; b) were >40 years old; and c) resided in Northern Manhattan for ≥ 3 months, in a household with a telephone. Subjects were identified by random-digit dialing, and interviews were conducted by trained bilingual research assistants. The telephone response rate was 91%. Subjects were recruited from the telephone sample to have an in-person baseline interview and assessment. The enrollment response rate was 75%, the overall participation rate was 69%, and a total of 3,298 subjects were enrolled with an average annual contact rate of 95%. For this study we excluded participants with missing information on egg consumption (N=423) and additionally those with a myocardial infarction prior to baseline (N=206). Of the 3298 NOMAS subjects, 1,788 had ultrasound measurements of IMT and carotid plaque. Of these participants, dietary information was lacking on 359 participants, so the study population for the analysis of carotid IMT and plaque included 1,429 NOMAS participants with both carotid ultrasounds and diet measured. The study was approved by the Columbia University and University of Miami IRBs and all subjects provided written informed consent.

Baseline evaluation

Data were collected through interviews with trained bilingual research assistants in English or Spanish. Physical and neurological examinations were conducted by study neurologists. Race-ethnicity was based upon self-identification through a series of questions modeled after the US census and conforming to standard definitions outlined by Directive 15.[12] Standardized questions were adapted from the Behavioral Risk Factor Surveillance System by the Centers for Disease Control regarding hypertension, diabetes, smoking, and cardiac conditions.[13] The questionnaire included a question about history of stroke and MI among brothers and sisters. Hypertension was defined as a blood pressure ≥140/90 mmHg (based on the average of two measurements during one sitting), the patient's self-reported hypertension, or use of anti-hypertensive medications. Diabetes mellitus was defined as fasting glucose ≥126 mg/dl, the patient's self-reported diabetes, or use of insulin or oral anti-diabetic medication. Fasting lipid profile was measured at enrollment as previously

described.[14] Body mass index (BMI) was examined continuously in kg/m^2. Smoking was categorized as never smoking, former smoking, and current (within the past year) smoking. Physical activity was defined as the frequency and duration of 14 different recreational activities during the 2-week period beforethe interview, as described previously.[15] Moderate alcohol use was defined as current drinking of >1 drink per month and ≤2 drinks per day.

Diet

At baseline, participants were administered a modified Block National Cancer Institute food frequency questionnaire by trained research assistants, in English or Spanish.[16] This food frequency questionnaire listed 207 foods (HHHQ version Full87, Form A, Form B) and is intended to represent typical food consumption over the previous year. The questionnaire contained questions regarding the average consumption of eggs, with a medium portion size identified as 2 eggs. The possible responses were: never or < 1/month, 1/month, 2-3/month, 1/week, 2/week, 3-4/week, 5-6/week, 1/day, 2+/day.

In order to account for confounding by overall dietary habits, we also included as a covariate a Mediterranean-style diet score, with a higher score on a 0-9 scale representing increasing adherence to a Mediterranean-style diet. In NOMAS, we have previously shown this score to be inversely associated with the risk of vascular events, and details about the calculation of the score have been described.[17]

Carotid Ultrasound

High-resolution B-mode ultrasounds (GE LogIQ 700, 9- to 13-MHz linear-array transducer) were performed by trained and certified sonographers as described previously.[18] Presence of plaque is defined as a focal wall thickening or protrusion in the lumen more than 50% greater than the surrounding thickness. Carotid plaque area (mm^2) and thickness (mm) were measured using an automated computerized edge tracking software M'Ath (Paris, France).[19] Total plaque area (TPA) was defined as the sum of all plaque areas measured in any of the carotid artery segments within an individual. IMT in all carotid segments was measured in areas without plaque. IMT was calculated as a composite measure of IMT in the near and the far walls of the CCA, bifurcation and ICA of both sides of the neck, and examined continuously as a mean of the maximum measurements of the 12 carotid sites.[18]

Prospective Follow-up and Clinical Outcomes

Annual telephone screening was conducted to determine changes in vital status, detect neurologic events, document interval hospitalizations, and review risk factor status, medication changes, and changes in functional status. Persons who screened positive had an in-person assessment, including chart review and physician examination. Outcome events were detected through ongoing hospital surveillance of admission and discharge data from all area hospitals, including screening of International Classification of Diseases-9 codes. The outcomes were (a) a combined incident vascular event (incident stroke, MI, or vascular death) as well as (b) incident stroke, (c) incident MI, and (d) vascular death. Vascular death included death due to stroke, MI, heart failure, pulmonary embolus, cardiac arrhythmia, or other vascular cause. Follow-up procedures and outcome classifications were detailed previously.[20] Briefly, all hospitalization medical records were reviewed to confirm the

details of suspected events. Outcome events were reviewed by a specially trained research assistant and, when available, medical records were reviewed for all outcome events. Two neurologists independently classified the strokes after review of the data, and one of the principal investigators (RLS, MSVE) adjudicated disagreements.

