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Dietary Cholesterol from Eggs Increases Plasma HDL Cholesterol in Overweight Men Consuming a Carbohydrate-Restricted Diet[1,2]

Gisella Mutungi,[3] Joseph Ratliff,[3] Michael Puglisi,[3] Moises Torres-Gonzalez,[3] Ushma Vaishnav,[3] Jose O. Leite,[3] Erin Quann,[4] Jeff S. Volek,[4] and Maria Luz Fernandez[3]*

[3]Department of Nutritional Sciences and [4]Department of Kinesiology, University of Connecticut, Storrs, CT 06269

Abstract

Carbohydrate-restricted diets (CRD) significantly decrease body weight and independently improve plasma triglycerides (TG) and HDL cholesterol (HDL-C). Increasing intake of dietary cholesterol from eggs in the context of a low-fat diet maintains the LDL cholesterol (LDL-C)/HDL-C for both hyper- and hypo-responders to dietary cholesterol. In this study, 28 overweight/obese male subjects (BMI = 25–37 kg/m^2) aged 40–70 y were recruited to evaluate the contribution of dietary cholesterol from eggs in a CRD. Subjects were counseled to consume a CRD (10–15% energy from carbohydrate) and they were randomly allocated to the EGG group [intake of 3 eggs per day (640 mg/d additional dietary cholesterol)] or SUB group [equivalent amount of egg substitute (0 dietary cholesterol) per day]. Energy intake decreased in both groups from 10,243 ± 4040 to 7968 ± 2401 kJ ($P < 0.05$) compared with baseline. All subjects irrespective of their assigned group had reduced body weight and waist circumference ($P < 0.0001$). Similarly, the plasma TG concentration was reduced from 1.34 ± 0.66 to 0.83 ± 0.30 mmol/L after 12 wk ($P < 0.001$) in all subjects. The plasma LDL-C concentration, as well as the LDL-C:HDL-C ratio, did not change during the intervention. In contrast, plasma HDL-C concentration increased in the EGG group from 1.23 ± 0.39 to 1.47 ± 0.38 mmol/L ($P < 0.01$), whereas HDL-C did not change in the SUB group. Plasma glucose concentrations in fasting subjects did not change. Eighteen subjects were classified as having the metabolic syndrome (MetS) at the beginning of the study, whereas 3 subjects had that classification at the end. These results suggest that including eggs in a CRD results in increased HDL-C while decreasing the risk factors associated with MetS. J. Nutr. 138: 272–276, 2008.

Introduction

Overweight and obesity have continued to increase rapidly in the United States, affecting both adults and young children. This is in general a result of genetics and lifestyle consisting of low levels of physical activity and consumption of excess carbohydrate (1). In obesity, the main health risks are a result of increased adipose tissue. Adipose tissue synthesizes and secretes biologically active molecules believed to affect metabolic syndrome (MetS)[5] and cardiovascular diseases (2). Carbohydrate-restricted diets (CRD) have been shown to reduce weight and hence reduce these risks (3,4). In numerous studies evaluating the effect of CRD on weight loss, a significant reduction in weight mostly from the abdominal area has been reported (3). This area has been associated with increased lipolytic activity of abdominal adipose tissue, leading to higher plasma free fatty acid concentrations, which, in turn, decrease both hepatic removal of insulin and insulin-stimulated glucose uptake by peripheral tissues (5). Compared with a low-fat diet, a CRD results in preferential loss of fat in this region (6).

According to the National Cholesterol Education Program adult treatment panel III (ATP III) diagnostic criteria, the parameters associated with MetS include levels of plasma fasting glucose > 100 mg/dL, (5.5 mmol/L), triglycerides (TG) > 150 mg/dL (1.88 mmol/L), blood pressure (BP) > 130/85 mm Hg, low levels of HDL cholesterol (HDL-C) <40 mg/dL in men and <50 mg/dL in women (1 mmol/L in men and 1.3 mmol/L in women), and waist circumference (WC) > 88 cm in women and >102 cm in men (7). From 1994 to 1998, there were ~45–50 million Americans (24%) who met the ATP III diagnostic criteria for MetS, of which 37% were Hispanic women and 16% were men of African-American origin (8). There also have been dramatic and rapid increases of MetS and diabetes among children and teens, which are not due to the results in the

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[2] Supplemental Figure 1 is available with the online posting of this paper at jn.nutrition.org.
[5] Abbreviations used: ATP III, adult panel treatment III; BP, blood pressure; CRD, carbohydrate-restricted diet; DEXA, dual-energy X-ray absorptiometry; EGG, 3 liquid eggs per day; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MetS, metabolic syndrome; SUB, same amount of egg substitute; TC, total cholesterol; TG, triglyceride; WC, waist circumference.
* To whom correspondence should be addressed. E-mail: maria-luz.fernandez@uconn.edu.

