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Effect of Egg Consumption on Blood Pressure: a Systematic Review and Meta-analysis of Randomized Clinical Trials

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Abstract

Purpose of Review—We identified and quantified the results of randomized controlled trials (RCTs) that have assessed the impact of egg consumption on blood pressure in adults.

Recent Findings—We conducted a comprehensive search of medical bibliographic databases up to February 2019 for RCTs investigating the effect of egg consumption on blood pressure in adults. Fifteen RCTs were included with a total of 748 participants. Overall, egg consumption had no significant effect on systolic blood pressure (weighted mean difference (WMD) = 0.046 mmHg; 95% CI – 0.792, 0.884) and diastolic blood pressure (WMD = – 0.603 mmHg; 95% CI – 1.521, 0.315). Subgroup analyses had no effect on pooled results and no heterogeneity was found among included studies.

Summary—Egg consumption has no significant effects on systolic and diastolic blood pressure in adults. Due to several limitations among existing studies, general conclusions cannot be drawn regarding the beneficial or neutral impact of egg consumption on blood pressure in adults.

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Author Contribution RKM screened and selected the trials, extracted the data, and wrote the manuscript. MM screened and selected the trials, extracted the data, and assessed quality of included studies. ZSC reviewed and edited the manuscript. SZS screened the trials. NP screened and selected the trials and assessed quality of included studies. MKS screened the trials. SS conceived the idea, conducted the research, analyzed the data, and performed statistical analysis and had primary responsibility for final content. All authors read and approved the final manuscript.

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Keywords

Egg; Systolic blood pressure; Diastolic blood pressure; Meta-analysis

Introduction

Cardiovascular diseases (CVD) are the leading cause of death in the developed world [1]. Hypertension (HTN) is a key contributor to the global burden of CVD [2] and overall death, leading to 10.5 million deaths annually [3]. The prevalence of HTN in the adult population is estimated to reach 1.56 billion by 2025 [4]. However, HTN is a modifiable risk factor for CVD, and as such, with proper treatment and control, risk of CVD is significantly reduced [2]. Various antihypertensive medications are often used for treatment of HTN, but many of these medications have adverse side effects and require lifelong adherence [5].

In recent years, the use of food for prevention and management of HTN has become a growing interest [6]. Among these foods, eggs have received much attention. Eggs are an economic and nutritious food commodity, which contain highly bioavailable proteins, essential fatty acids, antioxidants, choline, essential vitamins, and minerals [7•]. Despite being an excellent source of nutrients, the cholesterol content of eggs has been a matter of concern [8]. The current (2015–2020) Dietary Guidelines for Americans have removed the recommendation of limiting cholesterol intake and have explicitly stated that cholesterol is not a nutrient of concern for overconsumption; however, the current Dietary Guidelines for Americans also state that individuals should consume as little dietary cholesterol as possible [9]. A recent meta-analysis of ten prospective cohort studies revealed that higher dietary cholesterol intake was not associated with an increased risk of CVD [10]. Additionally, another meta-analysis of prospective cohort studies demonstrated no association between daily egg consumption and risk of coronary heart disease (CHD) [11•]. Interestingly, daily egg consumption was actually accompanied with a 12% reduction in stroke risk [11•].

A recent systematic review and meta-analysis of three prospective cohort studies by Zhang et al. showed the egg consumption was associated with lower risk of HTN (relative risk (RR) = 0.79; 95% CI 0.68–0.91; $P=0.001$) [12••]. In contrast, the results of human randomized controlled trials (RCTs) investigating the effect of egg consumption on blood pressure have been inconsistent [13–27] with some studies showing beneficial effects of egg consumption on systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) [16, 23], while others have shown no effect [13–15, 17–22, 24–27]. The primary purpose of the current study was to conduct a systematic review and meta-analysis of the published RCTs to comprehensively evaluate and quantify the effects of egg consumption on blood pressure in adults. The secondary purpose was to establish evidence that could potentially inform future dietary guidelines for the management of HTN.

Methods

Protocol and Registration

The current systematic review and meta-analysis was carried out and reported in accordance with the preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines [28] and the study protocol was registered in the international prospective register of systematic reviews (PROSPERO) database as CRD42019127500.

Search Strategy

We performed a search of PubMed, Ovid Medline, Scopus, and the Cochrane Central Register of Controlled Trials (Central) databases from inception up to 25 February 2019 for studies that described the effects of egg consumption on blood pressure in adults using the keywords egg and dietary cholesterol which were paired with hypertension or blood pressure (supplementary Table S1). The search was restricted to clinical trials. No limit was placed on language or date of publication during the literature search. We also reviewed reference lists of all retrieved publications again to obtain further relevant articles. Attempts were also made to contact investigators for additional information and the full-text article if the article could not be retrieved during the original search.