Statistical Analysis

The primary aim of this study was to examine the association between egg consumption and carotid atherosclerosis phenotypes. First we examined the frequency of egg consumption categorically in relation to the demographic variables and vascular risk factors among those with carotid ultrasound. The frequency of the categorical covariates and the mean and standard deviation of the continuous variables across categories of egg consumption were calculated. Next, we examined the associations of egg consumption (continuous and categorical) with carotid IMT and plaque phenotypes. For the analyses of IMT, linear regression models were constructed with IMT as the dependent variable. Logistic regression models were constructed to examine the association between egg consumption and the plaque presence. Due to the non-normal distribution of plaque thickness and area with a large percentage of the study population having no plaque, we used quantile regression to examine plaque thickness and area as continuous outcomes. For individuals without plaque, a value of 0 was assigned for plaque thickness and area. We chose the median (50^{th} percentile) and 75^{th} percentile as our cutpoints of interest.

As the primary exposure of interest, egg consumption was examined continuously as eggs per week, after assigning the middle value for each category with a medium portion size of 2 eggs. Egg consumption frequency was also examined as a categorical variable with a reference category of <1 time/month and a category for highest consumption of 2+ times/ week corresponding to >2 eggs/week, consistent with the consumption level examined in Spence's study. We also examined the potential presence of a U-shaped relationship between egg consumption and the outcomes of interest by adding a quadratic term for egg consumption to the models.

A sequence of three models was constructed as follows: Model 1 was unadjusted, Model 2 adjusted for demographics only (age, sex, race/ethnicity), Model 3 additionally adjusted for vascular risk factors (BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol, triglycerides, cholesterol-lowering medication use, moderate alcohol use, moderate-heavy physical activity, smoking, and education level), and Model 4 additionally adjusted for total daily kilocalories consumed and the Mediterranean-style diet score. Model 5 included the variables in model 3 as well as history of stroke among siblings, history of MI among siblings, daily consumption of saturated fat, unsaturated fat, protein and carbohydrates (in grams). A secondary sensitivity analysis additionally controlling for the inflammatory marker high sensitivity C-reactive protein was conducted among the subset of participants with data available for this biomarker.

The second aim was to examine the association between egg consumption and clinical vascular events. Cox proportional hazards models were used to examine the association between egg consumption and vascular events, and hazard ratios (HR) and 95% confidence intervals (CI) were calculated. Person-time of follow-up was accrued from baseline to the

end of follow-up (September, 2013), outcome event, death or loss to follow-up, whichever came first. The same sequence of multivariable-adjusted models, as described above for the carotid atherosclerosis outcomes, was constructed.

Because self-reported total daily kcal <500 or >4000 might indicate inaccurate reporting of dietary information, we conducted sensitivity analyses excluding these participants (total N=78 and N=43 with carotid ultrasound, respectively).

Results

In the subcohort with carotid ultrasound measured, the mean age was 65.8±8.8 years, 40% were male, 18% white, 20% black, and 60% Hispanic. In response to the frequency of whole egg consumption with a medium portion size of 2 eggs, 23% of the cohort reported that they consumed eggs less than once per month, 26% 1 time/month, 16% 2-3 times/month, 30% 1 times/week, 3% 2 times/week, 2% 3-4 times/week, 1% 5-6 times/week, and nobody reported consuming eggs daily. Table 1 shows the distribution of the demographics and vascular risk factors in the study population overall and by categories of egg consumption frequency.

The mean total IMT was 0.91±0.08 mm. The prevalence of carotid plaque in the cohort was 58%. The median plaque thickness was 1.48mm, 75^{th} percentile=2.17mm (2.09mm and 2.52mm among those with plaque respectively). The median plaque area was 4.41mm^2, 75^{th} percentile=15.87mm^2 (13.78mm^2 and 26.30mm^2 among those with plaque respectively).

