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The Effects of a Plant-Based Diet with Eggs on the Parameters of Metabolic Syndrome, Insulin Resistance, and Dietary Choline and Carotenoids

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Abstract

Objective: Plant-based (PB) diets have been shown to positively affect the parameters of Metabolic Syndrome (MetS). The addition of eggs, which are rich in choline and carotenoids, could also complement the beneficial effects of PB diets by increasing HDL-C and improving the other parameters of MetS.

Methods: Twenty-four subjects with MetS completed this 13-week randomized, controlled, crossover clinical trial. Following a 2-week run-in period where subjects followed a lacto-vegetarian diet, subjects were randomly allocated to consume 70g of spinach with either 2 whole eggs or the equivalent amount of egg substitute. At the end of 4 weeks, subjects underwent a 3-week washout period before switching to the alternate diet. Anthropometric measurements, blood pressure, and plasma lipids and glucose were assessed at the beginning and end of each intervention period and after the wash-out. Plasma concentrations of insulin and insulin resistance were collected at calculated following completion of the study.

Results: Plasma insulin concentrations and insulin resistance were slightly higher after the SUB phase compared to EGG phase and baseline, but the differences were non-significant. For the parameters of MetS, body weight and BMI were significantly reduced ($p<0.05$) following the EGG phase compared to baseline, but not following the SUB phase. HDL-C was also significantly higher following the EGG phase ($p<0.05$) compared to baseline and the SUB phase. Dietary carotenoids were significantly higher ($p < 0.025$) after both treatments compared to baseline. The EGG phase resulted in highest choline intakes ($p<0.025$).

Conclusions: The inclusion of eggs in a plant-based diet increased dietary intake of choline, reduced dyslipidemias, and resulted in better weight loss outcomes for individuals with MetS.

1. Introduction

Metabolic Syndrome (MetS) is a cluster of conditions including elevated waist circumference, dyslipidemia (i.e., high triglycerides and low HDL-C), hypertension, hyperglycemia; together, these factors represent a fivefold increased risk for the development of type 2 diabetes (T2D) and a twofold increased risk for cardiovascular disease [1,2]. Based on available NHANES data, the prevalence of MetS in the U.S. has been relatively steady, with a small decrease in 2017-2018 to 38.3% from 39.9% the previous year [3].

As a key regulator of glucose metabolism, defective insulin signaling and its associated pathways are detrimental towards health. In healthy individuals, pancreatic beta cells increase insulin supply in response to peripheral demand from the liver, muscles, and adipose tissue in a tightly regulated negative feedback loop [4]. In insulin-resistant individuals, insulin production steadily increases until the pancreatic beta cells are unable to fully compensate for decreased insulin sensitivity, ultimately leading to the hyperglycemia observed in some individuals classified with MetS. Chronic, low-grade inflammation is a hallmark of many chronic conditions such as T2D, CVD, obesity, and MetS. Unlike acute inflammation, which is caused by infection/injury and is resolved promptly, low-grade inflammation persists and is the result of cellular adaptation to prolonged stress on tissues [5,6]. Clinically, inflammation can be measured by analyzing serum levels of pro-inflammatory factors such as TNF-alpha, IL-6, MCP-1, and C-reactive protein (CRP).

Despite being a rich source of high-quality protein, fat-soluble vitamins, choline, and other micronutrients, the public discourse surrounding egg intake remains controversial due to their cholesterol content, in spite of studies that demonstrate the favorable effect that eggs have on lipoprotein profiles [7,8,9]**.** Moreover, a growing body of research suggests that dietary cholesterol (from eggs or other sources) does not correspond to an elevated risk for CVD development in healthy individuals, nor does it play a significant role in plasma cholesterol levels [10,11].

As a precursor of CVD and other chronic diseases, the recommended treatment(s) are aggressive lifestyle interventions such as incorporating more physical activity and implementing healthy dietary changes. Plant-based diets, which are characterized by ample consumption of plant foods and reduced consumption of animal products (e.g., MedDiet, DASH, lacto-ovo vegetarian, etc.), have been shown to positively affect all MetS parameters; previous studies have demonstrated the effectiveness of plant-based diets in weight loss [12,13,14] as well the management of dyslipidemias [14,15], hypertension [14,16], and hyperglycemia-associated insulin resistance [12,17].