Study Selection

Studies were included in this meta-analysis if they met the following criteria: (1) the study was a RCT with either a parallel or a crossover design; (2) the participants used whole egg matched by a suitable control arm; (3) the study reported baseline and post intervention values (or their differences) for SBP, DBP or both with SDs, SEMs, or 95% CIs for each group; and (4) the study was conducted on an adult population. Study exclusion criteria were as follows: (1) non-RCT studies; (2) nonhuman studies; (3) trial conducted on pregnant women or children; (4) studies which used eggs enriched with different nutrients in the experimental group but not in the control group; and (5) studies that evaluated egg components such as egg yolk, egg white, or bioactive peptides derived from eggs.

Data Extraction

Two authors (RKM, MM) independently assessed the abstract and the full text of eligible articles and extracted the following data: (1) study characteristics (first author's name, country, year of publication, sample size, study design, type and amount (number of eggs consumed per day) of intervention, specific diet adherence, and study duration); (2) population information (sex, age, BMI, and health status); and (3) mean $\pm$ SD for baseline, post intervention, and changes from baseline for SBP and DBP in experimental and control groups. Any disagreement in abstracted data was resolved through discussion and consultation with a third author (SS).

All study durations were converted to weeks from days or months. In the case where results were reported separately for hypo and hyper-responders to dietary cholesterol intake, we combined both groups using a fix model to retrieve an overall effect.

Quality Assessment and Quality of Evidence

Two independent authors (MM and NP) assessed the quality of included trials using the Cochrane Collaboration's tool for the following domains: (1) random sequence generation; (2) allocation concealment; (3) blinding (participants, personnel, and outcome assessors); (4) incomplete outcome data; (5) selective outcome reporting; and (6) other sources of bias and each RCT stratified as good, fair, or poor quality according to each domain [29].

The overall quality of the studies included in this meta-analysis was also evaluated by the use of NutriGrade scoring system which comprises the following items: (1) risk of bias, study quality, and study limitations (0–3 points); (2) precision (0–1 point); (3) heterogeneity (0–1 point); (4) directness (0–1 point); (5) publication bias (0–1 point); (6) funding bias (0–1 point); and (7) study design (+ 2 points). This scoring system recommends four categories to judge the meta-evidence as high meta-evidence (≥ 8 points); moderate meta-evidence (6–7.99 points); low meta-evidence (4–5.99 points); and very low meta-evidence (0–3.99 points) [30].

Statistical Analysis

Intervention effects were defined as weighted mean differences (WMD) and 95% CIs calculated for net changes in SBP and DBP values with the use of the random effects models [31]. Heterogeneity of studies was examined with the use of Cochran's test and the inconsistency index I^2 with an I^2 of 25%, 50%, and 75% indicating low, medium, and high heterogeneity, respectively [32]. Pre-defined subgroup analysis based on sex (male, female, or both), population health status (healthy, type 2 diabetic and metabolic syndrome, patients with coronary artery disease (CAD) and hyperlipidemia), hypertension (patients who had SBP > 120, DBP > 80 mmHg or used antihypertensive drugs and who did not have hypertension as an inclusion criteria) and obesity status (nonobese or overweight/obese), duration (less than 12 weeks or ≥ 12 weeks) and design (parallel or crossover) of study, diet adherence (usual diet or specific/restricted diet), and amount of egg consumption in intervention group (one egg/day or greater than one egg/day) was conducted to detect potential sources of heterogeneity. Furthermore, the potential nonlinear effects of egg consumption (number/day) and study duration (week) on SBP and DBP were evaluated using fractional polynomial models [33]. Publication bias was tested using Begg's and Egger's tests [34]. Sensitivity analysis using the "leave one out" approach was also conducted to evaluate the impact of one study on overall pooled estimates and heterogeneity [35]. Alpha was set at 0.05 and significance was determined at $P < 0.05$. Data analyses were conducted using Stata version 13 (Stata Corp LP, College Station, TX, USA).

Results

Results of the Literature Search

Initial database search yielded 3589 articles, of which 79 articles were assessed in full text for inclusion in the meta-analysis. With the 79 articles assessed, fifteen trials were eligible for inclusion. Excluded studies are reported in Fig. 1.

