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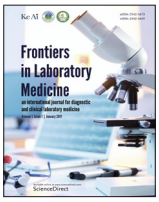

Using the VAP lipid panel for the detection, evaluation, and treatment of patients "at risk" for CAD

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ABSTRACT

In the past several decades, multiple clinical trials have demonstrated the effects of dyslipidemia beyond low density lipoprotein cholesterol (LDL-C) on predicting risk for atherosclerosis and cardiovascular disease. In recent years there has been a proliferation of lipoprotein markers that, when used with LDL-C, help healthcare providers assess risk of patients on the basis of the cardiovascular risk spectrum. In this review, we will discuss some of the important reasons why traditional lipoprotein testing has failed in high risk populations and how unique lipoprotein testing by the Vertical Auto Profile (VAP) Lipid panel is to provide significant clarity to a difficult disease for its management and treatment. We will also discuss some of the new trials that address newer markers of risk that have robust outcomes even after adjusting for traditional cardiovascular disease risk factors.

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The VAP Lipid Panel is a comprehensive assessment for patients at risk for Coronary Artery Disease (CAD) and metabolic syndrome. This recommendation rests on the inadequacy of the ordinary lipid panel to identify patients at risk for myocardial infarction,[1] and similarly, the inadequacy of fasting glucose and insulin testing to identify many patients with metabolic syndrome.[2] Through direct measurement of the five major lipoprotein classes: high density lipoprotein cholesterol (HDL-C), lipoprotein little "a" (Lp(a)-C), low density lipoprotein cholesterol (LDL-C), intermediate density lipoprotein cholesterol (IDL-C) and very low density lipoprotein cholesterol (VLDL-C), including the LDL-C density pattern and key HDL-C/LDL-C/VLDL-C subclasses, the VAP Lipid panel increases detection rates of all patients who are at risk for coronary atherosclerotic disease.[3] In addition, the presence of the lipid triad of high triglycerides, low HDL_2-C and dense LDL-C particles is a very specific and early indicator of insulin resistance.[4]

Almost half of all patients who have a heart attack have "normal" cholesterol and only 25% of patients with premature coronary artery disease have abnormal LDL-C levels.[1] Premature CAD is not

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rare, and published data show that 25% of acute myocardial infarction in community hospitals occurs in men under 55 and women under 65.[5] In fact, 58% of these patients had LDL-C <130 mg/dL. Also 80% of patients who had an event in the Framingham study had ordinary lipid profiles identical to the population that was event free.[6]

Accurate LDL cholesterol

LDL-C is the primary target for risk assessment and treatment of coronary artery disease. In May, 2002 National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATPIII) Guidelines called for new methods to directly measure LDL-C that is unaffected by elevated triglycerides when above 200 mg/dL. These same guidelines recognized non–HDL-C as a secondary target of therapy in patients with triglycerides >200 mg/dL. As early as 1995, the NCEP Working Group on Lipoprotein Measurements pointed out that, patients with fasting triglyceride concentrations above 250 mg/dL warrant further evaluation in any case (NIH Consensus Conference 1984, 1993), which at least in some which would usually require more extensive analytical procedures than use of the Friedewald equation.[8] Significantly, LDL-C has not been directly measured in today's ordinary lipid panels, rather it is estimated using the Friedewald equation:

$$[\text{LDL-C}] = [\text{Total Cholesterol}] - [\text{HDL-C}] - [\text{Triglycerides}/5]$$