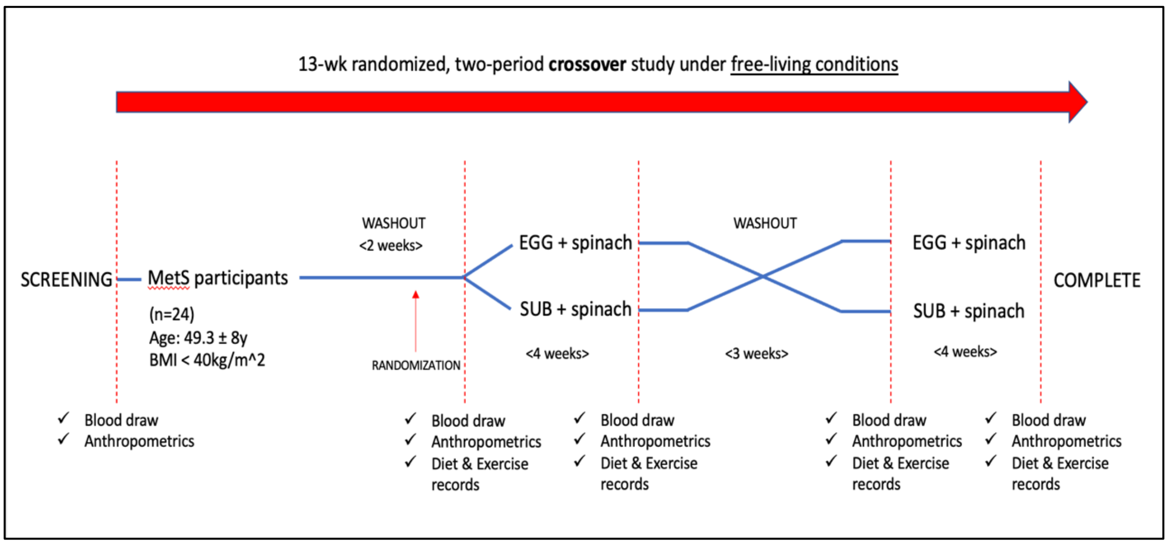
The purpose of project was to ascertain whether the addition of eggs in a lacto-vegetarian diet would result in significant improvements in fasting insulin levels, insulin resistance, and the parameters of MetS compared to a plant-based diet without eggs. We hypothesized that the inclusion of the eggs would effect these changes in part due to increased dietary intake of choline and carotenoids.

2. Materials & Methods

2.1 Experimental Design

The intervention design is depicted in Figure 1. Twenty-four men and women classified with MetS according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria [18] were recruited to participate in this 13-week randomized, controlled two-period crossover clinical trial. According to NCEP-ATP III criteria, MetS is classified when three of the following conditions are met: WC ≥102cm (men), WC ≥88cm (women); blood pressure (BP) ≥ 135/85 mmHg; HDL-C <40 mg/dL (men) or HDL-C <50 mg/dL (women); triglycerides (TG) ≥150 mg/dL; fasting blood glucose (FBG) ≥100 mg/dL. Other inclusion criteria for participation include an age range of 35-70 years old and a willingness to follow a plant-based diet. The following individuals were excluded from the study: 1—individuals with liver disease, renal disease, diabetes, cancer, history of stroke, or heart disease; 2—individuals taking glucose-lowering drugs/supplements; 3—individuals with plasma triglycerides > 500 mg/dL, glucose > 126 mg/dL, or total cholesterol > 240 mg/dL; 4—individuals with blood pressure > 145/100 mmHg; 5— individuals with egg allergy or spinach intolerance.

Figure 1. Cross-over intervention scheme



Following a 2-week washout period with no egg or spinach consumption, participants were randomly allocated to consume 70 grams of spinach with either 2 whole eggs or the equivalent amount of egg substitute at breakfast for the four week treatment period. After the first treatment period, participants underwent a 3-week washout before crossing over to the opposite treatment for the remainder of the study. A total of 5 blood draws (including initial screening for eligibility) were taken following each wash-out and treatment period. Outside of egg/substitute and spinach provision, the study was conducted under free-living conditions with no restrictions on energy intake.