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changes of the criteria by AHA and the National Heart Lung and Blood Institute but rather, from complications developing earlier in their lives due to overweight/obesity and diabetes (9).

In this study, we used eggs as part of a CRD due to their high protein and low carbohydrate content. Because eggs contain substantial amounts of dietary cholesterol (10), we were able to evaluate the effects on weight loss and features of MetS of a CRD that was either low or high in cholesterol. Results from previous studies in our laboratory revealed that hyper-responders to dietary cholesterol (a response higher than 0.06 mmol/L for each additional 100 mg of dietary cholesterol) in the context of a low-fat diet increased both LDL-C and HDL-C concentrations while maintaining the LDL-C:HDL-C ratio, whereas the cholesterol carried by these lipoproteins did not change in hypo-responders (11,12).

The objective of this study was to compare the effects of a CRD high in cholesterol (provided by eggs) to one low in cholesterol (using an egg substitute) on the variables of MetS. We hypothesized that including eggs in the CRD would not alter the beneficial effects of the CRD on plasma lipids and body composition.

Methods

Materials. Liquid whole eggs and cholesterol-/fat-free eggs were purchased from Vistar. The composition of these products is as follows: 3 eggs are the equivalent to 1.76 g carbohydrate, 18.95 g protein, 22.99 g fat, and 1239 kJ and cholesterol-/fat-free eggs are the equivalent to 2.90 g carbohydrate 19.79 g protein, 0.31 g fat, and 394 kJ.

Kits for total cholesterol (TC) and TG were from Roche Diagnostics; glucose kits were from WACO (Waco Diagnostics).

Study design. We recruited 31 men between the age of 40 and 70 y with a BMI of 26–37 kg/m^2 from the university and the surrounding community and randomly assigned them to consume the equivalent of 3 liquid eggs per day (EGG) or the same amount of egg substitute (SUB). Three individuals dropped out of the study due to compliance issues. Subjects were excluded if they had hypothyroidism, documented heart disease, type I diabetes, gout, or egg allergies. All subjects followed a CRD for 12 wk. Similar to other studies in our laboratory (4,6), carbohydrates were restricted to 10–15% of total energy. The energy percent contribution was set at 10–15% from carbohydrates, 25–30% from protein and 55–60% from fat. This was a parallel, randomized, placebo-controlled, single-blinded study. The substitute had the same color and consistency as the eggs. Fifteen subjects from the EGG group and 13 subjects from the SUB group completed the study.

Blood samples, body composition, food records, BP, and anthropometrics were collected at baseline, wk 6, and wk 12. Logs were provided to subjects to record physical activity at baseline and each week during the intervention. All study protocols were approved by the University of Connecticut Institutional Review Board and all subjects signed an informed consent form before participating in the study.

Diet. These were free-living subjects who were not provided with any other foods apart from either eggs or egg substitute to consume as part of their diet and energy intake was not restricted. Subjects received individual and personalized dietary counseling from registered dietitians prior to the dietary intervention. Detailed dietary booklets, specific to each dietary treatment, were provided outlining dietary goals, lists of appropriate foods, recipes, sample meal plans, and food record log sheets. No explicit instructions were provided regarding energy intake for either diet to allow expression of any noncognitive aspects on food intake. Subjects received weekly follow-up counseling during which we measured body mass, assessed compliance, and provided further dietetic education. A 3-d weighed food record was obtained at baseline to assess nutrient intake and 5-d records were completed during wk 1, 6, and 12 of the intervention.

Subjects were given specific instructions regarding the type of foods that must be avoided as a result of following a CRD and they could not consume any additional eggs beyond what was provided to them weekly. Subjects in the EGG group were taking an additional 640 mg/d of cholesterol, whereas this product was excluded from the SUB group diet. They could consume unlimited amounts of meat and fish, moderate amounts of cheese, vegetables and salad dressings with low carbohydrate content, and small amounts of seeds and nuts. There were no restrictions on the type of fats consumed. Subjects were asked to maintain their normal routine of physical activity during the course of this study.

