Abbott Vascular, Medtronic, CSI, St. Jude Medical, and Boston Scientific; and is on the advisory boards of Abbott Vascular, Medtronic, and Philips. Dr. Moses is a consultant for Boston Scientific and Abiomed. Dr. Kirtane has received institutional research grants to Columbia University from Boston Scientific, Medtronic, Abbott Vascular, Abiomed, St. Jude Medical, Vascular Dynamics, and Eli Lilly. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Deepak Bhatt, MD, MPH, served as Guest Editor-in-Chief for this paper. James B. Young, MD, served as Guest Editor for this paper.

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Role of Adiponectin

Important or Null?

Mechanick and colleagues (1) described recent information about adipokine effects on the cardiovascular system. We already discussed that adiponectin plays an important role in metabolic and cardiovascular homeostasis, and circulating adiponectin levels might act as a biologic marker by having insulin-sensitizing, anti-inflammatory, and antioxidant effects (2,3). With regard to the potential association of adiponectin with clinical outcomes, longitudinal studies have indicated that hypoadiponectinemia is an important risk factor for atherosclerosis, and that hypoadiponectinemia is independent of traditional cardiovascular risk factors, including hypertension and diabetes.

In contrast, Borges et al. (4) investigated the causal effect of adiponectin on coronary heart disease (CHD) risk by performing a Mendelian randomization study using data from genome-wide association studies consortia. Findings from the liberal approach (including variants in any locus across the genome) indicated a protective effect of adiponectin that was attenuated to the null after adjustment for known CHD predictors. Therefore, this study does not seem to support a causal role of adiponectin levels in CHD etiology. It is used by the most updated technique. Furthermore, several recent papers have suggested that high adiponectin levels are linked to unfavorable patient outcomes, particularly in older adult populations (5). What is the clinical meaning of these studies? Unfortunately, this aspect has not yet been investigated much; therefore, further studies in this field should be investigated.

Recently, a high-throughput screening assay was developed to determine adiponectin secretion modulators in 3T3-L1 adipocytes. These compounds could be useful drug candidates for cardiometabolic disorders. Such tools might be applicable to screening for other adipokine modulators that could be useful for the treatment of other conditions.

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REPLY: Role of Adiponectin

Important or Null?

We thank Dr. Koh for these comments that point to examples of discrepant data pertaining to adiponectin's role in cardiometabolic disease. We also have a primary research interest in adiponectin and have shown that it can contribute to both vascular and metabolic disease components (1). Regarding vascular disease, it has a direct action on macrophages to inhibit lipid accumulation and foam cell formation when exposed to oxidized low-density lipoprotein (2,3). In adipose tissue, it acts as an autocrine and/or paracrine factor to increase insulin sensitivity, augment lipid storage capacity, and decrease the