Table 2 shows the association between egg consumption and the carotid IMT and plaque phenotypes. When assessed continuously, increasing egg consumption was inversely associated with IMT. Increasing egg consumption was also associated with a decreased risk of having plaque. In model 3, for every additional egg consumed per week, the risk of plaque decreased by 11% (95% CI 3%-18%). Higher egg consumption was also associated with a lower median and 75^{th} percentile for carotid plaque thickness and TPA. The associations persisted when adjusting for vascular risk factors and dietary variables. The same findings remained consistent in secondary sensitivity analyses in which those with improbably low or high total daily kilocalories were excluded (data not shown). In this analysis and after controlling for the inflammatory biomarker high-sensitivity C-reactive protein (N=1043) in model 3, the results remained consistent (per additional egg/week: IMT beta=-0.0031, p=0.09; plaque presence OR=0.89, 95% CI=0.80-0.98). The power of this analysis was limited as it was conducted in a restricted subcohort of the study population. When a quadratic term for egg consumption was added to models 3 and 4, a potential U-shaped relationship was only suggested in relation to IMT ($p<0.05$, data not shown).

Potential effect modification by the demographic variables, lipid variables, diabetes, and Mediterranean-style diet score was explored using interaction terms in model 3, but there was no evidence of any suggested interactions with egg consumption in relation to IMT or plaque ($p>0.05$).

The categorical analysis of egg consumption frequency suggested that consuming eggs two or more times per month, with a medium portion size of 2 eggs, was inversely associated with IMT and plaque presence, thickness, and burden. However, a clear dose-response

relationship may not exist. In the categorical analysis we did not see a significant association between consuming eggs 2+ times/week vs. never or <once/month and increased IMT or plaque presence or TPA, as shown in Table 2. However, the power of these analyses was limited, as only a small percentage of our study cohort consumed whole eggs more frequently than once per week. Furthermore, we did see that those who consumed eggs 2+ times/week had a lower median plaque thickness as compared to those who consumed eggs <once/month.

In the full cohort analysis of egg consumption in relation to clinical vascular events (N=2,669), the mean age at baseline was 68.8±10.3, 36% were male, 21% white, 24% black, and 53% Hispanic. The distribution of egg consumption in the full cohort was the same as that for the subcohort with carotid ultrasound, suggesting that selection bias for the previous analysis was unlikely. Twenty-three percent of the full NOMAS cohort consumed less than 1 egg per month, 25% 1/month, 16% 2-3/month, 30% 1/week, 3% 2/week, 2% 3-4/week, 1% 5-6/week, and nobody reported consuming eggs daily. Over a mean follow-up of 11 years (SD=5) 719 incident vascular events occurred, including 266 strokes, 226 MIs, and 452 vascular deaths. Table 3 shows the relationship between egg consumption, assessed both continuously and categorically, and the incidence of clinical vascular events, combined and assessed separately in the sequence of three models. As shown, there was no association between egg consumption and risk of any of the clinical vascular outcomes after adjustment for covariates. The results remained consistent in sensitivity analyses. Lastly, we explored potential effect modification by the demographic variables, lipid variables, diabetes, Mediterranean-style diet score, and plaque by individually including interaction terms between these variables and eggs/week in model 3 for combined vascular events, but there was no evidence of any effect modification ($p>0.05$).

Discussion

In this multi-ethnic population-based cohort study, we observed an inverse association between egg consumption and several distinct imaging biomarkers of carotid atherosclerosis including carotid IMT, plaque presence, plaque thickness, and total plaque area. The inverse association persisted without attenuation after adjustment for demographics, traditional vascular risk factors, dietary habits, and inflammation. Our results suggest that egg consumption, in the low to moderate range, is not associated with an increase in carotid atherosclerosis. The findings do not support advice to limit whole egg consumption in reference to this important risk factor for stroke and vascular outcomes, and are in contrast to the findings of a positive association between frequent egg consumption (>2/week) and carotid plaque.[7] Because of the limited range of whole egg consumption in our cohort, with few participants consuming eggs more than twice per week, our results do not support a dose-response relationship within the moderate range, hence the exact nature of the relationship between egg consumption and atherosclerosis markers is not conclusive.

Despite the strong association between carotid atherosclerosis and clinical vascular events, particularly stroke, we did not observe an association between low to moderate frequency egg consumption and risk of clinical events, combined or separately, after adjustment for potential confounders. The etiologies of stroke and MI are very complex and heterogeneous

and it is unlikely that any one single dietary item would have an independent effect on the risk. However, our results are not consistent with the hypothesis that egg consumption in the low to moderate range, would have a deleterious effect on vascular risk. The stated results are consistent with a large body of evidence which suggests that the consumption of up to 1 egg per day in healthy, non-diabetic, individuals is not associated with increased cardiac risk [8, 10, 21-23] and may, in fact, be protective for stroke risk.[24-26] A recent meta-analysis further supports the lack of harm from egg consumption, and concludes that consumption of up to one egg per day was not associated with increased risk of CVD.[27] The safety of egg intake has been a controversial issue, but close examination of individual trials reveals that residual confounding, and covariance of dietary risk factors such as cholesterol with saturated fat and decreased fruit and vegetable intake, likely explain inconsistencies in the data. Specifically, many of the earlier studies did not control for overall dietary patterns, and hence are of limited value.

