

LIPID TOPICS

by Mark Deeg, MD, PhD

Benefits of Direct LDL Measurement

Calculated LDL

Historically, LDL cholesterol has been calculated from the Friedewald equation, which states:

$$\text{LDL Cholesterol} = \text{Total cholesterol} - \text{HDL Cholesterol} - \text{triglycerides}/5.$$

Since total cholesterol, triglycerides, and HDL cholesterol can be measured, LDL can be calculated. Since there are other cholesterol-carrying lipoproteins in serum, the calculated LDL also includes lipoprotein(a) and intermediate density lipoproteins. Usually, this only adds 5 to 10 mg/dL to the LDL cholesterol.

Unfortunately, once triglycerides exceed 250 mg/dL, the accuracy of the calculated LDL begins to deteriorate and once triglycerides exceed 400 mg/dL (1), LDL cannot be calculated. In addition, the accuracy of calculated LDL is reduced when LDL is less than 100 mg/dL (2).

Direct LDL

Within the last ten years, newer assays have been developed that measure LDL directly rather than calculating it. This test has been called the "direct" LDL or "quantitative" LDL. The first direct LDL test utilized antibodies to recognize LDL and had to be run in a clinical laboratory. Third generation tests of direct LDL methods utilize various means to block or dissolve lipoproteins to isolate LDL cholesterol. There is now a point-of-care test available that determines direct LDL.

Calculated vs. Direct LDL

The biological and analytical variation of both the calculated and direct LDL is 5 to 7%, i.e., the day-to-day variation of both tests is similar.

There are, however, numerous differences between the calculated and direct LDL, most significantly:

- The direct LDL, under most circumstances should be 5 to 10 mg/dL lower than the calculated LDL since the calculated LDL includes intermediate density lipoproteins and lipoprotein(a). If the difference is larger this may indicate the presence of an abnormally high level of intermediate density lipoproteins, which is seen in type III dyslipidemia. Such patients should be referred to a lipid specialist.

- It should be kept in mind that the LDL goals set by the ATP III panel are based upon calculated LDL. Hence, the direct LDL target should be set slightly lower than the ATP III LDL goal based upon the patient's risk for cardiovascular events.
- The direct LDL test is not affected by serum triglycerides. Since LDL cholesterol does not change during the post-prandial state, direct LDL can be measure any time of the day regardless of whether the patient is in the fasting state or not. In addition, new technology has been developed so that direct LDL may be determined rapidly by a handheld device, allowing for point-of-care testing.

Having the direct LDL available as a point of care test allows rapid clinical decision making regarding lipid management without having the patient to have blood testing before or after the office visit and without requiring them to fast beforehand.

- Calculated LDL accuracy is reduced when LDL is less then 100 mg/dL or triglycerides exceed 250 mg/dL. LDL cholesterol can not be calculated when triglycerides exceed 400 mg/dL
- LDL determined by the direct method will be 5 to 10 mg/dL lower than the calculated LDL, and goals shall be set accordingly
- Calculated LDL is influenced by serum triglycerides but direct LDL is not
- Direct LDL can be measured in non-fasting patients

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