2.2 Dietary and Exercise Records

Participants were asked to complete and return 3-day diet and exercise records for each wash-out and intervention period in order to assess compliance. Diet records were analyzed using Nutrition Data System for Research (NDSR) software, and total nutrient reports were averaged after each phase of the study.

2.3 Anthropometric Measurements and Plasma Biomarkers

Height, weight, and waist circumference were measured at each participant visit following each phase of the study. Height (cm) was measured using a stadiometer, weight (kg) was measured with a digital scale, and waist circumference was recorded using a tape measure over the iliac crest and/or navel. Blood pressure was measured using an automatic blood pressure machine. Anthropometric measurements and blood pressure readings were all recorded three times for an average value. Plasma total cholesterol (TC), HDL-C, triglycerides (TG), glucose, and liver enzymes were measured using a COBAS c-111 analyzer. Plasma LDL-C was calculated using the Friedewald equation: LDL-C = TC – HDL-C – (TG)/5.

2.4 Plasma insulin and insulin resistance

Plasma insulin was measured using a solid-phase sandwich Enzyme-Linked Immunosorbent Assay (ELISA), which used specific antibodies to capture insulin and the chromogenic substrate necessary for detection by a plate reader. Each sample was assessed in duplicate, and plasma insulin was assessed at baseline and following each treatment period. Insulin resistance was approximated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) formula: fasting insulin (mU/L) * fasting glucose (mg/dL)/405.

2.5 Statistical Analysis

Repeated measures ANOVA was used to analyze plasma lipids, glucose, CRP, liver enzymes, insulin, and insulin resistance. A paired t-test was used to evaluate differences in the dietary records between the EGG and SUB phases.

3. Results

3.1 Dietary Components

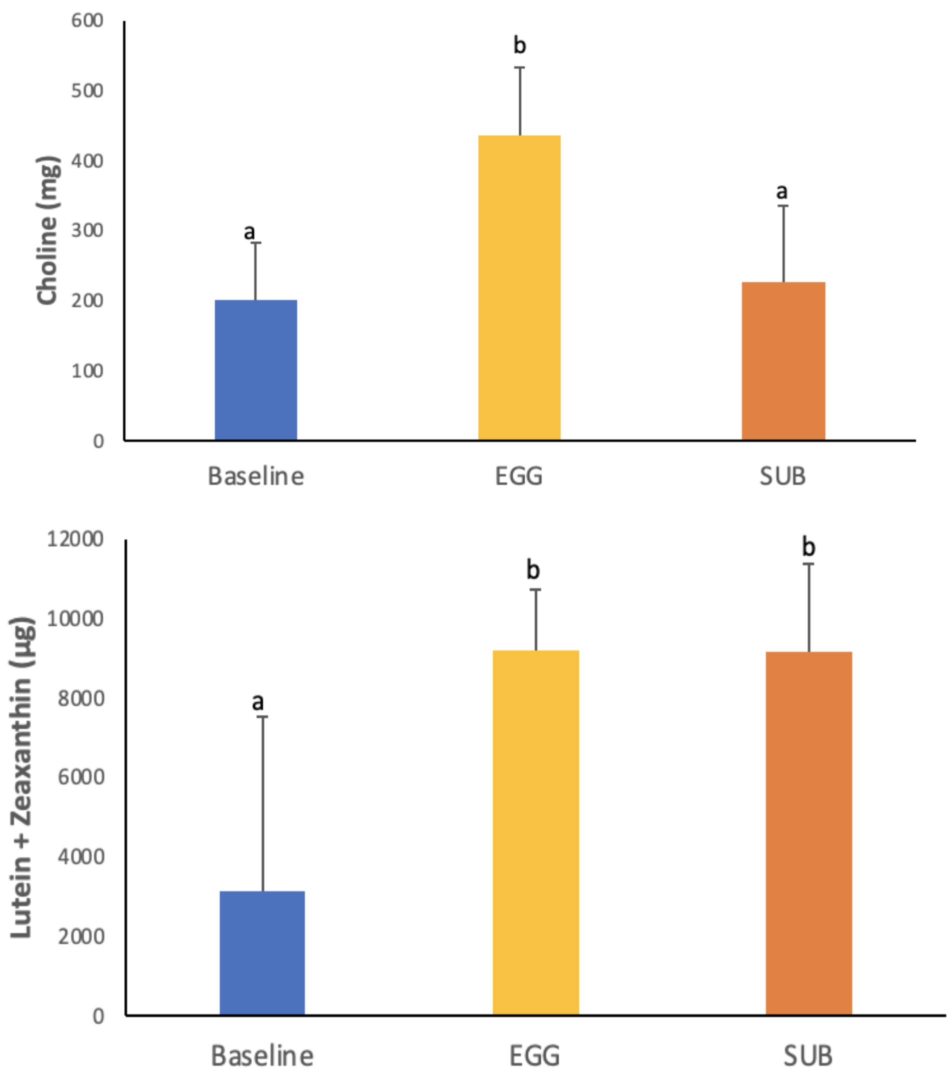
Compared to the SUB treatment, the EGG phase resulted in significant increases ($p<0.025$) in dietary choline. Both the SUB and the EGG phases increased dietary intake of carotenoids compared to baseline ($p<0.025$), however there was no significant difference between the EGG and SUB phase.