Study Characteristics

The characteristics of included studies are displayed in Table 1. Fifteen articles with 748 participants and mean age range from 23.3 to 67.1 years old were included in this systematic review and meta-analysis. Included studies were published between 1984 and 2018 and were conducted in the USA ($n = 10$) [15, 16, 18–24, 27], Australia ($n = 2$) [17, 25], Mexico ($n = 1$) [13], Colombia ($n = 1$) [14], and Thailand [26] ($n = 1$). Ten studies used a crossover design [13, 16, 18–22, 24, 26, 27] and five studies used a parallel arm design [14, 15, 17, 23, 25]. Of the fifteen studies, one study was conducted only in women [18] and one conducted only in men [23]; all of the remaining studies were conducted in both men and women [13–17, 19–22, 24–27]. Four trials were conducted in participants with type 2 diabetes [13, 17, 24, 25], one trial conducted in participants with the metabolic syndrome [14], one trial included patients with hyperlipidemia [26], one trial selected patients with CAD [20], and eight studies used healthy participants [15, 16, 18, 19, 21–23, 27]. Four studies included participants who were taking blood pressure lowering medications or who had SBP/DBP $> 120/80$ mmHg [13, 17, 23, 25]. Nine studies included participants that were overweight and obese [13–15, 17, 19, 20, 23–25]. All included studies used whole egg as an intervention which varied from one egg/day to three eggs/day and duration of supplementation ranged from 3 to 12 weeks. In some studies, egg consumption in the intervention group was compared with less [17, 26] or no egg consumption [16, 24, 27] in the control group, while other studies compared egg consumption with egg substitute [14, 18, 23], egg beater [20], oatmeal [13, 19, 22], bagel [15], lean animal protein [25], and choline bitartrate supplementation [21] in the control group.

Effect of Egg Consumption on SBP and DBP

The overall effect of egg consumption on SBP was 0.046 mmHg (95% CI – 0.792, 0.884; $P = 0.914$) and there was no heterogeneity among studies ($I^2 = 0.0\%$, $P = 0.453$) (Fig. 2). The nonlinear dose-response analysis failed to show a significant effect of egg consumption (P -nonlinearity = 0.07) and study duration on SBP (P -nonlinearity = 0.61). The overall effect of egg consumption on DBP was – 0.603 mmHg (95% CI – 1.521, 0.315; $P = 0.198$) and there was no heterogeneity among studies ($I^2 = 38.1\%$, $P = 0.067$) (Fig. 3). Nonlinear dose-response meta-analysis did not reveal a significant effect of egg consumption (P -nonlinearity = 0.76) and study duration on DBP (P -nonlinearity = 0.63). Subgroup analyses based on study design, sex, population health status, obesity and hypertension status, diet adherence, study duration, and amount of egg consumption did not affect the overall effects of egg consumption on SBP and DBP values (supplementary Table S2 and Table S3).

Sensitivity Analysis and Publication Bias

Sensitivity analysis indicated that excluding each trial did not significantly change the overall observed effects of egg consumption on SBP and DBP values. No evidence of publication bias was seen in the meta-analyses of SBP (Begg's $P = 0.235$, Eggers's $P = 0.433$) and DBP (Begg's $P = 0.254$, Eggers's $P = 0.267$).

Data Quality

The quality of selected trials was diverse with one trial classified as high quality (score 6) [17], 7 trials were classified as fair (score 4) [13, 18–20, 23–25], and the remaining 7 trials were classified as poor quality (score = 2 or 3) [14–16, 21, 22, 26, 27]. Qualities of included studies are presented in supplementary Table S4. Additionally, the NutriGrade meta-evidence rating was 6.86 in this meta-analysis which suggests that there is a moderate confidence in effect estimate and further research may change the effect estimate (supplementary Table S5).

Discussion

The overall outcome of this meta-analysis from fifteen eligible RCTs showed no significant effect of egg consumption on blood pressure. Subgroup analyses showed that the pooled effects of egg consumption on SBP and DBP were not influenced by study design, sex, population health status, obesity and HTN status, diet adherence, study duration, and number of eggs consumed.

HTN is a strong risk factor for CVD and strokes [36]. The results from our study are in accordance with a meta-analysis of cohort studies that reported intake of one egg/day compared with low egg intake (approximately < 2 eggs/week) was not associated with increased risk of CHD [11•]. Similarly, a systematic review and meta-analysis by Shin et al. showed that high (> 1 egg/day) vs low egg consumption (< 1 egg/week or never) was not associated with an increased risk of CVD, ischemic heart disease (IHD), stroke, and cardiac mortality in the general population [37]. In relation to blood pressure, a systematic review and meta-analysis of three prospective cohort studies showed that egg consumption was associated with a reduced risk of HTN [12••]. In contrast, Wang et al. recently reported that consumption of > 4 whole eggs/week compared with < 4 whole eggs/week intake did not influence blood pressure in middle-aged and older adults [38].