Dietary assessment. We analyzed dietary intake using the Nutritional Data System 5.0 (University of Minnesota). The mean values were obtained for nutrient intake at each data collection point. Values for total energy as well as absolute and percent contribution from the macronutrients were obtained. Contributions from different dietary fats and cholesterol were also calculated.

Blood collection. After overnight food deprivation, blood (12-h fasting) was collected from an antecubital vein into EDTA tubes and was immediately centrifuged at 2000 × *g*; 20 min. Preservatives (1 mL/L sodium azide, 1 mL/L phenylmethylsulfonyl fluoride, and 5 mL/L aprotinin) were added to the plasma once separated from red blood cells. The plasma was then aliquoted and frozen at −80°C and the plasma to measure lipids was stored at 4°C. The subjects were requested to fast on 2 d in the same week to average their plasma lipids.

Plasma lipids: TC, TG, LDL-C, HDL-C, and plasma glucose. Plasma TC concentration was measured by enzymatic methods using Roche Diagnostics standards and kits (13). We measured plasma HDL-C concentration in the supernatant after precipitation of Apo B-containing lipoproteins (14) and we measured plasma LDL-C concentration using the Friedewald equation (15). The TG concentration was determined using Roche Diagnostic kits, which adjust for free glycerol (16). Glucose was determined by a colorimetric method as previously reported (3).

Anthropometrics and BP. Anthropometrics and BP were measured at baseline, 6 wk, and 12 wk. Weight was measured to the closest 0.5 lb (0.25 kg) and height to the closest 0.5 inch (1 cm) on a portable stadiometer/scale. Weight and height were converted into metric units to calculate BMI (kg/m^2). WC was measured mid-way between the lowest rib and iliac crest to the nearest 0.1 cm. BP was measured on the right arm using a Welch Allyn, Tycos BP cuff with the participant seated, following a 5-min rest. BP and anthropometrics were measured twice by the same individual during the same week to account for variability.

Body composition/dual-energy X-ray absorptiometry scan. Body mass and body composition were measured in the morning after an overnight fast. Body mass was recorded to the nearest 100 g on a calibrated digital scale with subjects wearing only underwear. We assessed whole body and regional body composition using a state-of-the-art fan-beam dual-energy X-ray absorptiometry (DEXA) (Prodigy, Lunar). Analyses were performed by the same technician who was unaware of study details.

Statistics analyses. Two-way repeated measures ANOVA was used to determine diet effects and time effects on plasma lipids, food intake, body composition, and BP. Each individual's response to the intervention over time was the repeated measure and EGG vs. SUB were the between-subject factors. $P < 0.05$ was considered significant. SPSS version 13.0 for Windows was used to perform the statistical analyses and the data are reported as means ± SD.

Results

Dietary analysis. Energy intake decreased during the intervention compared with baseline in both groups ($P < 0.05$; **Table 1**). Energy contribution from carbohydrates was reduced from 42.4% at baseline to 14.9% at wk 12 in the EGG group, whereas these changes were from 41.5 to 19.1% ($P < 0.0001$) in

TABLE 1 Baseline dietary intakes of overweight men and intakes when they consumed a CRD including 3 eggs (EGG) or an egg substitute (SUB) for 12 wk[1]

Variable	Baseline	Wk 1	Wk 6	Wk 12	*P*-value (time effect)
Total energy, *kJ/d*					
EGG	2544 ± 921	1821 ± 311	1909 ± 641	1962 ± 691	<0.05
SUB	2318 ± 1030	1973 ± 465	1985 ± 738	1821 ± 408	
Carbohydrate, *% en*					
EGG	42.4 ± 8.3	11.1 ± 5.0	13.8 ± 7.7	14.9 ± 9.3	<0.0001
SUB	41.5 ± 9.5	15.6 ± 8.8	17.8 ± 9.7	19.9 ± 12.1	
Fat, *% en*					
EGG	39.9 ± 7.2	57.9 ± 6.6	58.1 ± 9.5	56.1 ± 10.3	<0.0001
SUB	39.2 ± 8.4	54.5 ± 7.4	54.7 ± 8.6	54.9 ± 13.8	
Protein, *% en*					
EGG	17.1 ± 3.7	28.9 ± 5.1	25.9 ± 5.8	26.9 ± 6.5	<0.0001
SUB	18.6 ± 5.9	27.9 ± 4.1	25.1 ± 3.5	24.5 ± 3.6	
Cholesterol, *mg/d*					
EGG	319 ± 150	778 ± 240	832 ± 253	827 ± 192	<0.0001
SUB	354 ± 170	403 ± 174*	337 ± 133*	277 ± 100*	