Table 1. Mean dietary intake of various nutrients at baseline and post intervention with EGG and SUB. Values in the same row with different superscripts are significantly different a $p < 0.025$.

Dietary Component	Baseline	EGG	SUB
Energy (Kcal)[2]	1677 ± 573^{a}	1798 ± 579^{a}	1699 ± 512^{a}
Total fat (%)	35.6 ± 6.5^{a}	40.9 ± 7.2^{b}	35.4 ± 6.4^{a}
Total CHO (%)	49.6 ± 4.7^{a}	43.7 ± 7.7^{b}	47.1 ± 7.9^{ab}
Total Protein (%)	13.3 ± 3.0^{a}	14.8 ± 2.9^{b}	15.4 ± 2.8^{b}
SFA (g)	21.8 ± 2.8^{a}	29.2 ± 1.3^{b}	24.2 ± 11.2^{ab}
MUFA (g)	23.5 ± 9.3^{a}	28.6 ± 10.9^{b}	23.4 ± 9.1^{a}
Cholesterol (mg)	102 ± 86^{a}	438 ± 135^{b}	143 ± 115^{a}
Omega-3 fatty acids (g)	1.6 ± 0.7^{a}	2.0 ± 0.9^{b}	2.0 ± 0.7^{b}
Added sugars (g)	45.7 ± 36.2^{b}	32.4 ± 30.0^{a}	32.0 ± 21.2^{a}
Beta-Carotene (µg)	4084 ± 2890^{a}	6357 ± 2527^{b}	7684 ± 3387^{b}

Lutein + Zeaxanthin (µg)	3151 ± 4382^{a}	9190 ± 1527^{b}	9179 ± 2188^{b}
Choline (mg)	200.7 ± 82.9^{a}	436.0 ± 96.9^{b}	226.7 ± 109.4^{a}
Vitamin A (µg)	1207 ± 538^{a}	1643 ± 493^{b}	1748 ± 640^{b}
Vitamin D (µg)	3.3 ± 2.3^{a}	5.4 ± 2.3^{c}	4.3 ± 1.7^{b}
Selenium (µg)	78.6 ± 38.9^{a}	106.6 ± 29.4^{b}	101.0 ± 29.3^{b}

Figure 2. Dietary choline and carotenoids (lutein + zeaxanthin) at baseline and after interventions. The EGG breakfast resulted in highest intakes of choline ($P < 0.025$) as indicated by different superscripts. Dietary lutein + zeaxanthin increased significantly after both interventions compared to baseline ($P < 0.025$) as indicated by different superscripts.