Hu *et al.* examined the association between egg consumption and risk of CHD and stroke using data from the Health Professionals' Follow-up Study (1986-1994) and the Nurses' Health Study (1980-1994) and found no significant increase in CVD risk after extensive adjustment for vascular risk factors, dietary habits, and demographics.[8] Similar results were obtained recently by two additional studies that controlled extensively for vascular risk factors and diet: Zazpe *et al.*, which examined egg consumption and CVD incidence in 14,185 Spanish University graduates,[28] and Houston *et al.*, which examined the association between dietary fats, cholesterol, eggs and CVD risk in 1,941 community-dwelling adults aged 70–79.[29] All three of these studies detected an association between high egg consumption and overall unhealthier behavior patterns. The higher egg consuming groups were more sedentary, with more than double the rates of active smoking (Hu: men 7.2% versus 14.6% and Houston 6.2% versus 11.9 % active smoking). An unhealthier overall eating pattern was also noted, including decreased intake of fruits and vegetables and increased intake of saturated fat.

The socio-temporal context of the data is worthy of consideration. Hu *et al.'s* data was collected from physicians and nurses from 1980-1994, living in the United States: a time when Americans were strongly advised against consuming eggs. To a certain extent, this cultural bias persists today. Any health professional consuming seven eggs per week in the 1980's was knowingly violating accepted health norms. As such, heavy egg consumption may be a marker of other unhealthy behaviors, resulting in unmeasured confounding. Egg is an extremely nutrient dense food. It provides high quality protein, many vitamins, minerals, and essential fatty acids. An atheroprotective effect of egg is biologically plausible based on its various components. Egg supplies arginine which is a precursor of nitric oxide, a key molecule in maintaining vascular health via its effect as a mediator of vasodilation.[30] Egg is one of the few dietary sources of choline, a potent antioxidant, that has been shown to lower homocysteine levels and decrease inflammation, [20, 31, 32] as well as other antioxidants including vitamin E, and the carotenoids zeaxanthin and lutein. Additionally, egg supplies vitamin D which may also confer an atheroprotective effect.[33] Furthermore, human feeding studies demonstrate that egg consumption exerts favorable effects on a healthy individual's lipoprotein profile. The LDL-HDL ratio, a strong predictor of CVD risk, is unaffected in

humans fed 3 eggs per day for one month in egg feeding studies.[34] Low HDL is an important risk factor for CVD, particularly in the elderly and egg consumption increases HDL.[35] Finally, egg consumption was shown to increase LDL size and causing a shift to more buoyant, larger LDL particles associated with anti-atherogenic pattern A.[36] The safety of egg consumption in healthy individuals is further supported by post-prandial testing of endothelial function via brachial flow mediated vasodilation (FMD). This measure of endothelial function used to gauge CVD risk and risk reduction, and has been studied extensively with regards to foods and nutrients. One trial of 49 healthy adult males fed 2 eggs per day for 6 weeks demonstrated no effect on FMD versus the control group. [37] In contrast, Vogel *et al.* demonstrated a fall in flow mediated vasodilatation persisting up to four hours after a high fat meal. Remarkably, no fall in FMD was witnessed after subjects consumed the same meal with antioxidant vitamin C and E pretreatment,[38] suggesting oxidative stress as a likely mechanism, and demonstrating an atheroprotective effect of antioxidant containing foods or supplements if consumed with a high fat diet.

Despite the clear nutritional benefits of egg, and its lack of harm in the healthy, the literature does indicate an association with increased CVD risk among diabetics who consume eggs frequently.[8, 21, 29] Indeed, a recent meta-analysis by Shin *et al.* demonstrated a pooled HR (95% CI) of 1.69 (1.09,2.62) for overall CVD in diabetics consuming ≥ 1 egg/day versus those consuming < 1 egg/day.[39] Both Hu and Houston demonstrated increased cardiovascular risk in diabetics consuming more than one egg per day, a finding that warrants further study among this patient population.