The beneficial effects of egg consumption on blood pressure in humans may be attributed to the presence of nutrients with antioxidant and antihypertensive effects in whole eggs [7•, 39]. For example, beneficial effects of egg white derived peptides on blood pressure have been shown in animal studies. In these studies, orally administered IQW (Ile-Gln-Trp) and LKP (Leu-Lys-Pro) (tripeptides provided by enzymatic digestion of the ovotransferrin) decreased mean blood pressure in hypertensive rats [40]. Additionally, orally administered egg white hydrolysate [41] and an antihypertensive tripeptide Ile-Arg-Trp (IRW) [42•] reduced blood pressure in hypertensive rats. In these studies, reduction of blood pressure was concomitant with increased nitric oxide (NO) mediated vasodilatation, angiotensin converting enzyme (ACE) inhibition, reduced vascular inflammation and oxidative stress, reduced ACE and angiotensin II type 1 receptor expression, and increased ACE2 expression [40, 41, 42•].

We considered several possible explanations for the lack of association between egg consumption and blood pressure in the current meta-analysis. Firstly, blood pressure was not a primary objective in the majority of the trials included in this meta-analysis, which may have resulted in inadequate statistical power to detect significant changes regarding the

effects of egg consumption on blood pressure. Secondly, it is possible that lifestyle factors associated with egg consumption may influence HTN, as higher egg consumption tends to be associated with smoking, physical inactivity, and increased consumption of red and processed meat [12••, 43]. These factors tend to exaggerate the association between egg consumption and HTN [43]. Thirdly, heterogeneity of control interventions is an important factor which can significantly alter blood pressure results. In three of the fifteen studies included in the current meta-analysis, egg consumption was compared with consumption of oatmeal [13, 19, 22]. A recent systematic review and meta-analysis demonstrated that β -glucan can decrease SBP by 0.22 mmHg per gram consumed [44], and oatmeal intake in the studies included in the present systematic review and meta-analysis varied between 40 and 60 g. Additionally, two studies used lean animal protein [25] and choline bitartrate supplement [21] as control.

Fourthly, baseline characteristics of the studied populations must be considered. Thus, we performed subgroup analyses for baseline characteristics for all studies included in the present meta-analysis. However, due to small number of trials in each subgroup, we could not find association in this regard. Of the fifteen trials included in the current meta-analysis, thirteen trials found that egg consumption did not affect blood pressure [13–15, 17–22, 24–27], while in one trial, consumption of three eggs per day in overweight or obese participants significantly reduced SBP and DBP relative to the control group [23]. Additionally, one study demonstrated that consumption of three eggs per day in healthy participants significantly reduced DBP but had no effect on SBP [16]. Taken together, these data suggest that high egg intake, baseline characteristics of participants (healthy not sick), and intervention in the control group (low or no egg consumption or egg substitute) have an important role in the association between egg consumption and blood pressure. Finally, most of the included studies in this meta-analysis utilized a crossover design with short washout periods ranging from 0 to 6 weeks [13, 16, 18–22, 24, 26, 27]. Inadequate and/or inconsistent washout periods from one intervention to the next may lead to inaccurate results, potentially due to carryover effects from the first arm into the second.

To our knowledge, the current systematic review and meta-analysis of RCTs is the first to evaluate the effect of egg consumption on blood pressure in general adult population. We performed several subgroup analyses to identify the possible source of heterogeneity that may be influencing the relationship between egg consumption and blood pressure. Moreover, doing comprehensive literature search to include available RCTs is examining the effect of egg consumption on blood pressure. As with all systematic reviews and meta-analyses, the current analysis has some limitations. First, blood pressure was not a primary objective in almost all included studies, so it is possible that the study sample size was not sufficient to detect significant relationship. Second, the number of RCTs assessing the association between egg consumption and blood pressure was small and most studies were of low or fair quality, which can be attributed mostly to lack of blinding of participants, personnel, and outcome assessment. These issues should be addressed in future studies. Third, the different types of placebo in control groups may have imposed effects on our results. Fourth, most included studies did not adjust the effect of confounding factors including medications, physical activity, and dietary habit which may have affected the results regarding the relationship between egg consumption and blood pressure.

