Editorial

Current management of cholesterol for atherosclerotic cardiovascular disease (ASCVD) in clinical medical practice

Hiroshi BANDO[1,2]

Medical Research[1] / Tokushima University[2], Tokushima, Japan

Editorial

In recent years, lifestyle-related diseases and metabolic syndrome have been increasing due to changes in people's lifestyles [1]. They include obesity, diabetes, hypertension and dyslipidemia, and a particularly important point would be the prevention of arteriosclerosis [2]. Especially, elevated values of low-density lipoprotein cholesterol (LDL-C) and glycosylated hemoglobin (HbA1c) have been known to become risk factors for atherosclerotic cardiovascular disease (ASCVD) [3]. Consequently, control of cholesterol profile has become essential for coronary heart disease.

From personal life point of view, the regular healthy lifestyle would be basically necessary for managing lipids problems [4,5]. Even if a person has some genetic increased risk for cholesterol, one can reduce the risk level by half degree associated with continuing adequate lifestyle [6]. For obtaining healthy lipid profile, maintaining optimal levels of body weight, blood glucose and physical activity would be beneficial as well as reducing of intake of refined carbohydrates and simple sugars [7,8]. After these recommended healthy strategies were tried, pharmacotherapy would be considered.

Historically speaking, it was the Framingham Heart Study that has identified cholesterol as one of the risk factors for coronary heart disease [9]. After that, there have been lots of papers and randomized clinical trials (RCTs), in which elevated LDL-C would be a major factor to ASCVD [10]. Consequently, beneficial managements for lipid profile have included the predominant target of apolipoprotein B, LDL-C, non-HDL-C and triglyceride (TG) [11].

Recently, there were some guidelines for clinical management for lipids. The American College of Cardiology–American Heart Association (ACC–AHA) published the guideline in 2018 [8]. Successively in the next year, it presented the guidelines for primary prevention of cardiovascular disease. Both have shown the recommendations for evaluation of risk factors and adequate management of lipid profile [5]. By utilizing these guidelines, physicians can give preferable management of lipid profile for clinical prevention of ASCVD.

From these situations mentioned above, this article introduces some hints and tips that will help clinicians in their daily medical practice. It cannot cover everything, but most common five suggestions are described.

Firstly, LDL-C is recommended to be reduced. The direct relationship has been reported between LDL-C value and the risk of atherosclerotic cardiovascular disease [12]. Then, there has been the recommendation that can simply describe "lower is better". As to the value of LDL-C, each 39 mg/dL

decrease would reduce cardiovascular events by 22% and overall mortality by 10% [13]. Furthermore, not only the conventional upper limit of LDL but also the reduction percentage has been described in recent guidelines [13]. It has been meaningful for the present of a linear correlation between LDL-C and cardiovascular risk.

From data of 29069 patients with statin therapy, LDL-C showed 39% of reduction without a significant change in lipoprotein(a) [14]. As a result, elevated baseline and on-statin lipoprotein(a) have showed the presence of approximately linear relation with cardiovascular disease risk. Furthermore, the magnitude of event reduction has reported to be proportional to the reduced degree of LDL-C [12,15]. Consequently, both of the degree of absolute risk and reduced ratio of LDL-C achieved have been important.

Secondly, physician will talk with the patient about the risk factors and show the risk for the next 10 years [13,16]. When boundary value is found, coronary artery calcium (CAC) score could be also performed and calculated. Risk factors for ASCVD include the following: high blood pressure, diabetes, smoking, pre-eclampsia, early menopause, rheumatic disease, HIV infection, family history of young coronary artery disease, South Asian ancestry, chronic kidney disease (CKD), elevated triglyceride, ankle-brachial index (ABI) <0.9, high sensitivity C-reactive protein (CRP) > 2mg/L, high lipoprotein (a) and high apolipoprotein B .

Calculating the risk of ASCVD (ACC / AHA, next 10 years) requires age, gender, race, T-cho, HDL-C, SBP, DBP, hypertension treatment, history of diabetes and smoking. The possible estimated age ranges 40-75 years old. Value of LDL-C must be maintained during 70-190 mg / dL [13,16].

Thirdly, there are strong recommendations for diabetes and previous cardiovascular disease [13]. The guideline recommends statin therapy for patients 40-75 years with LDL-C more than 69 mg/dL who have diabetes or a 10-years risk of ASCVD equal to or greater than 7.5% [13]. Similarly, additional considerations should be made for younger or older adults. Medical staff calculates patient's 10-year risk of ASCVD, and then risk assessment can be individualized by considering any risk-enhancing factors [13]. The patient's CAC score would be measured, if the situation is possible.

Fourthly, key points from the 2018 ACC-AHA guidelines were described in scheme for everyone to understand easily and well [13]. It includes a) promote a healthy lifestyle, b) share decision making with the patient, c) determine candidates for pharmacotherapy, d) adopt a personalized approach and e) monitor responses to treatment and lifestyle.

There are several important managements in the part c) as follows: i) reduce LDL-C level by >= 50% with high-intensity statin for clinical ASCVD, ii) prescribe high-intensity statin (up to highest tolerated dose) and consider addition of nonstatin if needed for severely elevated LDL-C, iii) prescribe moderate-intensity statin and consider reducing LDL-C by >= 50% in diabetic patients at high risk, iv)   reduce LDL-C by >= 30% for 10-yr risk of ASCVD >= 7.5% (or >= 50% if 10-yr risk >= 20%) [13].