Strengths of this study include the use of a large multi-ethnic population-based cohort of adults living in the same community with available information on many traditional and novel vascular risk factors. In addition, we examined several distinct phenotype biomarkers of atherosclerosis including the more novel marker of carotid plaque burden (total plaque area). Some important limitations are worthy of mention. Most importantly, the analysis of eggs and carotid plaque measures is cross-sectional and therefore we can't make assumptions about temporality or causality. Despite the use of a validated and reliable Block food frequency questionnaire, there are some important limitations to our diet data. First, misclassification due to self-reported diet consumption is possible, although the misclassification is most likely random resulting in bias towards the null, suggesting that the true association may in fact be stronger than that observed here. However, we excluded those with improbably low or high self-reported total daily kilocalorie consumption in sensitivity analyses with the goal of minimizing misclassification bias. Although the food frequency questionnaire is designed to measure average consumption over the previous year, information on food consumption was collected at a single time point (baseline) and we lacked information on long-term egg consumption as well as changes in consumption over time. This analysis did not address eggs consumed as ingredients in other food sources, such as baked goods. Therefore, our conclusions only apply to the consumption of whole eggs and further research is needed to examine the potential impact of egg consumption in the overall diet including baked goods. Although it is possible that some participants cooked their eggs without egg yolks included, we lacked information on this and considered it unlikely. As mentioned previously, due to the collection of egg consumption data using

categorical responses and the limited number of people with high egg consumption, we are not able to speculate on the relationship between very frequent egg consumption and atherosclerosis or risk of clinical vascular events. While we controlled for many potential confounders that are known risk factors for atherosclerosis and vascular events, residual confounding by unmeasured and measured risk factors, including correlated dietary habits, is possible and could account for the associations observed. Given the slightly more favorable vascular risk profile detected among higher egg consumers with regards to blood pressure, CRP, BMI, and cholesterol lowering medication usage, reverse confounding resulting from higher risk individuals deliberately avoiding eggs cannot be ruled out. This would likely be counterbalanced by the presence of other significant risk factors such as more active smoking, less physical activity and greater caloric consumption. Because physical activity levels fluctuate with time, our assessment of physical activity, which was performed over a two week period prior to the interview, may not be an accurate reflection of the individual's baseline activity level. Lastly, an observational study like ours is unable to shed light on the underlying mechanisms by which egg consumption might be associated with a reduced risk of atherosclerosis, and further research in this area is needed.

In conclusion, the results of this study showed an inverse relationship between the frequency of egg consumption in the low to moderate range and several markers of carotid atherosclerosis, and no association with clinical vascular events, including stroke. Therefore, our findings are inconsistent with any nutritional guidelines suggesting the avoidance of egg consumption due to its cholesterol content for the purposes of vascular health promotion. Due to the observational nature of this study and the cross-sectional design of the carotid atherosclerosis component, we recommend further research in other large and diverse prospective community-based cohorts to further elucidate the independent relationship between egg consumption, carotid atherosclerosis, and risk of clinical cardiovascular and cerebrovascular outcomes. Such studies are needed to clarify dietary recommendations for public health.

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Highlights

- The association between egg intake and carotid plaque phenotypes was studied.
- Frequent egg consumption was inversely related to several atherosclerosis phenotypes.
- No association with clinical vascular events was detected among frequent egg eaters.
- Our findings do not support limiting egg consumption for vascular health promotion.

Table 1

Characteristics of the study cohort overall and by *frequency* of egg consumption category (medium portion size=2 eggs)

