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SYSTEM BRIEF

Calculated Results on the Cholestech LDX™ Analyzer

LOW DENSITY LIPOPROTEINS

Total cholesterol in blood is distributed among very low density lipoproteins (VLDL), low density lipoproteins (LDL), intermediate density lipoproteins (IDL), high density lipoproteins (HDL) and lipoprotein(a) (Lp(a)). LDL-cholesterol (LDL-C) contains more lipids than protein and carries most of the circulating cholesterol from the liver to various tissues. Because of this, increased LDL-C constitutes a major risk factor for the development of coronary heart disease (CHD). However, IDL and Lp(a) are also important atherogenic particles. Their concentrations can be expected to be higher in patients with CHD and in patients at risk for CHD.[1]

LDL-C has been measured by one of two methods in almost all epidemiological and case control studies that form the basis for the estimates of association between LDL-C concentrations and CHD risk. The first method is beta quantification, which is the recognized reference method for measuring LDL-C. It is not commonly used because it requires an ultracentrifuge to prepare a plasma or serum faction that contains only LDL-C and HDL-C. In this method, the total cholesterol and HDL-C contents of the fraction are measured and the LDL-C is calculated by subtracting HDL-C from total cholesterol.

The second and more practical method utilizes a fasting lipid panel – total cholesterol (TC), HDL-C and triglyceride (TRG) measurements – to obtain a calculated LDL-C. It is calculated using the Friedewald formula as follows:

LDL-C = TC – HDL-C – (TRG/5)

The fasting triglyceride value is divided by 5 to estimate VLDL-C levels. This model is based on the fact that most of the circulating triglyceride is carried by VLDL, the composition of which is relatively constant. The Friedewald formula is generally considered to be valid when triglycerides are below 400 mg/dL.

As mentioned, this second calculated method has been used in various studies that have contributed to the epidemiological database relating LDL-C to CHD risk. Calculated LDL-C has also been used in most clinical trials that form the evidence base for lipid-lowering treatment and is the most widely used LDL-C method in clinical practice. What is commonly regarded today as LDL-C is actually the sum of cholesterol carried by LDL, Lp(a) and IDL particles.

NON-HDL CHOLESTEROL

Non-high density lipoprotein cholesterol (non-HDL-C) is total cholesterol minus HDL-C. It can be measured via the classic lipid profile and does not require fasting measurements. Reducing LDL-C has long been the goal of therapy to prevent CHD. But researchers are finding that other lipoproteins appear to be involved in developing heart disease. These include VLDL and IDL, which also carry non-HDL-C. Non-HDL-C reflects the levels of all of the highly atherogenic fractions: VLDL-C, IDL-C, Lp(a)-C, as well as LDL-C.

Studies have shown that the general category of non-HDL-C is a strong predictor of heart disease in people who have not yet developed signs of heart problems. Non-HDL-C was introduced as a secondary target of treatment in clinical practice guidelines for adults widely used between 2001 and 2013 because it provides the cholesterol content of all the atherogenic lipoproteins.[2]

In the Friedewald formula, VLDL-C is calculated as TRG divided by 5. The therapeutic goal for TRG defined in the 2001 adult guidelines was a value less than 150 mg/dL.[2] Therefore, VLDL-C was recommended to be less than 30 mg/dL (150÷5). Under these guidelines, once the LDL-C goals had been reached, the non-HDL-C was an indicator of whether further treatment was needed in individuals with TRG >200 mg/dL.[2] The non-HDL-C goal was therefore the LDL-C goal plus 30 mg/dL. Under the 2013 cholesterol management guidelines for adults, target levels of LDL-C and non-HDL-C are not utilized.[3] However, 2011 guidelines for cardiovascular health and risk reduction in children and adolescents recommend using non-HDL-C for risk assessment.[4]

FASTING IS NOT A REQUIREMENT

An added advantage of non-HDL-C measurements is that they can be taken even when the individual has eaten. By comparison, LDL-C measurements can be taken only when the individual fasts, as food intake can raise TRG and lower LDL-C. The latest adult guidelines do not include a significant role for measuring non-HDL-C. They do note, however, that non-HDL-C may be an indicator of genetic hypercholesterolemia if measured in individuals that are nonfasting.[3] The pediatric guidelines recommend using nonfasting non-HDL-C for risk assessment for its practicality.[4]

Non-HDL-C rather than LDL-C level may be particularly useful in risk assessment for some specific patient populations. For example, patients with type 2 diabetes have elevations in TRG levels, often making the calculation of LDL-C level by the Friedewald formula potentially inaccurate. One report has suggested that non-HDL-C levels be used as a primary risk assessment tool in patients with diabetes.[5] Non-HDL-C level might also identify a group of individuals who have a genetically influenced atherogenic lipoprotein phenotype, characterized by high VLDL and IDL levels, a low HDL level, and an LDL level within the reference range. About 20% of the American population are estimated to have this phenotype.[6]

TC:HDL-C RATIO

Total cholesterol and HDL-C can be measured in the nonfasting state, with reduced analytical variability.[7] The ratio of total cholesterol to good cholesterol (HDL-C) provides even better information with regard to an individual's risk for heart disease. Despite an apparently normal total cholesterol level, low HDL-C will place an individual at an increased risk. Multivariate analysis of the Framingham Heart Study and the Physician's Health Study demonstrated that the TC:HDL-C ratio is independently related to CHD in elderly men and women.[8] TC:HDL-C ratios are used in principle in Framingham risk assessment scoring. Some experts have suggested that the goal for the ratio is a value less than 4.5.[9]

Clinical practice guidelines do not set any desirable levels or therapeutic targets for the TC:HDL-C ratio, preferring instead that clinicians focus on each lipoprotein fraction separately,[10] or not addressing the ratio at all.[3,4] Many clinicians, however, will focus on the ratio for its simplicity in identifying two powerful components of risk.

LDL-C:HDL-C RATIO

The LDL-C:HDL-C ratio is similar to the TC:HDL-C ratio, in that it integrates a measure of "bad" cholesterol and one of "good" cholesterol into a single parameter. The predictive value of the LDL-C:HDL-C ratio is similar to the TC:HDL-C ratio,[7,8] though it has not been as widely adopted by clinicians. Guidelines do not set any desirable levels or therapeutic targets for the LDL-C: HDL-C ratio.

1. Working Group on Lipoprotein Measurement. National Cholesterol Education Program: recommendations on lipoprotein measurement. NIH Publication No. 95-3044, 1-186. 1995. National Institutes of Health, National Heart, Lung, and Blood Institute.
2. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97.
3. Stone NJ, Robinson J, Lichtenstein AH, Merz CN *et al*. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. Published online before print November 12, 2013.
4. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics 2011;128;S213-S256.
5. Lu W, Resnick HE, Jablonski KA, Jones KL *et al*. Non-HDL cholesterol as a predictor of cardiovascular disease in type 2 diabetes: the Strong Heart Study. Diabetes Care 2003; 26:16-23.
6. Cui Y, Blumenthal RS, Flaws JA, Whiteman MK *et al*. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. Arch Intern Med 2001; 161:1413-9.
7. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. Ann Intern Med 1994; 121:641-7.
8. Castelli WP. Lipids, risk factors and ischaemic heart disease. Atherosclerosis 1996; 124 Suppl:S1-S9.
9. Castelli WP, Abbott RD, McNamara PM. Summary estimates of cholesterol used to predict coronary heart disease. Circulation 1983; 67:730-4.
10. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 1-284. 2001. National Institutes of Health.

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