

Egg intake and cardiometabolic diseases: an update

Part 2

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Abstract

Following on from the previous publication (part 1) summarizing study results on the association between egg intake and risk of cardiovascular diseases, the aim of this article was to assess the association between egg intake and risk of type 2 diabetes mellitus and the effect on cardiometabolic risk factors. Overall, study results from previous meta-analyses, systematic reviews and recently published cohort and intervention studies show no clear negative or positive effects of egg intake on the investigated outcomes. Therefore, the focus should be placed on overall nutrition quality rather than a discussion on limiting egg intake or associated dietary cholesterol.

Keywords: egg intake, cardiovascular diseases, cholesterol, type 2 diabetes mellitus, cardiometabolic risk factors

Introduction

The association between egg intake and risk of type 2 diabetes mellitus has been investigated in recent years in several prospective observational studies, which show contradictory results [1–4]. Previous estimates from population-based surveys in Germany assume 7–8% of type 2 diabetics in the adult population [5–7] with a proportion of unrecognized (untreated) diabetes mellitus among the overall prevalence of over 20 and up to 50% [5, 7–9]. Results vary however depending on the age group studied and the data pool used [10]. In one recent study a 9.5% prevalence of type 2 diabetes mellitus was calculated based on overall accounting data from German physicians who treat state-insured patients [11]. This article presents the results of systematic reviews and meta-analyses as well as more recent intervention and cohort studies examining the effects of egg intake on the risk of type 2 diabetes mellitus and cardiometabolic risk factors. Taking account of the previous article (part 1) which presented, inter alia, the status of current studies on the association between egg intake and cardiovascular diseases, the results are then discussed.

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Methodology

Systematic literature research for systematic reviews and meta-analyses of intervention and cohort studies was done using the database NCBI PubMed covering studies from January 2008 to August 2018.

In addition to this a systematic search was done for current studies not considered in systematic reviews and meta-analyses up to now. The search strategy included, inter alia, the English language terms “egg”, “diabetes

mellitus type 2”, “blood lipids”, “insulin”, “fasting blood glucose” and the search terms “meta-analysis”, “systematic review”, “interventional trial” and “cohort”.

Results

Egg intake and risk of type 2 diabetes mellitus

In four of seven meta-analyses of prospective cohort studies examining the association between egg intake and risk of diabetes mellitus type 2, the analyses (highest vs. lowest intake, dose-response analyses) showed no association [12–15]; three meta-analyses indicated a risk increasing association [16–18]. In a systematic review two prospective cohort studies showed a positive association between egg intake and risk of diabetes; one study showed no association [19] (♦ Table 1).

One current prospective cohort study has not been considered in systematic reviews and meta-analyses up to now. Among the participants in the Caerphilly prospective cohort study (CAPS) who did not show neither cardiovascular diseases nor type 2 diabetes mellitus at baseline, a total of 120 cases of disease were proven during the average follow-up duration of 22.8 years. In both the unadjusted and the multi-adjusted models no association was shown between egg intake and risk of diabetes [20].

Egg intake and effect on cardiometabolic risk factors

The effect of egg intake on cardiometabolic risk factors was examined in two systematic reviews and one meta-analysis of randomized controlled intervention studies [19, 21, 22] (♦ Table 2). Predominantly no negative effect could be determined on serum lipids and glucose metabolism.

Further intervention studies

In recent years other intervention studies of various designs have been published examining the effect of egg intake on cardiometabolic risk factors.

Wright et al. examined the effect of a protein-rich diet (1.4 g of protein/kg body weight/day) with an intake of three eggs per day and an egg-based snack compared to a diet with a daily protein intake of 0.8 g of protein/kg body weight without egg intake on, inter alia, cardiometabolic risk factors over a period of twelve weeks using 22 overweight or obese participants. At the end of the study the treatment group without egg intake showed a reduction of low-density lipoprotein (LDL) cholesterol. There was however no significant difference to the comparison group. For other serum lipids and glucose metabolism parameters there were no differences within and between the treatment groups after twelve weeks [23].

Comparative results were achieved by Fuller et al. [24]. They conducted a nine-month intervention study (subsequent to a three-month weight retention phase) in which the participants with diabetes mellitus type 2 or pre-diabetes and (pre)obesity underwent a three-month weight reduction program with a subsequent six-month follow-up phase. In addition, the participants in the

intervention group consumed two eggs per day (12 eggs/week) and those in the control group less than two eggs per week. Over the study period there were no significant differences between the two treatment groups for the serum lipids or the parameters for glucose metabolism.