Covariates	Study population (N=1429)	≤1x/mo. (N=711)	2x/mo.-1x/wk, (N=648)	≥2/wk. (N=70)
Age years mean±SD	65.80±8.80	65.94±8.78	65.63±8.70	65.77±9.99
Male sex N (%)*	577 (40)	260 (37)	276 (43)	41 (59)
Race/ethnicity N (%)				
White	257 (18)	122 (17)	124 (19)	11 (16)
Black	282 (20)	131 (18)	133 (21)	18 (26)
Hispanic	858 (60)	443 (62)	375 (58)	40 (57)
Other	32 (2)	15 (2)	16 (2)	1 (1)
High-school completion N(%)	668 (47)	312 (44)	318 (49)	38 (54)
BMI kg/m^2 mean±SD	28.12±5.08	28.17±5.13	28.13±5.00	27.51±5.37
Moderate alcohol use N (%)*	550 (38)	254 (36)	273 (42)	23 (33)
Moderate-heavy physical activity N (%)	149 (10)	69 (10)	76 (12)	4 (6)
Smoking N (%)				
Never	682 (48)	342 (48)	311 (48)	29 (41)
Former	517 (36)	260 (37)	231 (37)	26 (37)
Current	230 (16)	109 (15)	106 (16)	15 (21)
Diabetes N (%)	283 (20)	121 (17)	137 (21)	15 (21)
Hypertension N (%)	1012 (71)	520 (73)	447 (69)	45 (64)
LDL-C mg/dL mean±SD*	120.34±36.30	133.10±34.89	125.99±35.01	124.42±31.73
HDL-C mg/dL mean±SD	50.07±16.32	45.66±13.86	46.23±14.11	44.17±14.46
TGs mg/dL mean±SD*	130.80±81.23	141.42±85.16	127.79±69.69	135.86±97.57
Cholesterol-lowering medication use N (%)*	212 (15)	130 (18)	77 (12)	5 (7)
Mediterranean-style diet score mean±SD	4.43±1.63	4.45±1.68	4.42±1.58	4.27±1.46
Total kilocalories/day mean±SD*	1598.07±728.04	1430.57±632.01	1705.41±739.40	2282.21±915.89
Total fat g/day mean±SD*	61.97±33.04	52.73±27.24	67.76±33.31	97.38±41.03
Saturated fat g/day mean±SD*	20.56±12.47	17.09±10.17	22.78±12.60	33.58±15.33
Carbohydates g/day mean±SD*	191.52±91.21	179.02±83.60	201.55±95.16	238.33±102.81

Covariates	**Study population (N=1429)**	**≤1x/mo. (N=711)**	**2x/mo.-1x/wk, (N=648)**	**≥2/wk. (N=70)**
Protein g/day mean±SD*	62.87±30.97	55.22±26.91	67.55±30.34	95.59±36.95
History of stroke in siblings N (%)	171 (12)	83 (12)	80 (12)	8 (11)
History of MI in siblings N (%)	182 (13)	98 (14)	77 (12)	7 (10)
CRP mg/L mean±SD	4.62±7.12	4.51±6.36	4.82±8.09	3.92±4.16
cIMT mm mean±D*	0.91±0.08	0.92±0.09	0.90±0.08	0.91±0.08
Plaque presence N(%)*	823 (58)	436 (61)	350 (54)	37 (53)
Plaque Thickness mm mean±SD	1.32±3.08	1.36±1.21	1.30±4.38	1.15±1.16

Mo., month; wk., week; SD, standard deviation; BMI, body mass index; LDL-C, low-density lipoprotein; HDL-C, high-density lipoprotein; TGs, triglycerides; CRP, C-reactive protein; cIMT, carotid intima media thickness

*P<0.05 across categories of egg consumption using ANOVA for continuous variables and chi-square tests for categorical variables

Table 2

Egg consumption and atherosclerosis in NOMAS

N=1429	cIMT (mean of the max) Beta, p-value	Plaque presence vs. no plaque OR (95% CI)	Plaque thickness 50% effect, p-value	Plaque thickness 75% effect, p-value	Plaque area 50% effect, p-value	Plaque area 75% effect, p-value
Egg consumption, *continuous*						
Eggs/wk.						
Model 1	-0.00261, 0.09	0.92 (0.85-0.99)	-0.0652, 0.22	-0.0401, 0.06	-0.4449, 0.001	-1.2347, 0.0001
Model 2	-0.00369, 0.01	0.90 (0.83-0.98)	-0.0958, <0.0001	-0.0622, 0.01	-0.2478, 0.01	-1.1850, <0.0001
Model 3	-0.00328, 0.03	0.91 (0.83-0.99)	-0.0788, 0.001	-0.0660, 0.01	-0.1749, 0.18	-1.0168, <0.0001
Model 4	-0.00379, 0.02	0.89 (0.82-0.97)	-0.0882, 0.001	-0.0737, 0.003	-0.3858, 0.001	-1.1078, <0.0001
Model 5	-0.00296, 0.08	0.89 (0.81-0.98)	-0.0752, 0.003	-0.0772, 0.003	-0.2320, 0.09	-1.0272, <0.0001
Egg consumption, *frequency*						
0 or <1x/mo.	ref	ref	ref	ref	ref	ref
1x/mo.						
Model 1	-0.00176, 0.78	0.99 (0.73-1.34)	0.0000, 1.00	-0.0712, 0.43	-0.1633, 0.91	0.4337, 0.87
Model 2	-0.00353, 0.56	0.95 (0.69-1.30)	-0.1245, 0.43	-0.0378, 0.71	-1.4828, 0.11	-0.5734, 0.78
Model 3	-0.00304, 0.62	0.96 (0.69-1.35)	-0.0443, 0.73	0.0593, 0.53	-0.5599, 0.55	-0.0322, 0.99
Model 4	-0.00304, 0.62	1.02 (0.73-1.43)	-0.0878, 0.54	0.0009, 0.99	-0.5345, 0.57	0.4337, 0.83
Model 5	-0.00398, 0.52	0.93 (0.66-1.30)	-0.0400, 0.76	-0.0131, 0.90	-0.1380, 0.87	-0.6972, 0.72
2-3 x/mo.						
Model 1	-0.01617, 0.02	0.67 (0.48-0.95)	-0.1739, 0.73	-0.3321, 0.002	-2.1734, 0.28	-6.5917, 0.01
Model 2	-0.01752, 0.01	0.62 (0.43-0.89)	-0.5407, 0.01	-0.2721, 0.02	-2.7513, 0.001	-8.5923, <0.0001
Model 3	-0.01724, 0.01	0.64 (0.44-0.93)	-0.3110, 0.06	-0.1384, 0.29	-1.9672, 0.04	-6.2675, <0.0001
Model 4	-0.01717, 0.02	0.64 (0.44-0.94)	-0.3731, 0.02	-0.1645, 0.17	-2.2677, 0.02	-5.7141, 0.0002
Model 5	-0.01691, 0.02	0.63 (0.43-0.92)	-0.3935, 0.01	-0.1437, 0.23	-1.8842, 0.03	-5.3846, 0.0003
1x/wk.						
Model 1	-0.01460, 0.01	0.78 (0.58-1.04)	-0.0870, 0.53	-0.2451, 0.003	-0.6224, 0.63	-3.8163, 0.08
Model 2	-0.0181, 0.002	0.73 (0.54-0.99)	-0.3723, 0.04	-0.2108, 0.03	-2.4067, 0.0003	-5.2935, 0.001
Model 3	-0.0176, 0.003	0.72 (0.52-1.00)	-0.2818, 0.02	-0.1061, 0.28	-1.2815, 0.11	-4.0597, 0.004