Thus, the calculated LDL-C is speciously low in patients with elevated triglycerides (TG).[9] Although calculated LDL-C levels in healthy patients correlate well with directly measured LDL-C, they do not correlate well in patients with diabetes, coronary or other atherosclerotic disease.[10] A recently published study by J Am Coll Cardiol, Martin SS et al., found, in a 1.3 million patient cohort, there was a clinically significant misclassification of patients using the Friedewald formula compared to directly-measured VAP LDL-C by ultracentrifugation.[11] It also found in patients with abnormal triglycerides of 150–400 mg/dL, the reportable range for the Friedewald formula, a 25–60% of patients would be reclassified into a higher risk category. Likewise, in patients with normal triglycerides <150 mg/dL, they found that 10–20% of patients would be reclassified into a higher risk category. These limitations are problematic in 2017 as many patients present with disorders of triglyceride metabolism, who incidentally are excluded from clinical trials, and these are: patients with diabetes[7], hepatic disease[7], nephrotic syndrome or chronic renal insufficiency[7], clinical hypothyroidism[7], triglycerides >150 mg/dL[11], Type I, III or IV hyperlipoproteinemia[12], and patients receiving hormone replacement therapy.[13] Another strong reason to obtain a direct LDL is that a large percentage of patients sent for ordinary lipid panels do not fast correctly, so their calculated LDL cholesterol will be falsely low with a result that chylomicrons still present as the cause of a false increase in the VLDL-C calculation and subsequent LDL-C underestimation by the Friedewald formula. In contrast, the directly-measured LDL-C and VLDL-C cholesterol in the VAP lipid panel are accurate in these non-fasting persons.

Understanding LDL

Total LDL-C consists of three components: Lp(a)-C, $LDL_{4+3+2+1}$-C, and IDL-C. It is important to identify these three components separately, because they confer different risk, have different inheritance and require different treatment. Incidentally, in 1995, the Working Group on Lipoprotein Measurement discussed the need to develop methods that can measure LDL cholesterol independent of the Lp(a)-C and IDL-C contribution.[14] To date, the VAP lipid panel is the only commercially available method that can separately report these three atherogenic lipoproteins in a single test (see Fig. 1).[15] This unique view allows for better risk assessment, as two LDL-C levels equal in quantity do not mean equal risk, and allows for better treatment decisions leading to CVD risk reduction.

LDL density pattern

LDL-C can be small and dense, or large and buoyant. LDL-C buoyancy is increased when its core is rich in cholesterol, i.e. the particles are "more buoyant" by their core lipids. However, the dense particles are more atherogenic than their buoyant cousins, and they appear to penetrate endothelial wall more easily, deposit their cholesterol burden, and are more easily oxidized. Dense LDL-C occurs in 40% or 50% of patients with CAD and dense LDL-C (Pattern B) is associated with a 2–3-fold increased risk for CAD.[16] By contrast, even very high total cholesterol and total LDL-C are associated with only a 2-fold increase in risk for CAD.[17] Prospective study evidence for treating dense LDL-C is supported by at least

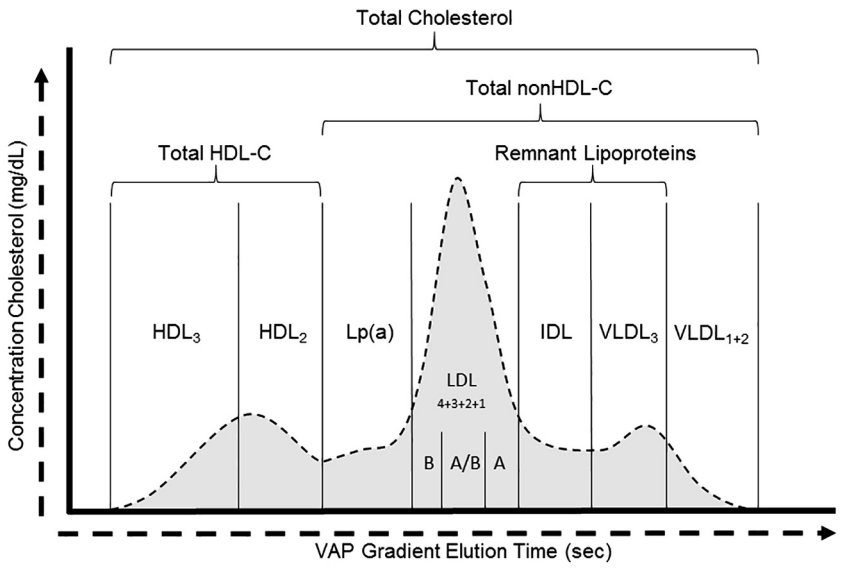

Fig. 1. The illustration is of the VAP Lipid test profile with clear demarcation of the different lipoprotein classes and subclasses.

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