

THE VAP[®] CHOLESTEROL TEST AS A REPLACEMENT FOR THE TRADITIONAL LIPID PROFILE

THE ROLE OF THE LIPID PROFILE

The role of cholesterol testing in clinical practice today is twofold: (1) to stratify a patient's risk for cardiovascular disease, and (2) to direct the initiation and titration of lipid-modifying therapy to reduce that risk. Accuracy and comprehensiveness in cholesterol testing are increasingly critical, as target LDLc (low-density lipoprotein cholesterol) levels have been lowered and evidence is uncovered about the important roles of other lipoprotein components in atherogenesis. As a result, routine cholesterol tests are increasingly being replaced by expanded lipid panels such as the VAP (Vertical Auto Profile) Cholesterol Test, which provide more accurate, directly measured LDL and quantify important emerging risk factors and secondary targets of therapy for cardiovascular disease.

LIMITATIONS OF THE ROUTINE CHOLESTEROL TEST

The routine lipid panel, which measures total cholesterol (TC), HDLc (high-density lipoprotein cholesterol), and triglycerides (TG) and calculates LDL, has been shown to have a 40 percent predictive value for coronary heart disease (CHD).¹ This low predictive value is cause for increasing concern among clinicians and is responsible for the fact that 80 percent of patients in the Framingham Study who had a cardiovascular event had routine lipid panels similar to the population that was event-free.² Part of the problem is the inaccuracies inherent in the formula used to calculate LDL.

THE FRIEDEWALD FORMULA

$$\text{LDL-c} = \text{TC} - \text{HDL-c} - (\text{TG}/5)$$

TG/5 represents VLDL-c

(very low-density lipoprotein cholesterol)

This formula was developed by Friedewald in 1972 and is used by labs to calculate LDL from total cholesterol, HDL and triglycerides. The formula, however, is generally agreed to be inaccurate in nonfasting patients and when triglycerides are greater than 400 mg/dL. The model

formula was developed in a population with significant elevations in LDLc. In 1972, for example, "normal" total cholesterol was 300 mg/dL, and only 3 percent of the data set had an LDL less than 100 mg/dL. In contrast, current National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines push LDL to less than 100 mg/dL in many patients — and in very high-risk patients, the LDL goal is less than 70 mg/dL.



Paul Ziajka, M.D., Ph.D.
Director, Florida Lipid Institute

Several key studies demonstrate the inaccuracy of calculated LDL. Marniemi compared Friedewald results with directly measured cholesterol in 1,215 samples in Finland. In this study, 36 percent of patients had an error of greater than 5 percent (underestimation) using the Friedewald formula. This underestimation resulted in 28 percent of patients being classified to the wrong CHD risk category. In addition, the inaccuracy increased dramatically in patients with triglycerides greater than 265 mg/dL.³

Lindsey compared the Friedewald formula with directly measured LDL in 19,343 samples, finding that the calculation underestimated LDLc an average of 19.5 mg/dL, with the error rate increasing as triglycerides increased. A total of 14,665 samples (76 percent) came from patients who had CHD or a CHD-risk equivalent, making their NCEP LDL goal below 100 mg/dL. Of these, 61 percent (8,966) were at goal when the LDL was calculated using the Friedewald formula. However, only 32 percent (4,738) of patients were at goal when LDL was measured directly.⁴

Scharnagl compared the Friedewald calculation with directly measured LDL in 176 patients pre- and post-LDL apheresis, finding biases (underestimations) of 3.8-18.5 percent (see table 1).⁵

In an era of lower LDL goals for high-risk patients, the Friedewald equation is too inaccurate for clinical use. Direct measurement of LDL cholesterol is needed if:

- LDLc is less than 100 mg/dL⁵
- Triglycerides are greater than 200 mg/dL³
- The specimen is from a non-fasting patient
- Patients are at moderate or high risk for CHD

UNCOVERING RESIDUAL RISK

While LDLc is the primary lipid marker for assessing the risk of cardiovascular disease, the NCEP ATP III guidelines state that emerging risk factors should be taken into consideration as optional modifiers of therapy. These include lipoprotein(a) [Lp(a)], LDL pattern density (small, dense Pattern B or large, buoyant Pattern A), HDL subtypes (HDL₂ and HDL₃), VLDL, and intermediate density lipoprotein (IDL). For example, LDLc accounts for only 25 percent of the risk of premature cardiovascular disease.⁶ The remaining 75 percent represents “residual risk” from these additional risk factors. These important components are directly measured by the VAP[®] Cholesterol Test in order to aid clinical judgment in assessing CHD risk, setting accurate LDL goals and determining optimal treatment plans.

The VAP Test uncovers residual risk by identifying:

- “Desirable” LDLc that actually is Pattern B
- “Desirable” LDLc with elevated Lp(a)
- “Desirable” HDLc with low HDL₂
- “Desirable” triglycerides with increased VLDL₃
- “Desirable” triglycerides with low HDL₂

Understanding residual risk is key to both setting the correct target LDL goal and determining the appropriate mix of therapies from among the growing list of available treatment options. It also allows treatment to be tailored to a patient’s specific lipid and lipid subclass abnormalities, increasing the effectiveness of therapy.

TARGETED THERAPY

The VAP Test can be used to direct therapy for lipid disorders, helping physicians decide, for example, which statin would be most effective for a particular patient. Table 2 illustrates statin effects on several VAP Test parameters.

The VAP Test also can point to the need for additional therapies, such as gemfibrozil, nicotinic acid and others, used alone or in combination with statins, to address particular lipid and/or lipid subclass abnormalities and lower CHD risk. For example, a statin plus fish oils (omega-3 fatty acids) or niacin can be used to increase

HDL, lower IDL, shift LDL pattern density from small and dense to large and buoyant, and decrease Lp(a). (For a copy of, “Using VAP[®] Expanded Lipid Testing to Develop Optimal Patient Treatment Plans,” please call 800-719-9807.)

CONCLUSION

The VAP Test provides twice the predictive ability in identifying CHD risk compared with traditional lipid panels. The test offers an affordable means to obtain a direct measurement of LDL cholesterol and identify the residual risk posed by components such as Lp(a), LDL Pattern B, low HDL₂ and others. Knowledge of the effects of lipid-lowering therapies on specific VAP Test parameters also can take the guesswork out of selecting therapeutic agents.

Friedewald LDL	Direct LDL	Bias in Estimated LDL
180	187	-3.8%
135	146	-7.3%
93	109	-14.5%
61	75	-18.5%

Agent	LDL Size	Lp(a)	HDL ₂	HDL ₃
Lovastatin	↑	↑	↑	↓
Pravastatin	↓/↔	↔	↑	↓
Simvastatin	↑	↔	↑↑	↓
Fluvastatin	N/A	N/A	↑	↓
Atorvastatin	↑	↑↑	↓	↓↓
Rosuvastatin	↑↑	↔	↑↑↑	↓↓

References

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- ⁶ Williams RR, Hunt SC, Hopkins PN, et al. Familial dyslipidemic hypertension. Evidence from 58 Utah families for a syndrome present in approximately 12% of patients with essential hypertension. *JAMA.* 1988;259(24):3579-3586.