N=1429	cIMT (mean of the max) Beta, p-value	Plaque presence vs. no plaque OR (95% CI)	Plaque thickness 50% effect, p-value	Plaque thickness 75% effect, p-value	Plaque area 50% effect, p-value	Plaque area 75% effect, p-value
Model 4	-0.0196, 0.002	0.68 (0.49-0.95)	-0.3790, 0.003	-0.1340, 0.21	-1.6238, 0.03	-3.9503, 0.01
Model 5	-0.0184, 0.004	0.66 (0.47-0.94)	-0.2674, 0.03	-0.1886, 0.06	-1.6685, 0.02	-3.5808, 0.03
≥2x/wk.						
Model 1	-0.00833, 0.44	0.70 (0.42-1.18)	-0.0852, 0.90	-0.1892, 0.16	-3.3163, 0.19	-3.2397, 0.41
Model 2	-0.01632, 0.12	0.63 (0.36-1.09)	-0.5729, 0.004	-0.1437, 0.33	-2.0621, 0.13	-7.3400, 0.001
Model 3	-0.01414, 0.19	0.64 (0.36-1.15)	-0.3945, 0.04	-0.2095, 0.34	-1.4839, 0.24	-5.0906, 0.08
Model 4	-0.01768, 0.11	0.59 (0.32-1.10)	-0.5132, 0.01	-0.3030, 0.18	-2.1244,0.09	-5.7478, 0.05
Model 5	-0.01324, 0.25	0.58 (0.31-1.07)	-0.3745, 0.09	-0.3472, 0.13	-1.6186, 0.16	-4.9831, 0.12

cIMT, carotid intima media thickness; CI, confidence interval; wk., week; mo., month

Model 1: unadjusted; Model 2: adjusted for age, sex, race/ethnicity; Model 3: adjusted for variables in model 1 + BMI, diabetes, hypertension, LDL, HDL, TG, cholesterol-lowering medication, moderate alcohol use, moderate-heavy physical activity, smoking, high-school completion; Model 4: adjusted for variables in model 3 + total daily kilocalories, MEDI diet score; Model 5: adjusted for variables in model 3 + family history of stroke in siblings, family history of MI in siblings, daily consumption of saturated fat, unsaturated fat, carbohydrates, and protein

