Egg consumption and incident type 2 diabetes: are there any advantages to excessive consumption of eggs?

Dear Editor:

In a recently reported study entitled “Egg consumption and risk of incident type 2 diabetes in men: the Kuopio Ischaemic Heart Disease Risk Factor Study,” which was a long-term cohort study, Virtanen et al. (1) concluded that a higher intake of eggs was associated with a lower risk of the development of type 2 diabetes (T2D) in 2332 men aged 42–60 y at baseline. The same trend without statistical significance was observed in relation to higher cholesterol intake and a lower risk of T2D. The authors also conducted a trend analysis on fasting plasma glucose (FPG), serum insulin, and serum C-reactive protein (CRP) over a follow-up period of 4 y and reported that egg consumption was inversely associated with the FPG and serum CRP. I have a comment on the setting of the reference group in their analysis.

A daily intake of 1 egg is considered to have no adverse effects on health, and the authors mentioned that the weight of a medium egg in their study was ~55 g. Namely, 377 subjects in the highest quartile (n = 582) consumed at least 1 medium egg/d. From the information obtained, the authors should not have selected the lowest quartile as the reference group for their Cox regression analysis. The lowest and the second-lowest quartiles included subjects with poor nutritional intakes with respect to eggs and cholesterol, which would lead to an increase in incident T2D.

The same situation can be observed in their trend analysis on FPG, serum insulin, and serum CRP. Linear trend analysis is not appropriate, and ANCOVA should be selected to analyze the elevated values of biomarkers in subjects in the lowest or second-lowest quartiles.

The authors cited 2 articles by Djoussé et al. (2, 3), which reported the lack of any association between egg consumption or dietary cholesterol and the risk of development of T2D (2) and a positive association between egg consumption and the risk of development of T2D (3). In addition, Zazpe et al. (4) reported that egg consumption was not associated with the development of T2D by comparing the highest with the lowest quartile of egg consumption (<4 eggs/wk compared with >1 egg/wk) with an OR of 0.7 (95% CI: 0.3, 1.7).

Virtanen et al. conducted a long-term cohort study by targeting middle-aged and older men at the baseline, and a sufficient number of events were observed. I suppose that a stable estimate of the development of T2D can be made only by the appropriate setting of the reference group, and their conclusion should be modified as “lower than recommended daily intake of egg is a risk factor for the development of T2D.”

The author had no conflicts of interest to disclose.

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REFERENCES


Reply to T Kawada

Dear Editor:

We thank Kawada for his interest in our article. He suggests that we should not have selected the lowest egg intake quartile as the reference group but instead investigated whether there is an increased risk in the lowest or the second-lowest quartile when compared with those with a high egg intake. We chose the lowest quartile as the reference, because in the previous population studies egg intake was associated with a higher risk of type 2 diabetes (T2D) or there was no association. Therefore, the use of the lowest quartile as the reference group was considered as a more appropriate setting. If, however, the highest egg intake quartile is used as the reference, the multivariate-adjusted [model 3 in the original analysis (1)] HRs are, from the highest to the lowest quartile, 1, 1.08, 1.63, and 1.83 (95% CI: 1.26, 2.64).

We considered the linear trend analysis to be appropriate for the assessment of the associations between egg intake and fasting blood glucose, serum insulin, and serum C-reactive protein, because the average values appeared to change linearly according to quartile of egg intake. For example, for fasting blood glucose, the multivariate-adjusted P value for trend across quartiles of egg intake was 0.002 (1). In the multivariate-adjusted ANCOVA (model 3 in the original analysis), the P values for the differences between the lowest and the second, third, and fourth quartiles were 0.09, 0.004, and 0.002, respectively. If the second-lowest egg intake quartile were used as the reference, the only significant difference is observed with the highest quartile (P = 0.05). This suggests that the use of a linear trend analysis is appropriate. It is, of course, possible that a more detailed analysis could reveal nonlinear associations, but that would require a larger study population.

We also thank Kawada for pointing out the omission of the study by Zazpe et al. (2), which had escaped our attention. In that study, egg intake was not associated with a risk of incident T2D among...
15,956 Spanish participants. However, the mean age of the cohort was 38.5 y, so only 91 incident T2D events occurred during the median follow-up of 6.6 y. The low number of events limits the power to draw conclusions from that study.