[1] Values are means ± SD, $n = 15$ (EGG), or 13 (SUB). There were no diet or diet × time effects for any of the variables except dietary cholesterol. *Different from EGG at that time, $P < 0.001$.

the SUB group. Carbohydrate intakes at baseline and 1, 6, and 12 wk for individuals are in Supplemental Figure 1. The contribution of energy from fat and protein increased after 12 wk ($P < 0.0001$). The only nutrient that differed between the groups was that of cholesterol. In the EGG group, dietary cholesterol increased from 319 ± 150 to 826 ± 192 mg/d ($P < 0.0001$), whereas it did not change in the SUB group (Table 1). Absolute protein and carbohydrate intakes (g/d) by all subjects changed during the study but that of fat did not, despite a change in its energy contribution (**Fig. 1**). Protein intake increased ($P < 0.01$) and that of carbohydrate decreased ($P < 0.01$). Physical activity did not change during the study (data not shown).

Anthropometrics and BP. The EGG and SUB groups did not differ in anthropometrics or BP. Body weight, BMI, and WC were reduced at wk 12 for all subjects (**Table 2**). Both systolic and diastolic BP decreased after the intervention. There was a significant reduction in the fat from the abdominal/trunk area as measured by DEXA (Table 2).

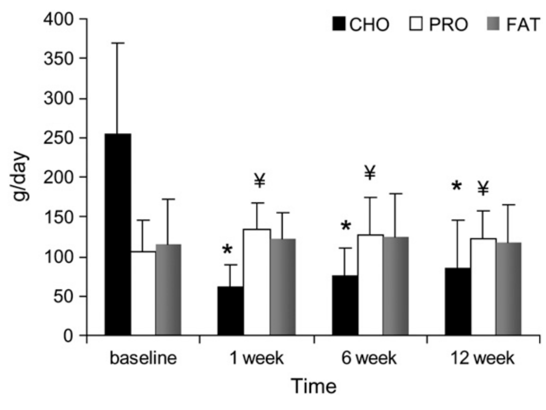

FIGURE 1 Baseline absolute macronutrient intakes of overweight men and intakes when they consumed a CRD including 3 eggs or an egg substitute for 12 wk. Values are means + SD, $n = 28$. Symbols indicate a difference from baseline: *, $P < 0.001$; ¥, $P < 0.05$. Groups were pooled because they did not differ.

Plasma lipids and glucose. Plasma TC and LDL-C ($P > 0.10$) concentrations and the LDL-C:HDL-C ratio ($P > 0.25$) did not change for either group despite the increased cholesterol intake by the EGG group (**Table 3**). The TG concentration in both groups was reduced by 45% from baseline ($P < 0.001$) as a result of CRD. However, the plasma HDL-C concentration increased only in the EGG group from 1.23 ± 0.39 at baseline to 1.47 ± 0.39 mmol/L at wk 12 (Table 3). The plasma HDL-C concentration did not change in the SUB group (Table 3). Thirteen of 15 subjects in the EGG group had increased HDL-C concentrations and only 3 subjects of 13 in the SUB group had increased HDL-C concentrations (**Fig. 2**). The fasting plasma glucose concentration, 5.1 ± 1.1 mmol/L at baseline and 5.2 ± 0.9 mmol/L after the intervention, did not change in either group.

TABLE 2 Body weight, anthropometrics, and BP at baseline, 6 wk, and 12 wk of subjects consuming a CRD in combination with either EGG or SUB[1]