Finally, a science advisory from the AHA has published the latest comments [17]. Among them, there are several key points about the relationship between dietary cholesterol and cardiovascular risk: a) previous guideline has eliminated specific dietary cholesterol target recommendation, then its role for CVD has been evaluated, b) a variety of meat contribute 42% of the total cholesterol intake, eggs 25%, and other food groups about a third, c) observational studies with 250,000 subjects from 1980-2012 have not shown the association between dietary cholesterol and CVD risk, and similarly egg intake is not associated with CVD risk, d) most observational studies of cholesterol intake on CVD risk are limited in value, and randomized controlled diet interventions showed a dose-response relationship, where every 100 mg/day increase in dietary cholesterol predicted an LDL-C increase of 1.90-4.58 mg/dl depending on the model, e) heart-healthy dietary patterns (Mediterranean-style and DASH-style diets) have a relatively high ratio of PUFA to saturated fatty acid and are low in cholesterol with typical menus. They are characterized by fruits, vegetables, whole grains, low-fat or fat-free dairy products, lean protein sources, nuts, seeds, and vegetable oils [17].

In summary, this article described current topics concerning the medical issues between cholesterol and ASCVD in the light of standard guideline. Furthermore, some related matters such as heart-healthy dietary patterns were also introduced. Author expects this report would become some reference in actual clinical practice.

Key words
cholesterol profile, low-density lipoprotein cholesterol (LDL-C), atherosclerotic cardiovascular disease (ASCVD), The American College of Cardiology–American Heart Association (ACC–AHA), coronary artery calcium (CAC) score
Abbreviation
low-density lipoprotein cholesterol (LDL-C), atherosclerotic cardiovascular disease (ASCVD), The American College of Cardiology–American Heart Association (ACC–AHA), coronary artery calcium (CAC) score

REFERENCES

[1] Bando H (2019) Adequate management for various problems of geriatric syndrome in elder diabetic patients. MOJ Gerontol Ger. 4(6):265–267. DOI: 10.15406/mojgg.2019.04.00218

[2] American Diabetes Association (2019) Standards of Medical Care in Diabetes 2019. Diabetes Care 42(Suppl. 1):S1–S193

[3] Boytsov S, Logunova N, Khomitskaya Y (2017) Suboptimal control of lipid levels: results from the non-interventional Centralized Pan-Russian Survey of the Undertreatment of Hypercholesterolemia II (CEPHEUS II). Cardiovascular Diabetology, 16(1). doi:10.1186/s12933-017-0641-4

[4] Eckel RH, Jakicic JM, Ard JD, et al. (2014) 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 129: Suppl 2: S76-S99.

[5] Arnett DK, Blumenthal RS, Albert MA, et al. (2019) 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 74: 1376-414.

[6] Khera AV, Emdin CA, Drake I, et al. (2016) Genetic risk, adherence to a healthy lifestyle, and coronary disease. N Engl J Med 375: 2349-58.

[7] Brinton EA (2015) Management of hypertriglyceridemia for prevention of atherosclerotic cardiovascular disease. Cardiol Clin 33: 309-23.

[8] Grundy SM, Stone NJ, Bailey AL, et al. (2019) 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 73: 3168-209.

[9] Kannel WB, Dawber TR, Kagan A, Revotskie N, Stokes J III (1961) Factors of risk in the development of coronary heart disease — six-year follow-up experience: the Framingham Study. Ann Intern Med 55: 33-50.

[10] Cholesterol Treatment Trialists' (CTT) Collaboration (2010) Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet 376: 1670-81.

[11] Cholesterol Treatment Trialists' (CTT) Collaboration (2012) The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 380: 581-90.

[12] Ference BA, Ginsberg HN, Graham I, et al. (2017) Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies: a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J 38: 2459-72.

[13] Michos ED, McEvoy JW, Blumenthal RS (2019) Lipid Management for the Prevention of Atherosclerotic Cardiovascular Disease. N Engl J Med 381(16): 1557–1567. doi:10.1056/nejmra1806939

[14] Willeit P, Ridker PM, Nestel PJ, Simes J, Tonkin AM, Pedersen TR, et al. (2018) *Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. The Lancet.* doi:10.1016/s0140-6736(18)31652-0

[15] Koskinas KC, Siontis GCM, Piccolo R, et al. (2018) Effect of statins and non-statin LDL-lowering medications on cardiovascular outcomes in secondary prevention: a metaanalysis of randomized trials. Eur Heart J 39: 1172-80.

[16] Thanassoulis G, Gregoire J, Pearson GJ (2019) The 2018 ACC/AHA Lipid Guidelines: A Little More or Less Canadian? Canadian Journal of Cardiology 35(5), 558–563. doi:10.1016/j.cjca.2019.03.003

[17] Carson JAS, Lichtenstein AH, Anderson CAM, Appel LJ, Kris-Etherton PM, Meyer KA, et al. (2020) Dietary Cholesterol and Cardiovascular Risk: A Science Advisory From the American Heart Association. Circulation. 2020;141:e39–e53. doi.org/10.1161/CIR.0000000000000743