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Understanding potential mechanisms linking low-fat diet to inflammation and metabolic syndrome

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Dear Editor-In-Chief,

We thank Dr. Kawada for his interest and comments regarding our recent publication on low-fat diet and C-reactive protein (CRP)¹ and welcome the opportunity to respond.

In our study, results showed that change in CRP was significantly greater in the low-fat diet group compared with the exercise group, but only in women classified with metabolic syndrome¹. The positive effects of a low-fat diet on inflammation were not found in men overall, women overall, men with or without the metabolic syndrome, or in women without the metabolic syndrome¹.

We agree with Dr. Kawada that dietary intake may be important for reducing inflammation, though the exact physiological mechanism relating low-fat diet to CRP is poorly understood. Increased intake of dietary fat can induce a pro-inflammatory profile increasing circulating levels of cytokines such as IL-6 and TNF- α ². Consumption of n-3 polyunsaturated fatty acids, a type of fat common in low-fat foods, can inhibit cytokine release directly from the endothelium in a vascular model of atherosclerosis³. The lower levels of cytokines may result in lower circulating CRP levels. Low-fat foods also may simultaneously change macronutrient intake and quality⁴. Individuals who consume low-fat diets also tend to increase intake of fruits, vegetables and whole grains⁴. Increased fruit and vegetable consumption can induce anti-inflammatory effects which may also lower CRP levels⁵. Meals that cause a rise in insulin and epinephrine output are associated with higher levels of CRP⁶. IL-6 release is also hypothesized to be stimulated by the amount of insulin and catecholamine in the bloodstream⁷. Thus, meals that limit the increase in postprandial glucose may also reduce levels of cytokines and CRP in the bloodstream⁸. In fact, consumption of meals which limit the rise in insulin and glucose, such as low glycemic diets, reduce CRP levels⁹. Our study does not allow us to comment if any of these potential mechanisms played a role in our results. Future studies are needed to elucidate the mechanism linking low-fat diet to inflammation.

Institution where work was done: University of Maryland, College Park, Kinesiology, School of Public Health

Conflicts: No conflict of interest to report

IRB approval: Stanford University Medical School (intervention and data collection) and University of Maryland (CRP and metabolic syndrome analyses)

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Dr. Kawada suggests that the possible explanatory physiological mechanism linking low-fat diet and CRP may be through obesity. If the low-fat diet from our research did promote a change in CRP through obesity, then changes in obesity (or body composition – namely adipose tissue) would be expected to predict the change in CRP. Our analysis included the covariate for percent body fat change. Results showed that the change in body fat was not a significant predictor for change in CRP in men, women, or in men and women with or without metabolic syndrome. Interestingly, women without metabolic syndrome did lose a significant amount of body fat in the low-fat diet group (–1.7%), but without any significant changes in CRP. In contrast, women with metabolic syndrome in the low-fat diet group had significant changes in CRP, but without significant reductions in body fat (–0.6%). Thus, results from a randomized controlled trial suggest that the link between low-fat diet and inflammation is not mediated through obesity per se.

In contrast to our results, Dr. Kawada's research in older habitually active women did not show a relationship between inflammation and metabolic syndrome. However, it is important to compare the overall sample characteristics and methodologies. Dr. Kawada's women were habitually active at least 1 day/week for the past 5 years, approximately 66 years of age, with CRP levels of 0.43 mg/L. Our women with metabolic syndrome were not habitually active at baseline, were approximately 10 years younger (~58 years of age), and had CRP values 5.5 times higher (~2.4 mg/L). The low level of CRP in Dr. Kawada's sample may explain why he did not observe the same results as ours. Dr. Kawada also speculated that the stratification of our sample by metabolic syndrome status could have been responsible for revealing this relationship. However, Dr. Kawada defined metabolic syndrome using the International Diabetes Federation (IDF) while we utilized the American Heart Association/National Heart, Lung and Blood Institute definition (AHA/NHLBI). It is important to consider that the IDF definition weights elevated waist circumference, a marker of obesity, as the most important component of the metabolic syndrome, whereas AHA/NHLBI weights all components equally. Our sample BMI in women was 26 kg/m², and only 14% of women were classified as obese. Naturally, those with metabolic syndrome did have higher mean BMI (~28 kg/m²). However, it is interesting to note that the two most common cardiovascular risk factors which classified women and men as having the metabolic syndrome were low HDL cholesterol (~98%) and elevated triglycerides (~86%), which is primarily due to recruitment of adults with elevated LDL and low HDL cholesterol. Thus, our sample has a unique metabolic profile, with little established obesity, and the results of our study may not be generalizable. Thus, the characteristics of women between the DEER study and Dr. Kawada's research were very different, as were the methodologies to assess metabolic syndrome. We would like to comment that instead of viewing these results as contrasting, the two studies are rather complementary, as they describe the relationship in two very different groups of women. Future studies are needed to rectify the complex relationship of low-fat diet, inflammation, metabolic syndrome and obesity across women with a range of adiposity and CRP levels.

Sincerely,

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Reference List

1. Camhi SM, Stefanick ML, Ridker PM, et al. Changes in C-reactive protein from low-fat diet and/or physical activity in men and women with and without metabolic syndrome. *Metabolism*. E-Pub: 2009.
2. Nappo F, Esposito K, Cioffi M, et al. Postprandial endothelial activation in healthy subjects and in type 2 diabetic patients: role of fat and carbohydrate meals. *J Am Coll Cardiol* 2002;39:1145–1150. [PubMed: 11923038]
3. De CR, Liao JK, Libby P. Fatty acid modulation of endothelial activation. *Am J Clin Nutr* 2000;71:213S–223S. [PubMed: 10617974]
4. Jenkins DJ, Kendall CW, Marchie A, et al. Direct comparison of dietary portfolio vs statin on C-reactive protein. *Eur J Clin Nutr* 2005;59:851–860. [PubMed: 15900306]
5. Middleton E Jr. Effect of plant flavonoids on immune and inflammatory cell function. *Adv Exp Med Biol* 1998;439:175–182. [PubMed: 9781303]
6. Liu S, Manson JE, Buring JE, et al. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. *Am J Clin Nutr* 2002;75:492–498. [PubMed: 11864854]
7. McCarty MF. Low-insulin-response diets may decrease plasma C-reactive protein by influencing adipocyte function. *Med Hypotheses* 2005;64:385–387. [PubMed: 15607574]
8. Clifton PM. Diet and C-reactive protein. *Curr Atheroscler Rep* 2003;5:431–436. [PubMed: 14525675]
9. Wolever TM, Gibbs AL, Mehling C, et al. The Canadian Trial of Carbohydrates in Diabetes (CCD), a 1-y controlled trial of low-glycemic-index dietary carbohydrate in type 2 diabetes: no effect on glycated hemoglobin but reduction in C-reactive protein. *Am J Clin Nutr* 2008;87:114–125. [PubMed: 18175744]