3.2 Anthropometrics and Plasma Biomarkers

Waist circumference and blood pressure remained relatively constant over the course of the study. Body weight, and consequently BMI, significantly decreased following the EGG phase compared to the SUB phase. TC, LDL-C, TG, glucose, and liver enzymes remained constant throughout the study. In terms of plasma lipids, the only significant result was the increase in HDL-C following the EGG phase ($p < 0.05$).

Table 2. Mean anthropometric measurements and plasma biomarkers at baseline and post intervention with EGG and SUB. Values in the same row with different superscripts are significantly different at $p < 0.05$.

Parameter	Baseline	EGG	SUB
Body Weight (kg)	99.4 ± 19.6 ^{b}	98.5 ± 19.2 ^{a}	99.6 ± 20.1 ^{b}
BMI	34.3 ± 4.8 ^{b}	33.8 ± 4.6 ^{a}	34.7 ± 4.6 ^{b}
WC (cm)	112.5 ± 11.9	113.4 ± 13.3	113.3 ± 12.7
Diastolic BP (mm Hg)	86.6 ± 5.6	86.2 ± 8.4	86.7 ± 6.6
Systolic BP (mm Hg)	183.0 ± 27.6	185.3 ± 29.0	179.1 ± 24.6
HDL-C (mg/dL)	42.1 ± 10.3 ^{b}	43.3 ± 10.7 ^{a}	41.5 ± 10.1 ^{b}
Triglycerides (mg/dL)	155 ± 68	149 ± 58	156 ± 66
LDL-C (mg/dL)	109.9 ± 26.6	112.3 ± 25.9	108.1 ± 19.8
LDL/HDL ratio	2.75 ± 0.88	2.72 ± 0.77	2.72 ± 0.73
Glucose (mg/dL)	103 ± 12	93 ± 11	92 ± 9
CRP (mg/dL)	0.25 ± 0.24	0.40 ± 0.57	0.27 ± 0.26
ALT (U/L)	29.42 ± 21.32	28.71 ± 13.84	29.42 ± 21..32
AST (U/L)	23 ± 7.7	23.88 ± 8.16	22.38 ± 7.63

Figure 3. Body weight was lower after the EGG treatment (P < 0.05) as indicated by different superscripts. Thus, BMI was also lower after the EGG treatment (P < 0.05) as indicated by different superscripts.

