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Adequate Control of Low-Density Lipoprotein Cholesterol (LDL-C) for Diabetic and Non-Diabetic Cases

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Abstract

For atherosclerotic cardiovascular disease (ASCVD), adequate control of low-density lipoprotein cholesterol (LDL-C) would be required. Discussion have been found concerning LDL-C borderline as 55, 70 or 100mg/dL by American College of Cardiology (ACC), American Heart Association (AHA) and European Heart Association (EHA). Latest study was reported from PEMA-study with 523 cases of diabetic (n=277) and non-diabetic (n=246). The protocol included the influence of LDL-C on the existence of plaque, using intravascular ultrasonography and near-infrared spectroscopy. As a result, targeting LDL-C <55 mg/dL would be effective for stabilizing plaques in non-diabetic, while it would be less effective in diabetic cases.

Keywords: Atherosclerotic cardiovascular disease (ASCVD); Low-density lipoprotein cholesterol (LDL-C); American College of Cardiology (ACC); American Heart Association (AHA); European Heart Association (EHA); Coronary artery disease (CAD)

Commentary Article

For decades, non-communicable diseases (NCDs) have been crucial medical and social problems worldwide [1]. Concerning their pathophysiology, inflammatory influence and oxidative stress have been observed [2]. Thus, actual clinical practice has included various medical problems of Atherosclerotic cardiovascular disease (ASCVD) [3]. Regarding the management of diabetes, American Diabetes Association (ADA) has announced the standard medical care in Jan 2022 [4]. The latest adequate recommendation of pharmacologic therapy has been also shown [5]. As to cardiology, American College of Cardiology (ACC) and American Heart Association (AHA) has continued the problem of heart failure in the committee [6]. Successively, 2022 AHA/ACC/HFSA guideline for the management of heart failure was presented [7].

For the protection against ASCVD, the concept has been known as lower is better for low density lipoprotein cholesterol (LDL-C). European Society of Cardiology (ESC) recommended the treat-to-target strategy for LDL-C control for <55 mg/dL. It was a treatment goal for related cases at high risk with the secondary prevention of ASCVDs [8]. In contrast, Japanese guideline for the prevention of ASCVDs has shown different target, where the recommended value would be <100mg/dL of LDL-C for secondary prevention [9]. However, it also states that strict target for 70 mg/dL of LDL-C should be considered for high-risk patients. The standard guideline of AHA reveals the recommendation of maximum LDL-C reduction using medical agents with no established target LDL-C levels [10]. Thus, several perspectives have been found for the target value of LDL-C.

Regarding the relationship of LDL-C and cardiovascular events, previous standard data showed that every 1 mmol/L (38.7 mg/dL) of LDL-C reduction can cause 5-year major CV events by 23% [11]. In order to clarify whether strict lowering LDL-C under 70 mg/dL would be effective, secondary prevention was studied [12]. The protocol included 344 cases with previous percutaneous coronary interventions, and patients were categorized into three groups, which are <70 mg/dL, 70-100 mg/dL, and ≥100 mg/dL. After 6 year-follow up, incidence of recurrent acute coronary syndrome (ACS) was significantly lower in the group of <70mg/dL than other two groups with p=0.009 and p=0.001,

respectively. Consequently, LDL-C seemed to be residual risk for recurrent-ACS.

The European Heart Association (EHA) has recently managed to target a stricter value (<55 mg/dL) than the conventional target value for lowering LDL-C (<70 mg/dL) in T2D with a history of developing cardiovascular disease. However, the plaque stabilizing effect of such potent LDL-C therapy has not been fully verified [13]. Then, clinical effect of strict LDL-C control on coronary plaque stabilization would be meaningful for diabetic and non-diabetic patients who have already developed CAD.

From the latest report of ACC, significant study was revealed from the National Cardiovascular Research Center (NCRC), Japan [14]. The enrolled patients were 523 cases of coronary artery disease (CAD), in which non-diabetic and diabetic was 277 and 246 case, respectively. The protocol included the influence of LDL-C on the existence of plaque, using intravascular ultrasonography and near-infrared spectroscopy. The combined investigation enables the visualization of tissue components in coronary plaque and the effectiveness on clarifying calcified components and lipids involved in the plaque instability. This study is from PEMA-CORE study in Japan, which stands for "Effect of PEMAfibrate on COronary plaques and REnal function in patients with cardiovascular disease and elevated fasting triglyceride", trial ID: jRCTs031210067 [15].

As a result, LDL-C value was attained <55 mg/dL in 6.4% of non-diabetic cases. In these non-diabetic cases with successfully strict LDL-C control, the presence of coronary plaque and calcification was rare. It suggests that strict LDL-C control would show effective management for stabilizing coronary plaque. In contrast, Type 2 diabetes (T2D) cases showed 13.0% patients achieved LDL-C <55mg/dL. Unlikely to non-diabetic cases, T2D cases showed that coronary plaques were rich in lipid components with mild calcification, even if the cases were under strict LDL-C control. From these results, targeting LDL-C <55 mg/dL would be effective for stabilizing plaques in non-diabetic cases, while it would be less effective in diabetic cases. Consequently, continuing LDL-C control cannot necessarily bring protection of CAD, because the vulnerable plaques may be present [14].

In the current report, vulnerable plaques which cause AMI still existed in T2D cases even continuing strong LDL-C control. T2D always includes some risk factors that bring arteriosclerosis such as hypertension, obesity and dyslipidemia. It is often accompanied by low HDL-C, high TG, and elevated oxidative/inflammatory stress. Consequently, it seems to be rather difficult to maintain stabilizing efficacy to plaque with only LDL-C intervention. Further, these results suggest the required strategies for LDL-C and also other risk factors in the case of T2D. Recently, hypertriglycemia has been in focus for a residual risk in T2D [14]. The intervention for high TG is expected to bring efficacy for preventing plaque development in T2D.

The PEMA-CORE research group by NCRC has continued specific investigation to verify the development and stabilization effect of the plaque. This clinical trials include joint research in 42 multi-centers, and will proceed the project for the purpose of establishing effective preventive strategy for T2D. Concerning statins on serial coronary calcification, 8 prospective randomized trials were conducted [16]. The study included the study of calcium indices (CaI) and percent atheroma volume (PAV) for three groups of high-intensity statin therapy (HIST), low-intensity statin therapy (LIST), and no-statin therapy. As a result, statins would promote coronary atheroma calcification, without the dependence of plaque-regressive effects. Previous studies showed that LDL-C control in our real life has been suboptimal in primary and secondary pretension [17]. Then, adherence for recommended guideline would be critical through adequate decision-making of patients and clinicians. It is accompanied with individual preferences, values, comorbidities and current situations.

In summary, various advances have been found as to cardiovascular events, such as coronary plaque imaging, risk stratification, hemodynamic factors and lipid monitoring [18]. Multi-modal imaging, high-risk plaque features and patient-oriented management would be crucial for future direction.

Conflict of Interest

The authors declare no conflict of interest.

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