In conclusion, our study is the only population-based study showing an inverse association between egg intake and risk of incident T2D. Although those with higher egg intakes were slightly younger and smoked less, egg intake was not systematically associated with either healthy or unhealthy lifestyle and dietary practices among the men in our study population, as shown in Table 1 in the original article (1). This lowers the possibility that those with a high (or low) intake would be a select group of individuals and that high (or low) egg intake would merely be a surrogate for some other factor or factors. However, Kawada’s suggestion for the conclusion from our study is as appropriate as was ours. That is, higher egg intake is not associated with a higher risk of T2D in this study population but may rather be associated with a lower risk.

The present study was supported by the University of Eastern Finland. None of the authors had conflicts of interest.

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REFERENCES


Is this the end of (−)-epicatechin, or not? New study highlights the complex challenges associated with research into the cardiovascular health benefits of bioactive food constituents

Dear Editor:

A considerable body of evidence supports the beneficial effects of dietary flavanols in relation to cardiovascular health, and the data for cocoa flavanols are particularly extensive and consistent. In addition to the reported results of individual studies, cocoa flavanol–related health benefits also have been substantiated by a Cochrane Review (1), as well as by a scientific consensus statement resulting in a European Food Safety Authority health claim (2). However, it is important to consider that the compound classes of flavanols and procyanidins include a variety of chemically distinct bioactives, one of which, (−)-epicatechin, has been identified as one of the bioactive flavonoid constituents of cocoa (3). Although food matrix properties and other constituents present in flavanol-containing foods are likely to contribute to, or modulate, the effects of (−)-epicatechin by affecting its bioactivity and/or bioavailability, we agree with Dower et al. (4) in a recent article in the Journal that it is important to investigate individual bioactives and to rigorously test on a larger scale the validity of previous findings. In their article, Dower et al. (4) investigated the effects of “pure epicatechin” in a controlled, double-masked, crossover study in humans and concluded that although (−)-epicatechin intake did not significantly increase flow-mediated arterial dilation (FMD; primary endpoint) or decrease blood pressure, it did have a significant beneficial effect on insulin resistance (secondary endpoint).

In an Editorial in the Journal that accompanied the Dower et al. article, Scalbert and Zamorros-Ros (5) emphasized that, “In contrast to the negative results observed on CVD [cardiovascular disease] markers, Dower et al. also observed a decrease in fasting plasma insulin...” We are concerned that the authors represent effects that are not statistically significant as “negative results” and that their interpretation does not distinguish between the primary endpoint the study was prospectively powered for, from outcomes representing secondary endpoints. So should the data by Dower et al. put to rest the idea that (−)-epicatechin represents a bioactive food constituent with cardiovascular health benefits? In other words, how rigorous are the data, what are the limitations of their interpretation, and how high is the risk of a false negative result? According to Dower et al. (4), “A 1% increase in FMD would be clinically relevant, because at a population level, a 1% increase in FMD is associated with a 13% lower risk of a cardiovascular event.” We fully agree with the statement and the reference provided in its support. Dower et al. reported that they observed an (−)-epicatechin intake-related increase in FMD of 1.1%, an outcome that did not reach statistical significance (P = 0.07; Table 2 in their article), because a hypothesized 1.3% change in FMD was the basis for their power calculation. Although we agree with the conclusion by Dower et al. that the statistical evaluation of their data disproves their hypothesis, we submit that drawing general conclusions from this work requires a careful consideration of all study limitations, including the question of sufficient statistical power in the context of a diverse study population. We appreciate the technical challenges of detecting a comparatively small change in FMD in healthy individuals in the context of a dietary intervention study of this scale. Although technical considerations are often overlooked and unappreciated, they can have a considerable impact on outcomes and final interpretations. One of the challenges encountered by Dower et al. (4) was the relatively large heterogeneity of their study population, especially considering the small total number of participants. The study population ranged in age from 48 to 79 y and in BMI (in kg/m2) from 20 to 35, and although the average systolic/diastolic blood pressure was 129/75 mm Hg, 22% of participants would be considered as hypertensive. These characteristics, which will very likely also result in a high interindividual variability in the primary endpoint of FMD, can represent a considerable challenge with regard to detecting small effect sizes. Moreover, the overall health status of the study population is an important consideration, especially when investigating the effects of a bioactive such as (−)-epicatechin in the context of health and nutrition. Although Dower et al. aimed at recruiting healthy individuals, the reported intervention-independent occurrence of 1 myocardial infarction and 1 fatal stroke, as well as the 22% prevalence of hypertension in the overall study population, indicates significant heterogeneity in vascular disease risk factor status. Further complicating the interpretation of the study, the primary endpoint of FMD was assessed with the use of a less-than-ideal methodology. Harris et al. (6), among others, demonstrated that an ultrasound transducer of 10–14 MHz is needed to optimally image superficial