Variable	Baseline	Wk 6	Wk 12	Absolute change	*P*-value (time)
Body weight, *kg*				*unit/12 wk*	
EGG	98.9 ± 15.3	93.5 ± 13.0	92.2 ± 12.7	−6.7	
SUB	97.6 ± 19.9	92.8 ± 18.5	91.7 ± 15.7	−5.9	<0.0001
Trunk fat, *%*					
EGG	37 ± 7.4	34.5 ± 8.6	31.6 ± 8.7	−5.4	
SUB	38.6 ± 6.6	36.3 ± 8	32.5 ± 8.3	−6.1	<0.0001
WC, *cm*					
EGG	107.9 ± 11.6	102.7 ± 10.4	101.5 ± 2.7	−6.4	
SUB	108.8 ± 15.8	104.3 ± 14.3	102.1 ± 14.7	−6.7	<0.0001
Systolic BP, *mm Hg*					
EGG	134.0 ± 12.4	125.6 ± 9.4	123.5 ± 14.0	−10.5	
SUB	136.2 ± 15.6	126.2 ± 9.6	126.1 ± 13.9	−10.1	<0.0001
Diastolic BP, *mm Hg*					
EGG	85.3 ± 5.2	77.7 ± 7.4	74.7 ± 7.7	−10.6	
SUB	82.3 ± 8.3	78.5 ± 9.0	77.7 ± 5.6	−4.6	<0.0001

[1] Values are means ± SD, $n = 15$ (EGG) or 13 (SUB). *P*-values are for time effects. There were no differences between groups or interactions in any variable, $P > 0.2$.

TABLE 3 Changes in plasma lipids, the LDL-C:HDL-C ratio, and glucose at baseline, 6 wk, and 12 wk of subjects consuming a CRD in combination with either EGG or SUB[1]

Variable	Baseline	Wk 6	Wk 12	Mean absolute change	*P*-value (Time)
Total cholesterol,[2] *mg/dL*				*unit/12 wk*	
EGG	198.3 ± 42.1	194.5 ± 40.6	202.2 ± 41.8	+3.9	
SUB	188.3 ± 33.7	178.7 ± 33.1	187.3 ± 39.5	+1.0	>0.1
TG,[3] *mg/dL*					
EGG	114.2 ± 49.4	72.7 ± 20.7	70.1 ± 20.8	−44.1	
SUB	126.1 ± 69.4	91.9 ± 31.3	76.7 ± 33.0	−49.4	<0.001
HDL-C,[3] *mg/dL*					
EGG	47.6 ± 15.1[b]	59.6 ± 14.5[a]	57.1 ± 15.1[a]	+12.0	
SUB	50.0 ± 9.7 [b]	49.4 ± 8.8[b]	48.8 ± 8.8[b]	−1.2	<0.01
LDL-C, *mg/dL*					
EGG	127.5 ± 42.2	121.2 ± 40.0	144.3 ± 45.1	+16.8	
SUB	110.8 ± 34.5	107.3 ± 34.4	121.5 ± 42.0	+13.5	>0.1
LDL-C/HDL-C					
EGG	2.27 ± 0.83	1.89 ± 0.75	2.46 ± 1.04	+0.19	
SUB	2.37 ± 1.14	2.23 ± 0.85	2.42 ± 0.78	+0.05	>0.25

[1] Values are means ± SD, $n = 15$ (EGG) or 13 (SUB). There were no diet or interactive effects for any of the variables except for HDL-C. Means without a common letter differ, $P < 0.01$.
[2] To convert to mmol/L, divide by 38.67.
[3] To convert to mmol/L, divide by 88.54.

MetS variables. According to the criteria definition of MetS by the National Cholesterol Education Program ATP III, there were 18 subjects at baseline (58% of total) classified as having MetS. We identified 18 subjects with MetS at the beginning of the study (11 in the EGG and 7 in the SUB group). Following the intervention, only 3 subjects remained in this classification and they were from the SUB group.

Discussion

Increased prevalence of obesity is positively associated with incidence of MetS, cardiovascular diseases, and type II diabetes (17–19). CRD reduce risks for cardiovascular diseases and MetS (3,4), problems that appear to be rapidly increasing in the younger population (20). Dietary cholesterol increases plasma cholesterol in those individuals who are classified as hyper-responders (21,22). However, in this study, we demonstrated that by including eggs as part of a low carbohydrate intervention, the plasma LDL-C concentration did not increase but the plasma HDL-C concentration did increase. Because low concentrations of HDL-C contribute to MetS, this is a very positive aspect of the intervention. To our knowledge, this is the first study to show that dietary cholesterol provided by eggs does not modify the beneficial effects of CRD in MetS. In addition, and considering the importance of HDL-C as a cardiovascular risk marker, these results point to eggs as a preferred food item for a CRD. These results confirm the findings of epidemiological studies where no relationship was found between egg consumption and the risk of coronary heart disease (23,24).

