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Editorial

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High-Density Lipoprotein Cholesterol Efflux Capacity as a Surrogate Marker for Major Cardiac Adverse Events in Japanese Patients

Tomohiro Komatsu[1, 2, 3] and Yoshinari Uehara[1, 2, 3]

[1]Research Institute for Physical Activity, Fukuoka University, Fukuoka, Japan
[2]Faculty of Sports and Health Science, Fukuoka University, Fukuoka, Japan
[3]Center for Preventive, Anti-aging and Regenerative Medicine, Fukuoka University Hospital, Fukuoka Japan

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Low cholesterol level in high-density lipoprotein (HDL) particles has been widely believed as an independent risk factor for cardiovascular diseases (CVDs). In contrast, HDL-increasing drugs such as cholesteryl ester transfer protein inhibitors failed to produce favorable outcomes for preventing CVDs[1]. Moreover, it has been recently indicated that high HDL cholesterol (HDL-C) level was associated with CVDs in Japan[2] and with all-cause mortality in other countries[3]. These findings make it difficult to understand the role of HDL despite the extensive knowledge from basic and clinical studies.

HDL has several functions, including antiatherosclerotic, anti-inflammatory, and antioxidant effects[4]. One of the most important HDL functions, the HDL cholesterol efflux capacity (CEC), is defined as the ability to mediate macrophage cholesterol efflux from atherosclerotic plaques and is also the most promising factor for the protective role in atherosclerosis. Initially, it was reported that CEC was related to an increased risk for CVDs and atherosclerosis in a clinical study, independent of the HDL-C level[5]. The most recent meta-analysis also demonstrated the inverse relationship between CEC and CVDs[6]. These findings have changed our belief that HDL CEC was important rather than HDL-C level **(Fig. 1)**.

In this context, Hisauchi and colleagues showed for the first time that the role of CEC in coronary artery disease onset would be a clinical prognostic maker for future major cardiac adverse events (MACE) in Japanese patients[7]. Therefore, this study investigated the importance of CEC, especially focusing on the secondary prevention of coronary artery disease. Moreover, this study provides the impact finding that CEC is a significant independent predictor of low-density lipoprotein cholesterol level. In addition, higher CEC could be a good protective surrogate even in older age individuals despite the low frequency occurrence of MACE compared with that in Western countries. This study revealed the extensive role of CEC in the prevention of atherosclerosis in CVDs.

In the real-world context, there is a further need to develop various components for CEC and analyze their clinical usefulness. First, it is necessary to unify the CEC expression value to some extent, including the absolute value or modified value. This is because CEC value showed much variation among reports. For instance, the CEC value in human subjects with genetic abnormalities of HDL metabolism, including ATP-binding cassette transporter A1, was expected to be very low, but it was much higher than the value observed in this study, despite using the same method[8]. Second, it is desirable to establish a simple method for determining CEC value because the method applied in this study used a radioactive tracer that could not be available in general laboratory. New simple tests for determining HDL-C efflux without the use of a radioisotope could be a breakthrough we all have been waiting for. Third, it is important to update our knowledge regarding the selection of the patient background for performing CEC tests by incorporating novel information as done in this study. Finally, more discoveries could be expected regarding strategies for upregulating CEC, such as lifestyle changes and drugs.

This study has clarified that a lower CEC value caused by HDL was a useful tool for detecting the

Address for correspondence: Yoshinari UEHARA, Faculty of Sports and Health Science, Fukuoka University, 8-19-1 Nanakuma, Jonan-ku, Fukuoka, 814-0180, Japan E-mail: ueharay@fukuoka-u.ac.jp
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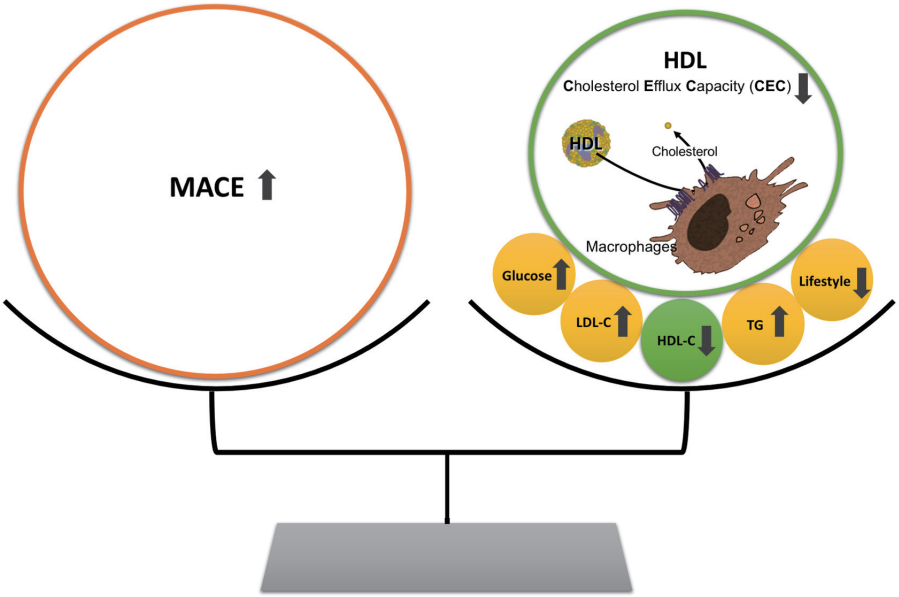

Fig. 1. The relationship between major cardiac adverse events (MACE) and various major factors

future progression of coronary artery disease. Therefore, the novel findings obtained in this study could add significant evidence regarding the importance of CEC for secondary MACE in Japanese patients.

Conflict of Interest

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