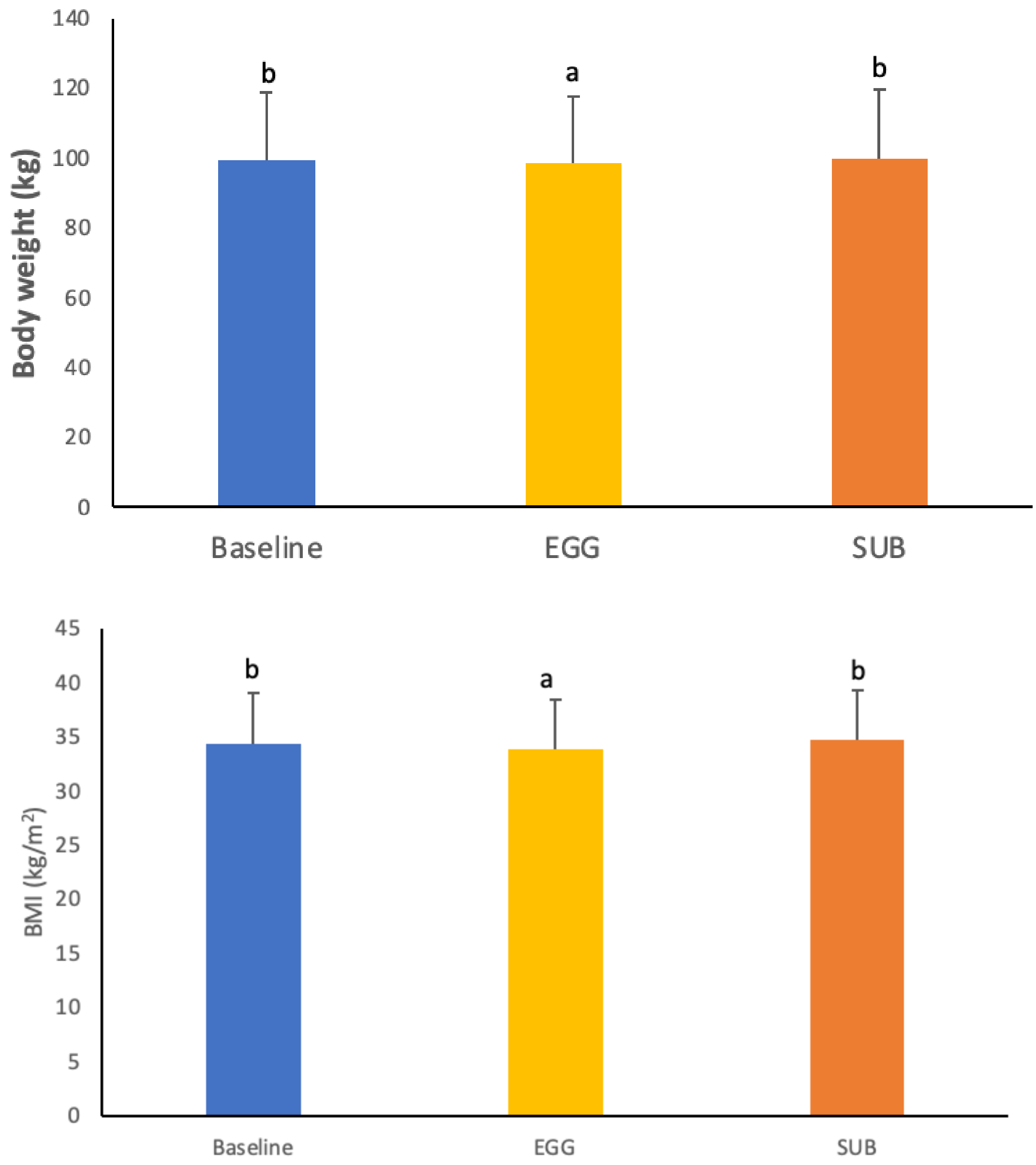
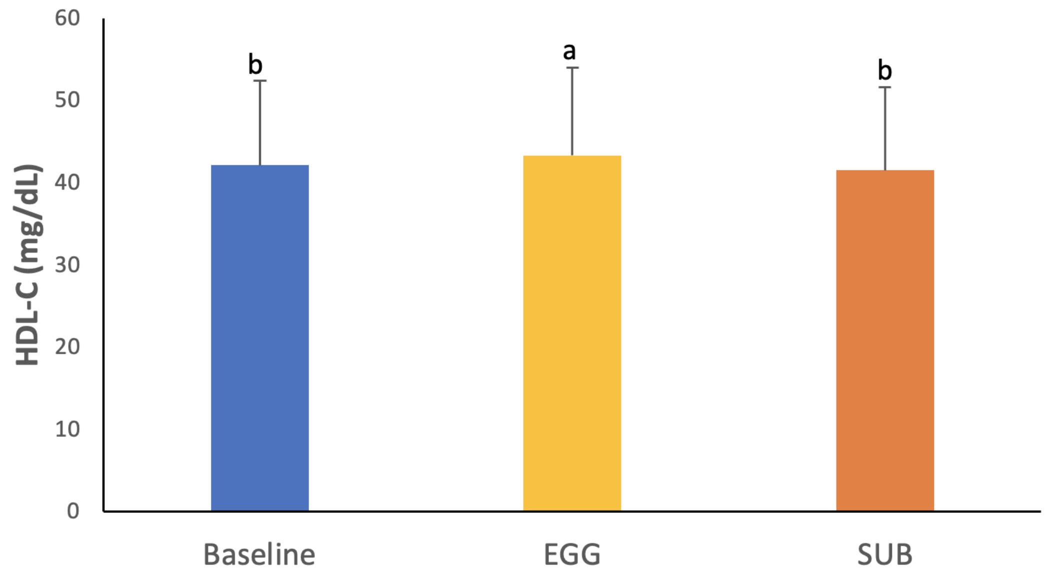


Figure 4. Concentrations of HDL-C at baseline and after interventions. The EGG breakfast resulted in higher concentrations of HDL-C ($P < 0.05$) as indicated by different superscripts.