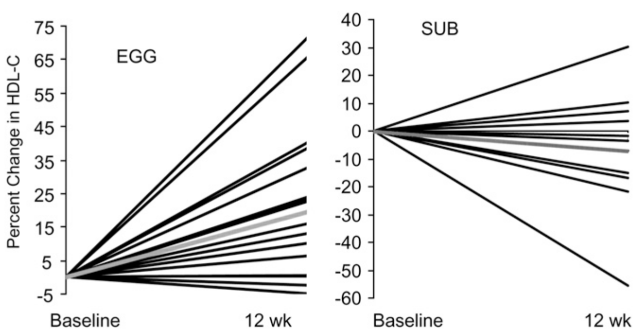

FIGURE 2 Percent changes in plasma HDL-C concentrations from baseline to 12 wk in overweight men who consumed a CRD including 3 eggs (EGG, $n = 15$) or an egg substitute (SUB, $n = 13$). The gray line indicates the mean of each group.

Dietary interventions have been and still are being used as a therapeutic mechanism to improve health status. During interventions with CRD, ad libitum food intake decreases total energy consumption even when energy intake is not restricted (25,26). The percentage of energy contribution from fat increases; however, the absolute amount of dietary fat consumed does not change, resulting in the reduction of total energy intake (4). Both observations were confirmed in this study. In the current study, the overall fat percent contribution increased from 39.6% at baseline to 55.6% at the end of wk 12. However, the absolute intake did not change throughout the study. The contributions of carbohydrate and protein to the diet were different at the end of the study compared with baseline. Carbohydrate intake was greatly reduced, whereas protein intake increased. These changes seem to be consistent with most of the studies following CRD (6). However, dietary cholesterol increased only in the EGG group. The absence of a dietary cholesterol increase in the SUB group might be explained by the fact that subjects were consuming daily a substantial portion of a cholesterol-free food (egg substitute), which very likely replaced the intake of other cholesterol-rich foods.

Due to CRD, body weight, WC, and trunk fat percent in all subjects were reduced independent of their groups. These favorable outcomes are not surprising, because it has been repeatedly shown that CRD can improve these variables (25–28). Independent of dietary intervention, weight loss is usually associated with beneficial overall health status (6,29). It is also clear that some diets present more benefits than others. Moreover, CRD can result in beneficial changes in plasma lipids even in the absence of weight loss (30). Regarding anthropometric measures, WC is a risk factor (31) that is considered a better predictor for MetS than BMI (32–34). CRD result in significant and preferential reduction of trunk fat (6) and hence WC. This was supported by the results in this study where the DEXA scan showed an overall fat reduction in the trunk area.

BP is another parameter used in the classification of MetS and cardiovascular disease risks (7). Both systolic and diastolic BP were significantly reduced in these subjects. We previously showed the reduction in systolic BP with CRD, with no changes in the diastolic BP (35). This study supports the previous findings of Yancy et al. (36) and of Shah et al. (37). CRD have been shown to reduce plasma TG concentrations and increase HDL-C concentrations (4,25). Studies from our laboratory have shown that in a normal weight maintenance diet, ~30% of the subjects undergoing a cholesterol challenge may show a significant increase in both plasma LDL-C and HDL-C (hyper-responders) concentrations, whereas those subjects classified as hypo-responders do not have increased cholesterol carried by LDL or HDL (11,12,28). In this study, carbohydrate restriction or weight loss seemed to have overridden this effect given that all of the subjects in the EGG group responded to the cholesterol challenge with an increase in plasma HDL-C without a change in LDL-C.

The beneficial effects of CRD on plasma lipids were not modified by the additional cholesterol consumed by the EGG group, because plasma TG was significantly reduced in both dietary groups. In contrast to other studies using CRD, subjects consuming the SUB did not increase HDL-C. An explanation for this observation is the reduction in consumption of other cholesterol-containing foods in subjects eating the high-protein SUB.

In summary, we have confirmed in this study that CRD improve all parameters related to MetS, including plasma lipids, fasting glucose, WC, and BP to the extent that 84% of the subjects who were originally classified as having MetS were no longer classified as such following the dietary intervention. We have also shown in this study that a challenge of dietary cholesterol during a weight loss intervention involving CRD does not alter the positive effects of a CRD on features of MetS but rather plays a major role in the positive effects on plasma HDL-C concentrations.

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