Pourafshar et al. also investigated the effect of egg intake (1 egg/day) in comparison to a control group (egg white) on 42 persons with pre-diabetes or type 2 diabetes mellitus and (pre)obesity. In the intervention group there was an increase in apolipoprotein A I and oxidized LDL and a reduction of plasma glucose compared to the control group after a twelve-week study phase [25].

Lemos et al. [26, 27] analyzed the effect of increased egg intake (3 eggs/day) compared to a choline bitartrate supplement (397.5 mg of choline, amount equivalent to that in 3 eggs) on the lipid profile, glucose metabolism and parameters for regulation of endogenous cholesterol synthesis [26, 27]. The study, which included a total of 30 participants, was conducted using a crossover design over 13 weeks with a two-week run-in phase and a three-week washout phase between each of the four-week intervention phases. In comparison to taking the choline supplement the daily intake of three eggs led to an increase in plasma concentrations of LDL, high-density lipoprotein (HDL) and total cholesterol, apolipoprotein A I and E, whilst no changes were observed in the LDL/HDL cholesterol ratio, apolipoprotein B, triglycerides and glucose. The daily egg intake resulted in an increase in fat as a proportion of overall energy intake, the intake of saturated and simple unsaturated fatty acids, vitamin E and cholesterol compared to the intake of the choline supplement.

Another study examined the influence of increasing egg intake from one, two and three eggs per day for four weeks each on 38 participants in a crossover design over 14 weeks (with a 2-week washout phase at the start of the study) [28]. The comparison of the daily egg intake of no, one, two and three eggs showed no difference in the effect on plasma concentrations of total cholesterol, triglycerides and glucose. In comparison to no egg intake, intake of one egg per day led to an LDL cholesterol reduction by approx. 11%. In the comparison of one and two eggs per day and two and three eggs per day there were no changes to be seen in LDL cholesterol con-

Author, Year	Study type Study region Follow-up duration	Study population/ No. of cases Age	Exposition estimate of nutrition factor	Results
Tian et al. 2017 [12]	Meta-analysis of 5 cohort studies USA, n=4; Europe, n = 1 Follow-up duration: n. d.	67,796/5,281 ^a ≥ 21 years ^a		Highest vs. lowest egg intake: RR 1.03 (95%-CI [0.64; 1.67])
Schwingshackl et al. 2017 [13]	Meta-analysis of 12 cohort studies USA, n=4; Europe, n = 7, Asia, n=1 5–23 years	315,358/17,629 ≥ 20 years	Range of egg intake: 0–60 g/day	Highest vs. lowest egg intake: RR 1.08 (95%-CI [0.95; 1.22]) Dose-response analysis (per increase in egg intake by 30 g/day): RR 1.08 (95%-CI [0.95; 1.22]) Non-linear dose-response analysis: No association between egg intake and diabetes risk (p = 0.09)
Tamez et al. 2016 [16]	Meta-analysis of 10 cohort studies USA, n=4; Europe, n = 5; Asia, n=1 5–23 years	251,213/12,156 38–95 years	Range of egg intake: 0–1.1 eggs/day 1 egg = 50 g	Dose-response analysis (per increase in egg intake by 1 egg/day): RR 1.13 (95%-CI [1.04; 1.22])
Wallin et al. 2016 [14]	Meta-analysis of 11 cohort studies USA, n=4; Europe, n = 6; Asia, n=1 5–23 years	287,963/16,264 ≥20 years	Range of egg intake: < 1 to ≥ 5 eggs/week 1 egg = 55 g	Dose-response analysis (per increase in egg intake by threefold/week): HR 1.03 (95%-CI [0.96; 1.10]) Non-linear dose-response analysis: No association between egg intake and diabetes risk (p ≥ 0.15)
Djoussé et al. 2016 [15]	Meta-analysis of 8 cohort studies USA, n=4; Europe, n = 3; Asia, n=1 5–20 years	219,979/8,911 20–98 years	Range of egg intake: 0 to ≥ 7 eggs/week 1 egg = 50 g	Highest vs. lowest egg intake: RR 1.06 (95%-CI [0.86; 1.30]) Non-linear dose-response analysis: No association between egg intake and diabetes risk (p = 0.36)
Tran et al. 2014 [19]	Systematic review of 3 cohort studies ^b USA n=2, Europe, n = 1 Follow-up duration: n. d.	88,036 /n. d. ≥ 40 years	Range of egg intake: 0 to ≥ 7 eggs/week	Two studies showed a risk increasing association between egg intake and risk of type 2 diabetes mellitus; one study found no association
Shin et al. 2013 [17]	Meta-analysis of 3 cohort studies from the USA 14.8 years	69,297/4,889 39–98 years	≥ 1 egg/day vs. <1 egg/week or never	Highest vs. lowest egg intake: HR 1.42 (95%-CI [1.09; 1.86])
Li et al. 2013 [18]	Meta-analysis of 2 cohort studies from the USA ^c 11.3–20 years	60,896/4,336 53.5–73.2 years	Range of egg intake: 0 to ≥ 1/day	Highest vs. lowest egg intake: RR 2.62 (95%-CI [1.48; 4.64])

