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NON-HDL CHOLESTEROL AND EVALUATION OF CARDIOVASCULAR DISEASE RISK

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Abstract
Cardiovascular disease (CVD), such as coronary heart disease (CHD), is the most frequent cause of death worldwide, especially in developed countries. The latest recommendations of European and American Cardiological Associations emphasize the role of non-HDL cholesterol (non-HDL-C) in evaluating the risk of CVD. Although this parameter has a lot of advantages, it is rarely used by general practitioners in lipid profile assessment.

The aim of this article is to present the recent informations on the usage of non-HDL-C in the primary prevention of cardiovascular disease and to compare its diagnostic value to traditional and new CVD risk factors.

INTRODUCTION

According to WHO's data from 2004 cardiovascular disease is the cause of death of over 17 million people worldwide [1]. Most often CVD is manifested in the form of coronary heart disease (CHD), myocardial infarction and stroke. The main cause of their development is atherosclerosis which is a chronic inflammatory disease of the arteries. Atherosclerotic plaques formation and pathological remodeling of vascular walls consequently lead to impaired tissue perfusion and ischemia. Many studies have shown that cholesterol is one of the key component of atherosclerotic plaques, therefore hyperlipidemia is considered as an essential risk factor for atherosclerosis [2, 3].

USE OF LIPID PROFILE IN THE ATHEROSCLEROSIS RISK ASSESSMENT

The basic laboratory exponent of cardiovascular risk is the elevated concentration of total cholesterol (TC) which mostly results from elevated LDL cholesterol (LDL-C) [4, 5]. Modified LDL particles, especially their oxidized forms (ox-LDL) may be freely taken up by macrophages whose scavenger receptors combine with apolipoprotein B100 (apoB). Subsequently arising foam cells form the fatty infiltrates in the artery walls which are the starting point for plaques [6,7].

LDL-C concentration reflects only the amount of cholesterol contained in LDL particles but does not provide information about their number and structure. In addition, LDL-C does not include the participation of other lipoprotein fractions (Lp (a), VLDL) that are essential in the development of atherosclerosis. LDL-C value is usually calculated with the Friedewald formula whereas this method has some limitations, predominantly hypertriglyceridemia [8]. It was shown that LDL-C is estimated with approximately 17% and 25% error at serum triglyceride concentration (TG) from 151-200 mg/dL and 201-300 mg/dL, respectively. Therefore apoB, the main protein of potentially atherogenic lipoproteins, seems to be a more reliable indicator. Clinical studies proved that apoB concentration highly correlates with the number of LDL particles, including small dense LDL (sd-LDL), having particularly strong atherogenic properties. Elevated apoB is considered one of the best prognostic factors of acute coronary events and deaths due to CVD [9, 10]. Nevertheless, determination of apoB requires the use of suitable methods and yet is not widely applied in routine laboratories.

NON-HDL CHOLESTEROL (NON-HDL-C) AS A RISK FACTOR FOR CARDIOVASCULAR DISEASE

Modern laboratory diagnosis of lipid disorders and cardiovascular risk should be based on the use of indicators which present full impact of all plasma lipid components involved in atherogenesis. Non-HDL-C is the sum of cholesterol accumulated in all lipoproteins, except HDL, such as: chylomicrones, VLDL and their remnants, IDL, LDL and Lp(a) [11]. The concentration of non-HDL-C is calculated using a simple equation:

non-HDL-C (mg/dL) = TC – HDL-C

Actually, little attention is being paid to the use of non-HDL-C but the latest Guidelines for both European and American Cardiological Societies emphasize the importance of this parameter for assessing the risk of atherosclerosis and coronary heart disease. Non-HDL-C concentration, as recommended by the NCEP Adult Treatment Panel III, should be higher by about 30 mg/dL than LDL-C (Table 1). Non-HDL-C is considered as the second, after the LDL-C goal of CVD therapy in patients with hypertriglyceridemia and should be calculated routinely in the lipid profile [12].