Conclusion

Overall our analysis has shown that egg consumption had no effect on blood pressure. However, high-quality RCTs with longer durations are needed to further confirm the effects of egg consumption on blood pressure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Availability of Data and Material It was registered in the PROSPERO (international prospective register of systematic reviews) database under the number CRD42019127500.

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Abbreviations

CVD	Cardiovascular diseases
HTN	Hypertension
CHD	Coronary heart disease
RR	Relative risk
RCTs	Randomized controlled trials
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
PRISMA	Preferred reporting items for systematic review and meta-analyses
PROSPERO	Prospective register of systematic reviews
WMD	Weighted mean differences
CAD	Coronary artery disease
IHD	Ischemic heart disease
IQW	Ile-Gln-Trp
LKP	Leu-Lys-Pro
IRW	Ile-Arg-Trp
NO	Nitric oxide
ACE	Angiotensin converting enzyme

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•• Of major importance

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Fig. 1.
Flow diagram for study selection procedure

Fig. 2.
Forest plot showing pooled weighted mean difference with 95% CI for SBP

Fig. 3.
Forest plot showing pooled weighted mean difference with 95% CI for DBP

Table 1

Summary of RCTs that assessed the impact of egg consumption on systolic and diastolic blood pressure

Author (year) [References]	Country	Sex	Mean age (year)	Study design	Egg group	Control group	Duration (week)	Population characteristic	Specific diet adherence	Outcome
Ballesteros (2015) [13]	Mexico	19 F/10 M	53.5	Crossover	1 egg/day	40 g oatmeal/day	5	T2DM	Usual diet	↔ SBP ↔ DBP
Blesso (2013) [14]	Colombia	25 F/12 M	51.9	Parallel	3 eggs/day	3 eggs substitute/day	12	MetS	Carbohydrate-restricted diets	↔ SBP ↔ DBP
Clayton (2015) [15]	USA	25 F and M	25.7	Parallel	2 eggs/day	9 cm bagel/day	12	Healthy	Not reported	↔ SBP ↔ DBP
DiMarco (2016) [16]	USA	19 F/19 M	24.1	Crossover	1 to 3 eggs/day	0 egg/day	4	Healthy	Usual diet	↔ SBP ↓ DBP
Fuller (2015) [17]	Australia	77 F/63 M	59.8	Parallel	12 eggs/week	< 2 eggs/week	12	Overweight and obese with T2DM	Usual diet	↔ SBP ↔ DBP
Herron (2002) [18]	USA	51 F	Not reported	Crossover	3 eggs/day	3 eggs substitute/day	4	Healthy	NCEP step I diet	↔ SBP ↔ DBP
Katz (2005) [19]	USA	19 F/30 M	56	Crossover	2 eggs/day	60 g oatmeal/day	6	Healthy	Usual diet	↔ SB ↔ DBP
Katz (2015) [20]	USA	6 F/26 M	67.1	Crossover	2 eggs/day	1/2 cup egg beaters	6	CAD	Usual diet	↔ SBP ↔ DBP
Lemos (2018) [21]	USA	16 F/14 M	25.5	Crossover	3 eggs/day	1.5 tablets choline bitartrate	4	Healthy	Usual diet	↔ SBP ↔ DBP
Missimer (2017) [22]	USA	26 F/24 M	23.3	Crossover	2 eggs/day	1 packet oatmeal/day	4	Healthy	Usual diet	↔ SBP ↔ DBP
Mutungi (2008) [23]	USA	31 M	Not reported	Parallel	3 eggs/day	3 eggs substitute/day	12	Overweight and obese	Carbohydrate-restricted diets	↓ SBP ↓ DBP
Njike (2016) [24]	USA	14 F/20 M	64.5	Crossover	2 eggs/day	0 egg/day	12	T2DM	Usual diet	↔ SBP ↔ DBP
Pearce (2010) [25]	Australia	65 F and M	59.7	Parallel	2 eggs/day	100 g lean animal protein	12	T2DM	Energy restricted diet	↔ SBP ↔ DBP
Putadechakum (2013) [26]	Thailand	63 F/8 M	50.79	Crossover	3 eggs/day	One egg/day	4	Hypertlipidemia	Usual diet	↔ SBP ↔ DBP
Sacks (1984) [27]	USA	13F/4M	Not reported	Crossover	1 egg/day	0 egg/day	3	Healthy	Usual diet	↔ SBP ↔ DBP

RCTs randomized controlled trials; F female; M male; gr gram; T2DM type 2 diabetes mellitus; MetS metabolic syndrome; CAD coronary artery disease; ↔, no change; ↓, significant reduction