3.3 Plasma Insulin and Insulin Resistance

Plasma insulin concentrations were slightly higher after the substitute phase compared to the egg phase and to baseline, and there were no differences in plasma concentrations between baseline and the egg phase. However, none of these differences were statistically significant. Similarly, insulin resistance remained constant between baseline and the egg phase and was the highest following the substitute phase, but the results were not significant.

Table 3. Mean fasting insulin concentrations and insulin resistance (HOMA-IR) at baseline and post intervention with EGG and SUB.

Parameter	Baseline	EGG	SUB
Insulin (pmol/L)	67.68 ± 34	67.45 ± 34.9	71.27 ± 39.2
Insulin Resistance (HOMA)	2.62 ± 1.5	2.62 ± 1.5	2.71 ± 1.6

Figure 5. Fasting plasma concentrations of insulin at baseline and post intervention with EGG and SUB.

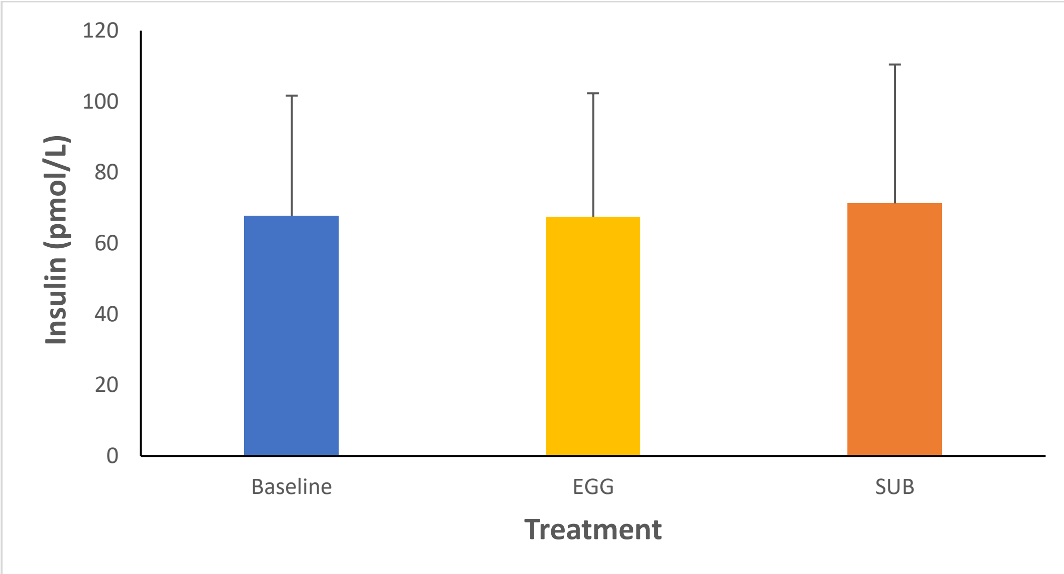
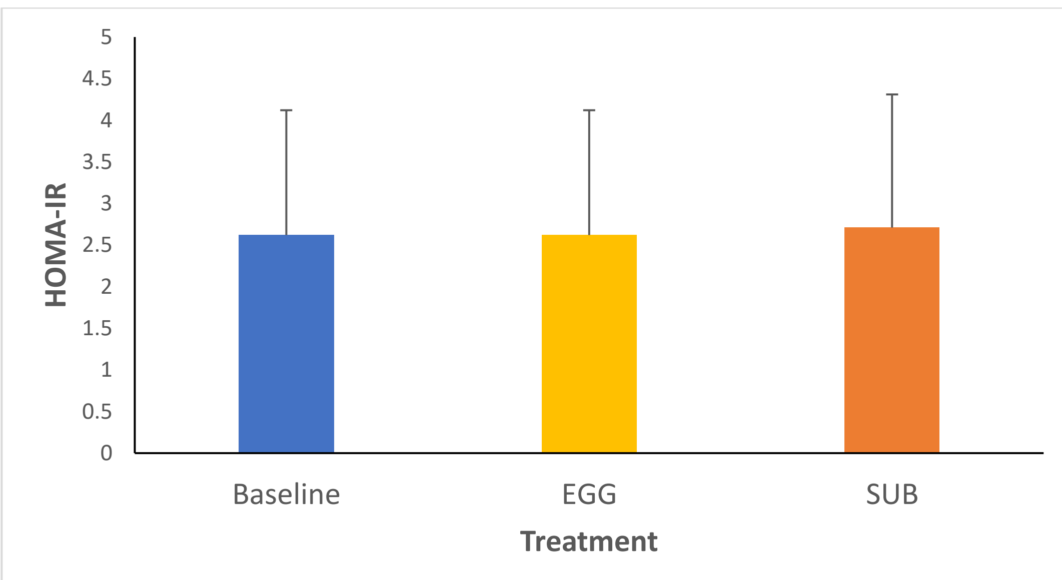


