Analysis of low-density lipoprotein in diabetic patients using the Martin/Hopkins and Sampson equations

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Dear Editor,

We read with great interest the article: Comparison of Novel Martin/Hopkins and Sampson Equations for Calculation of Low-Density Lipoprotein Cholesterol in Diabetic Patients. The study compared the Martin/Hopkins (LDL-Cmh), Sampson (LDL-Cs), and Friedewald (LDL-Cf) equations with directly obtained low-density lipoprotein (LDL-Cd). The aim was to analyze which would have a greater agreement with LDL-Cd in diabetic patients and investigate how these new equations could change clinical decision-making compared to LDL-Cf.[1]

It is already established in the literature that low-density lipoprotein (LDL-c) is strongly associated with cardiovascular diseases (CVD), and patients with diabetes mellitus (DM) are at increased risk due to the atherogenic capacity that LDL-c promotes, mainly to chronic endothelial damage developed by the hyperinflammatory state of persistent hyperglycemia.[2] Therefore, accurate measurement of LDL-c is essential for the clinical follow-up of these patients.

In the article, the use of LDL-Cmh and LDL-Cs showed a strong correlation with LDL-Cd, not requiring the reclassification of individuals. Both equations were better than LDL-Cf, especially triglyceride (TG) levels > 150 mg/dl. LDL-Cmh had an almost excellent agreement with LDL-Cd in individuals who had TG values between 150-400 mg/dl, requiring only 1.5% of patients to be reclassified when using LDL-Cmh. However, all equations behaved badly when the TG concentration was > 400 mg/dl, allowing only less than 90% of the individuals to be classified correctly. Furthermore, the concordance between LDL-Cd and calculated LDL-c was poor when the LDL-c value was < 70 mg/dl.[1]

The article's authors state that the equations for LDL-Cmh and LDL-Cs showed similar concordance for LDL-Cd. Thus, clinical decision-making should be similar in most patients, regardless of which equation is used. For those individuals with a TG of 150 to 400 mg/dl, LDL-Cmh presented an almost perfect agreement with LDL-Cd, concerning being within the LDL-C target, making it preferable for patients with DM in this range of TG.[1]

However, it was noticed that in the process of obtaining the population sample, even in diabetic patients, the statistical analysis considered only the TG variable on the behavior of agreement, underestimation, and overestimation in the analyzed equations. Therefore, since DM is a chronic, multifactorial process with different clinical presentations and therapeutic approaches, there may have been confounding factors in analyzing the behavior of the equations in diabetic individuals, because the patients were not stratified according to the type of DM, class of antidiabetics used, non-medication and medication adherence, anthropometric parameters, and liver function.

Keywords

Metabolic diseases; Dyslipidemia; Coronary artery disease; Diabetes Mellitus; Lipoprotein LDL

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Reply

Hypercholesterolemia is a primary determinant of atherosclerosis and complications of atherosclerotic disease in patients with diabetes. Correct identification of blood low-density lipoprotein (LDL) concentration is of utmost value to determine the risk of atherosclerosis associated with hypercholesterolemia in such patients. Due to the limited availability of direct measurement of LDL in healthcare centers, laboratories report LDL concentrations using indirect estimation methods. Of those methods, the Friedewald equation is the oldest and remains the most commonly used method to estimate LDL. Our study showed that novel equations were superior to the older Friedewald equation in assessing whether a diabetic patient was within the guideline-recommended LDL cholesterol target. However, the comparative advantage of using either equation over the Friedewald formula was rather minimal, and the risk associated with hypercholesterolemia could be correctly classified in most patients regardless of the equation used.[1,2]

Despite their differences, all three equations use the same variables, namely total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides, to calculate LDL cholesterol. Of those three variables, the total blood cholesterol concentration and the fraction of cholesterol transported by high-density cholesterol are measured directly, and therefore they are not responsible for the variations seen in the indirect calculation of LDL cholesterol. The cholesterol content of very-low-density lipoprotein (VLDL) is variable, and the cholesterol content of VLDL particles is estimated using triglyceride concentrations. The variation of the cholesterol content of VLDL particles is even more pronounced in those with high (i.e., >400 mg/dl) triglycerides, and this variation is responsible for the difference in LDL estimates when different equations are used. We have stratified the patients within different triglyceride strata to understand the performance of equations in patients with low or high triglyceride concentrations, as done in similar studies that analyzed the performance of these equations in different patient populations.[3-5]

While the individual characteristics of diabetic patients, such as the type and severity of diabetes or the number of drugs used, are clinically important, present results should nonetheless be valid regardless of such individual characteristics given that the same blood concentrations of total cholesterol, HDL cholesterol, and triglycerides are used in all three equations. That said, the individual risk of cardiovascular mortality for a given patient is undoubtedly affected by such individual clinical characteristics. However, unfortunately, none of the available risk stratification tools account for all variables associated with cardiovascular mortality risk in patients with diabetes. While this latter concern is a potential source of error, such errors stem from the relative imperfection of available risk stratification tools and are not directly related to our analysis methodology.

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