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EDITORIAL COMMENT

Oxidative stress and high-density lipoprotein cholesterol: Cause or consequence?

Stress oxidativo e colesterol de lipoproteínas de alta densidade – causa ou consequência?

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Atherosclerosis is a common underlying cause of cardiovascular disease (CVD). The American Heart Association reported that the prevalence of atherosclerosis is expected to increase by 18% by 2030.[1] Dyslipidemia, characterized by high levels of lipids (cholesterol, triglycerides, or both), is one of the main risk factors for atherosclerosis.[2] However, a low level of high-density lipoprotein cholesterol (HDL-C) is considered an independent risk factor for CVD.[3] Low HDL-C levels are inversely associated with cardiovascular risk and are a critical risk factor for estimating the 10-year risk of CVD.[3] Nevertheless, the relevance of HDL-C as an independent CVD risk factor when other lipids are normal is unclear. The atheroprotective properties of HDL-C include its ability to mediate macrophage cholesterol efflux, antioxidant and anti-inflammatory properties, and nitric oxide promoting activity.[4] However, HDL particles are complex and heterogeneous in composition and function, and HDL-C level may not be an independent modifiable and causal CVD-specific risk factor.[4] Additionally, naturally or pharmacologically induced high HDL-C was not associated with reduced CVD risk.[3,5,6]

As mentioned, HDL-C has antioxidant properties. Oxidative stress is defined as an imbalance between antioxidant factors and the production of reactive oxygen species (ROS) in favor of the latter, which results in oxidative damage.[7] Oxidative stress is thought to play a part in the pathogenesis of atherosclerosis, and HDL-C can potentially slow the development of atherosclerosis. Assessment of total antioxidant capacity (TAC) and total oxidant status (TOS) has been used to assess oxidant and antioxidant systems since, biologically, overall oxidant status may be more appropriate than the measurement of a single antioxidant. Moreover, the oxidative stress index (OSI), defined as the TOS/TAC ratio, as an indicator of oxidative stress, reflects the balance between oxidant and antioxidant agents.[7]

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These oxidative stress parameters are studied by Karabacak et al. in an analysis published in this issue of the *Journal*.[8] Their study aimed to analyze the favorable effects of HDL-C on the oxidative stress of patients with different HDL-C levels. The authors compared patients with low and high HDL-C and a group of matched controls with normal HDL-C, analyzing several oxidative stress parameters (TAC, TOS, OSI, total thiol levels, and arylesterase [ARES] activity). The authors reported that ARES activity and total thiol levels were significantly higher in patients with high HDL-C compared to those with low HDL-C. At the same time, TAC, TOS, OSI, uric acid, and gamma-glutamyltransferase were higher in low HDL-C patients.[8]

Establishing connections between known risk factors is a promising tool for identifying important molecules or signatures to improve current clinical biomarkers used for risk assessment, stratification, and therapeutic approaches. The study by Karabacak et al.[8] presents some limitations, which are acknowledged by the authors, the most important being the small sample size, single-center data, and a single time point of assessment. Overall, this paper contributes to knowledge improvement by showing a relationship between oxidative stress and low HDL-C, highlighting the correlation between these modifiable risk factors. A future follow-up study of these patients may help us to better understand the impact of the relationship between oxidative stress and low HDL-C and the role it plays as a risk factor for CVD.

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Conflicts of interest

The author has no conflicts of interest to declare.

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