Tab. 1: Egg intake and risk of type 2 diabetes mellitus: results of systematic reviews and meta-analyses of cohort studies

CI = confidence interval; HR = hazard ratio; n = study population; n. d. = no details; RR = relative risk

^a details relate only to 4 cohort studies; no details available for one cohort

^b 4 case control studies and 3 cohort studies were also cited; but these latter relate to dietary patterns or gestational diabetes and were therefore not included in this overview.

^c In the study by Li et al. (2013) [18] analyses were also cited which included additional case control and cross-sectional study results. Here only the results of the sub-group analysis of the cohort studies are presented.

centration. An increase in LDL cholesterol was shown in the case of the intake of three eggs per day compared to one egg per day, but not in comparison to no egg intake. At the same time intake of one egg per day compared to no egg intake led to an increase in HDL cholesterol, which persisted over the whole intervention period. The intake of one, two and three eggs per day resulted in a reduction of the LDL/HDL ratio in comparison to no egg intake. In the case of an intake of two to three eggs per day compared to intake of no to one egg per day, fat as a proportion of overall energy intake increased, whilst the carbohydrate proportion reduced. Increased egg intake also led to a reduced intake of fiber [28].

Njike et al. examined the effect of egg intake on glucose metabolism parameters in 34 type-2-diabetics. For the participants who consumed two eggs per day (10–14 eggs/week) over twelve weeks, in comparison to no egg intake (crossover design) no changes were to be seen in HbA_{1c}-concentration or homeostatic model assessment (HOMA) insulin resistance (IR)[29].

In a single-arm intervention study 14 women consumed one boiled egg for breakfast each

day over a period of four weeks. At the end of the intervention phase there were no significant changes in concentrations of glucose, insulin, total, HDL or LDL cholesterol or triglycerides[30].

Missimer et al.[31]compared the effect of egg intake(2 eggs/day)and intake of oatmeal (1 pack/day) on cardiometabolic risk factors in 48 women and men (mean age: 23.3 years) in a randomized crossover study. The daily intake of two eggs in comparison to intake of oatmeal led to an increase in LDL, HDL and total cholesterol concentrations. In terms of triglyceride concentration and LDL/HDL ratios there were no significant inter-group differences. The daily egg intake led to an increase of fat as a proportion of overall energy intake, an increased intake of saturated and unsaturated fatty acids and cholesterol and a reduction in carbohydrates as a proportion of overall energy intake and a reduction of fiber intake in the comparison to oatmeal consumption.

Discussion and conclusion

As regards the association between egg intake and risk of type 2 diabetes mellitus the results of the meta-analyses and systematic reviews of prospective cohort studies were contradictory. In the systematic reviews and one meta-analysis of randomized controlled intervention studies examining the effects of egg intake on cardiometabolic risk factors predominantly no negative effect on serum lipids and glucose metabolism could be determined. The picture was similar in the analysis of results from the cited intervention studies. In the previous article (Part 1) the meta-analyses and systematic reviews examining the association between egg intake and risk of cardiovascular diseases in diabetics determined a predominantly positive (risk increasing) association. In contrast to this in the majority of the intervention studies on people with pre-diabetes or type 2 diabetes mellitus no effect on cardiometabolic risk factors was determined (including insulin, glucose, LDL, HDL, total cholesterol, triglycerides) with increased egg intake.

