Calculated Results on the Alere 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 valid when triglycerides are below 400 mg/dL.

As mentioned, this second method has been used in various studies that have contributed to the epidemiological database relating LDL-C to CHD risk. The National Cholesterol Education Program (NCEP) ATP III medical decision points for classification of CHD risk were derived from this database.[2] What is commonly regarded today as LDL-C isactually 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. 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. As a result, the latest version of the NCEP guidelines recommends that doctors first target LDL-C, but also pay attention to non-HDL-C in individuals with high TRG. Non-HDL-C is introduced as a secondary target of treatment because it provides the cholesterol content of all the atherogenic lipoproteins.[2] 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.

In the Friedewald formula, VLDL-C is calculated as TRG divided by 5. The therapeutic goal for TRG is a value less than 150 mg/dL. Therefore, VLDL-C should be less than 30 mg/dL (150÷5). Once the LDL-C goals have been reached, the non-HDL-C is an indicator of whether further treatment is needed in individuals with TRG >200 mg/dL.[2] The non-HDL-C goal is the LDL-C goal plus 30 mg/dL as shown in the table below.

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.

Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for Three Risk Categories[2]

Risk Category	LDL-C Goal (mg/dL)	Non-HDL-C Goal (mg/dL)
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100	<130
Multiple (2+) Risk Factors and 10-year risk ≤ 20%	<130	<160
0-1 Risk Factor	<160	<190

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 level be used as a primary screening tool in patients with diabetes.[3] 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.[4]

TC:HDL-C Ratio

Total cholesterol and HDL-C can be measured in the nonfasting state, with reduced analytical variability.[5] 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.[6] 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.[7]

The NCEP ATP III 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.[8] 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,[5,6] though it has not been as widely adopted by clinicians. The NCEP ATP III guidelines do not set any desirable levels or therapeutic targets for the LDL-C: HDL-C ratio.

References

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