analysis. There is a possibility that dietary factor would relate to PAI-1 or hs-CRP via obesity, which can be speculated by the stratification of MetS presented by Camhi et al [1].

In parallel to clarify the significance of inflammation and coagulation factors to insulin resistance and MetS, dietary factor is indispensable to know the effect of lifestyle factors on systemic vascular marker and the component of MetS.

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Potential mechanisms linking low-fat diet to inflammation and metabolic syndrome

To the Editor:

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 syndrome [1]. 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 women without the metabolic syndrome [1].

We agree with Dr Kawada that dietary intake may be important for reducing inflammation, although the exact physiologic mechanism relating low-fat diet to CRP is poorly understood. Increased intake of dietary fat can induce a proinflammatory profile, increasing circulating levels of cytokines such as interleukin-6 and tumor necrosis factor−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 atherosclerosis [3]. The lower levels of cytokines may result in lower circulating CRP levels. Low-fat foods also may simultaneously change macronutrient intake and quality [4]. Individuals who consume low-fat diets also tend to increase intake of fruits, vegetables, and whole grains [4]. Increased fruit and vegetable consumption can induce anti-inflammatory effects, which may also lower CRP levels [5]. Meals that cause a rise in insulin and epinephrine output are associated with higher levels of CRP [6]. Interleukin-6 release is also hypothesized to be stimulated by the amount of insulin and catecholamine in the bloodstream [7]. Thus, meals that limit the increase in postprandial glucose may also reduce levels of cytokines and CRP in the bloodstream [8]. In fact, consumption of meals that limit the rise in insulin and glucose, such as low-glycemic diets, reduces CRP levels [9]. 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.

Dr Kawada suggests that the possible explanatory physiologic 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 percentage body fat change. Results showed that the change in body fat was not a significant predictor for change in CRP in men, in 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 d/wk for the past 5 years and were approximately 66 years of age, with CRP levels of 0.43 mg/L. Our women with metabolic syndrome were not necessarily 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, whereas we used the American Heart Association/National Heart, Lung, and Blood Institute definition. It is important to consider that the International Diabetes Federation definition weights elevated waist circumference, a marker of obesity, as the most important component of the metabolic syndrome, whereas the American Heart Association/National Heart, Lung, and Blood Institute definition weights all components equally. Our sample body mass index in women was 26 kg/m^2, and only 14% of women were classified as obese. Naturally, those with metabolic syndrome did have higher mean body mass index (~28 kg/m^2). However, it is interesting to note that the 2 most common cardiovascular risk factors that classified women and men as having the metabolic syndrome were low high-density lipoprotein cholesterol (~98%) and elevated triglycerides (~86%), which is primarily because of the recruitment of adults with elevated low-density lipoprotein and low high-density lipoprotein 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 (Diet and Exercise for Elevated Risk) 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 2 studies are rather complementary, as they describe the relationship in 2 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.

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