In a recently published meta-analysis which evaluated the individual data of approx. 30,000 participants from six prospective cohort studies, each increase in intake by half an egg per day or each increase in intake by

Author, Year	Study type Study region Follow-up/study duration	Study population Age	Intervention	Control	Results
Rouhani et al. 2018 [22]	Meta-analysis of 27 RCTs America, n = 19; Australia, n = 2; Asia, n = 2; Europe, n = 4 15–365 days	No. of study participants per RCT: 13–201 10-75 years	6 eggs/week to 3 eggs/day (or egg yolks) or additional palm oil, lacto-vegetarian or energy and carbohydrate-reduced diet, buttermilk, low-fat milk or corn oil and beef suet	Egg substitute and/or sugar-coated tablets, palm oil, lacto-vegetarian or energy and carbohydrate-reduced diet, buttermilk, low-fat milk, corn oil and beef suet, low-fat animal protein, NCEP diet or low egg intake (< 2 eggs/week)	Overall effect (Intervention vs. control): TC: 5.6 mg/dL (95%-CI [3.1; 8.09],p = 0.01) LDL-C: 5.55 mg/dL (95%-CI [3.14; 7.69],p < 0.0001) HDL-C: 2.13 mg/dL (95%-CI [1.10; 3.16],p < 0.0001) TG: -0.43 mg/dL (95%-CI [-3.77; 2.92], p = 0.80) TC/HDL-C: -0.01 mg/dL (95%-CI [-0.08; 0.07],p = 0.88) LDL/HDL-C: 0.16 mg/dL (95%-CI [-0.28; 0.59],p = 0.48) Dose-response analysis: Positive association between egg intake and HDL-C
Richard et al. 2017 [21]	Systematic review of 6 RCTs Study region: n. d. 12–20 weeks	No. of study participants per RCT: 31–221 ≥ 18 years	1–4 eggs/day or additional energy or carbohydrate-reduced diet or NCEP diet	Egg substitute and/or energy or carbohydrate-reduced diet, NCEP diet, low egg intake (< 2 eggs/week) or oatmeal with milk	In people with type 2 diabetes mellitus or an increased risk for this disease (pre-diabetes, insulin resistance, metabolic syndrome) the majority of studies showed no negative effect of increased egg intake on cardiometabolic risk parameters (including total, LDL-C, triglycerides, fasting glucose, insulin, C-reactive protein) compared to the control group. In 4 of 6 studies an increase in HDL-C was observed with egg intake.
Tran et al. 2014 [19]	Systematic review of 4 RCTs Study region: n. d. 12–20 weeks	No. of study participants: n. d. Age: n. d.	2–4 eggs/day or additional NCEP diet	Egg substitute and/or NCEP diet, carbohydrate-reduced diet	In non-diabetics with cardiovascular risk factors the majority of the studies showed no negative effects of increased egg intake on cardiometabolic risk parameters (including lipid profile, inflammation markers, insulin, HOMA-IR)

Tab. 2: Egg intake and cardiovascular risk factors: results of systematic reviews and meta-analyses of randomized controlled intervention studies

CI = confidence interval; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostatic model assessment-insulin resistance; LDL-C = low-density lipoprotein cholesterol; n = study population; NCEP = The National Cholesterol Education Program; n. d. = no details; RCT = randomized controlled trial; TC = total cholesterol; TG = triglycerides

300 mg of dietary cholesterol per day was associated with a risk increase for cardiovascular diseases and overall mortality. After adjustment for the intake of dietary cholesterol no further association between egg intake and the examined outcomes could be determined [32]. The results of this meta-analysis did not correspond to those of previous meta-analyses predominantly examining the association between egg intake and risk of stroke and coronary heart disease. Thus, the meta-analyses presented in part 1 of this article showed no association between egg intake and risk of stroke and coronary heart disease [17, 33–36] and the results of two meta-analyses on the association between egg intake and cardiovascular diseases in general were inconsistent [17, 18].

On the basis of the study results presented it is not possible to draw conclusions on concrete intake quantities for eggs. In the meta-analyses and systematic reviews of prospective cohort studies the exposure assessments varied considerably or no exact quantities were given for egg intake. This also applies to the results of intervention studies which did examine concrete intake quantities, but whose participants sometimes also followed a specific diet (e. g. energy or carbohydrate-reduced diet, National Cholesterol Education Program [NCEP] diet) or the study design showed limitations (e. g. no control group, different foods in the intervention group than the comparison group).

On the basis of the study results researched it is not possible to show any clear negative or any clear positive impacts of egg intake on the risk of cardiovascular diseases, type 2 diabetes mellitus or cardiometabolic risk factors. The current academic research suggests that no concrete quantitative recommendation can be derived for egg intake. Within an overall concept for a health-promoting, i.e. plant-based, diet, unlimited egg intake is however not recommended due to various premises, such as restricted energy intake. There is broad consensus that energy intake and overall dietary composition are decisive for a preventative nutritional effect rather than the focus on a single food (such as eggs) or one single nutrient or ingredient (such as cholesterol). In future these aspects will be given more attention in food-based dietary guidelines and consultation standards.

Conflict of Interest

The authors declare no conflict of interest.

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