Figure 6. Insulin resistance (HOMA-IR) at baseline and post intervention with EGG and SUB.



4. Discussion

We hypothesized that the inclusion of 2 eggs per day in a plant-based diet would significantly increase dietary intake of choline and carotenoids compared to a plant-based diet without whole eggs. We also hypothesized that whole egg intake would result in increased HDL cholesterol, which would then correlate with improvement in the other parameters of MetS.

We observed that compared to the egg-substitute breakfast, whole egg intake significantly increased dietary choline, while dietary carotenoids increased in both interventions compared to baseline. Regarding the parameters, HDL-C was significantly higher and body weight was significantly lower following the EGG phase compared to both baseline and following the SUB phase. Based on previous studies [19] and contrary to what we hypothesized, there were no observable differences in fasting insulin levels or insulin resistance, which may be in part due to the powerful effects of the plant-based diet, which subjects followed for the entire duration of the study. Some studies have shown that the replacement of SFA in a typical diet with more MUFA/PUFA (mono- and poly- unsaturated fatty acids) can improve insulin sensitivity [20,21,22]

In the context of MetS and the progression into more serious disease, body weight is relevant in that a buildup of excessive abdominal fat gives rise to the mobilization and ectopic deposition of metabolically active fatty acids to the rest of the body [23]. This impacts all the parameters of MetS: pancreatic beta cell dysfunction related to insulin resistance, an increase in the secretion of TG-rich by the liver, and the consequent decrease in HDL-C. The inverse relationship between HDL-C concentrations and atherosclerosis is supported by multiple lines of evidence, in large part due to the role that HDL particles play in reverse cholesterol transport and cholesterol efflux [24]. While HDL-C can serve as a biomarker for CVD risk, the functions of HDL may be more important than HDL-C when evaluating disease risk. Although this project focuses on plasma concentrations of HDL-C, previous studies have illustrated that whole egg intake has been shown to improve HDL functionality by increasing cholesterol efflux capacity [25,26].

The increases in dietary choline and carotenoids are both promising, as choline and carotenoids both play significant roles in cardiovascular and overall health. As an essential nutrient, choline is critical for a wide range of functions in the body, including cell structure integrity, cell signaling and neurotransmitter synthesis [27]. In addition to the crucial role of lutein and zeaxanthin in the maintenance of eye health, some studies suggest that lutein is able to protect against atherosclerosis and LDL oxidation [28,29], while choline from eggs in particular has been shown to protect against inflammation [30,31]. When LDL is oxidized, the altered particle is no longer recognized by the LDL receptor and remains in circulation where it is eventually recognized by the body's macrophages as a foreign substance. When the oxidized LDL is taken up by the macrophage, the subsequent formation of a foam cell precipitates the formation of atherosclerotic plaque. Preventing these oxidative processes and the inflammatory responses that follow are an important antiatherogenic strategy.

5. Conclusion

In conclusion, the inclusion of eggs in a plant-based dietary pattern increased intake of choline and carotenoids, increased circulating levels of HDL-C, and resulted in better weight loss outcomes for individuals classified with Metabolic Syndrome. To strengthen the findings from this study, future investigations should analyze plasma or serum concentrations of the aforementioned nutrients and examine other characteristics of HDL particles related to functionality.

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