Table 3
Egg consumption and clinical vascular events in NOMAS

N=2669	Combined vascular Events RR (95% CI)	Stroke RR (95% CI)	Myocardial infarction RR (95% CI)	Vascular death RR (95% CI)
Egg consumption, *continuous*				
Eggs/wk.				
Model 1	1.15 (1.06-1.25)	1.15 (1.00-1.31)	1.10 (0.95-1.29)	1.11 (1.00-1.24)
Model 2	1.10 (1.00-1.20)	1.11 (0.95-1.28)	1.03 (0.87-1.22)	1.08 (0.96-1.22)
Model 3	1.06 (0.96-1.16)	1.09 (0.93-1.27)	1.01 (0.84-1.21)	1.03 (0.91-1.17)
Model 4	1.02 (0.92-1.13)	1.05 (0.86-1.23)	1.00 (0.83-1.21)	0.98 (0.86-1.12)
Model 5	1.05 (0.95-1.16)	1.04 (0.88-1.22)	1.04 (0.87-1.26)	0.99 (0.87-1.14)
Egg consumption, *frequency*				
0 or <1x/mo.	ref	ref	ref	ref
1x/mo.				
Model 1	0.91 (0.74-1.12)	0.90 (0.65-1.25)	0.83 (0.58-1.19)	0.98 (0.76-1.28)
Model 2	0.97 (0.79-1.20)	0.94 (0.67-1.32)	0.85 (0.59-1.23)	1.05 (0.81-1.37)
Model 3	0.94 (0.76-1.17)	0.91 (0.65-1.29)	0.84 (0.58-1.24)	1.01 (0.77-1.33)
Model 4	0.97 (0.78-1.21)	0.98 (0.69-1.40)	0.81 (0.55-1.21)	1.06 (0.81-1.41)
Model 5	0.94 (0.75-1.16)	0.97 (0.69-1.37)	0.83 (0.57-1.22)	0.98 (0.74-1.28)
2-3 x/mo.				
Model 1	0.89 (0.70-1.13)	0.84 (0.57-1.24)	0.68 (0.44-1.06)	0.87 (0.64-1.19)
Model 2	0.81 (0.63-1.03)	0.83 (0.56-1.22)	0.63 (0.40-0.98)	0.76 (0.55-1.05)
Model 3	0.81 (0.63-1.05)	0.75 (0.50-1.14)	0.66 (0.41-1.07)	0.74 (0.53-1.04)
Model 4	0.79 (0.61-1.03)	0.73 (0.47-1.11)	0.66 (0.40-1.08)	0.74 (0.52-1.04)
Model 5	0.85 (0.66-1.09)	0.76 (0.50-1.14)	0.66 (0.40-1.06)	0.78 (0.56-1.08)
1x/wk.				
Model 1	1.13 (0.93-1.36)	1.02 (0.75-1.39)	1.09 (0.79-1.51)	1.29 (1.02-1.64)
Model 2	1.10 (0.91-1.33)	1.02 (0.74-1.39)	1.06 (0.76-1.48)	1.27 (1.00-1.62)
Model 3	1.00 (0.82-1.23)	0.91 (0.66-1.26)	1.06 (0.75-1.50)	1.12 (0.86-1.44)
Model 4	0.96 (0.78-1.18)	0.89 (0.63-1.24)	1.05 (0.74-1.50)	1.06 (0.81-1.38)
Model 5	0.96 (0.79-1.18)	0.83 (0.60-1.16)	1.09 (0.77-1.55)	1.09 (0.84-1.41)
≥2/wk.				
Model 1	1.50 (1.01-2.23)	1.48 (0.79-2.79)	1.20 (0.58-2.50)	1.42 (0.84-2.40)
Model 2	1.31 (0.87-1.99)	1.31 (0.65-2.62)	0.88 (0.40-1.93)	1.36 (0.80-2.31)
Model 3	1.10 (0.71-1.71)	1.25 (0.62-2.53)	0.69 (0.27-1.74)	1.18 (0.68-2.04)
Model 4	1.05 (0.67-1.63)	1.16 (0.57-2.37)	0.68 (0.27-1.72)	1.12 (0.64-1.95)
Model 5	1.03 (0.67-1.60)	1.18 (0.60-2.30)	0.81 (0.34-1.93)	1.00 (0.57-1.77)

CI, confidence interval; Wk., week; mo., month

Model 1: unadjusted; Model 2: adjusted for age, sex, race/ethnicity; Model 3: adjusted for variables in model 1 + BMI, diabetes, hypertension, LDL, HDL, TG, cholesterol-lowering medication, moderate alcohol use, moderate-heavy physical activity, smoking, high-school completion; Model 4: adjusted for variables in model 3 + total daily kilocalories, MEDI diet score; Model 5: adjusted for variables in model 3 + family history of stroke in siblings, family history of MI in siblings, daily consumption of saturated fat, unsaturated fat, carbohydrates, and protein