Table 1. LDL-C and non-HDL-C goals in three CHD risk groups by NCEP ATPIII (12)

Risk category	LDL-C (mg/dL)	non-HDL-C (mg/dL)
CHD and CHD risk equivalent (10-years CHD death risk >20%)	**<100**	**<130**
Multiple (≥ 2) risk factors (10-years CHD death risk <20%)	**<130**	**<160**
0-1 risk factor	**<160**	**<190**

The usefulness of non-HDL-C in the prevention of CVD was confirmed in numerous clinical trials. Liu et al. compared the diagnostic value of non-HDL-C as a prognostic factor of acute coronary events and myocardial infarction among healthy subjects and diabetics [13]. It was found that increased level of non-HDL-C by 1 mg/dL increases the risk of death due to cardiovascular disease by 5% and seems to be a better predictive indicator than the traditional lipid risk factors. Significantly higher concentrations of non-HDL-C and higher relative risk of coronary events among patients with diabetes were observed and the risk in particular grade levels of non-HDL-C was 1.5 to over 2.5 times higher in diabetics than in healthy subjects.

Ruminska et al. evaluated the usefulness of non-HDL-C in the lipid disorders in children and adolescents with simple obesity [14]. Patients with elevated non-HDL-C (> 123 mg /dL) had significantly higher values of waist circumference and serum TC, LDL-C, TG, TC: HDL-C, TG: HDL-C and lower HDL- C.

The impact of elevated TG levels in the calculation of LDL-C with the Friedewald formula suggests that non-HDL-C is beneficial in determining the risk of atherosclerosis and CVD in patients with hypertriglyceridemia [15]. It might be an important estimate for diseases such as diabetes and obesity, in which excessive triglyceride values increase the concentration of sd-LDL and decrease HDL-C. Numerous studies including Health Professionals Follow-up Study, Safari and the Copenhagen City Heart Study [16, 17, 18] indicated that non-HDL-C correlates better with apolipoprotein B100 than LDL-C and its diagnostic value as a risk factor is similar or as high as apoB.

The role of non-HDL-C in predicting and reducing CVD risk in patients treated pharmacologically due to dyslipidemia is noteworthy. In a meta-analysis of lipid-lowering therapies a 1:1 correlation between the 1% non-HDL-C lowering and CHD risk reduction by lipid-modifying drugs was observed [19]. Thus, not only lowering LDL-C, but also non-HDL cholesterol is an important goal of prevention and treatment of cardiovascular diseases.

Currently available clinical data describe the relationship between the concentration of non-HDL-C and methods of imaging of atherosclerosis. The effect of serum lipids on the process of coronary arteries calcification (CAC), regarded as an early marker of subclinical atherosclerosis was described in recent study by Orakzai et al. [20]. Of all lipid parameters, only the non-HDL-C showed a significant association with the process of atherogenesis. The Bogalusa Heart Study proved a relationship between the value of non-HDL-C in childhood and risk of cardiovascular disease in adulthood [21]. A strong association between non-HDL-C, denoted at the age of 5-17 years and the intima-media thickness (IMT) in carotid artery in adults was documented. Kawamoto et al observed excessive IMT value and CHD risk with the increasing non-HDL-C values in patients over 65 years old [22].

CONCLUSIONS

There is still much controversy about the use of non-HDL cholesterol in routine clinical/laboratory practice. Despite the numerous advantages it is not possible to exclude a higher diagnostic value of apolipoprotein B100 and apoB:apoAI ratio in the primary CVD prevention [23, 24]. Estimated non-HDL-C value, combined with apolipoproteins, hsCRP and LDL particle number (LDL-P) assessment is suggested to be the most optimal solution [25]. In summary, based on the available data, the use of a simple non-HDL-C calculation in a lipid profile testing, complemented by determination of the new risk factors, will allow a better assessment of the CVD risk.

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