

**ADVANCED LIPID PROFILE TESTING IN CARDIO  
VASCULAR RISK ASSESSMENT –A REVIEW****DR.MANJULA DEVI.A.<sup>1</sup> AND DR.RATHI ROOPAVATHY.J<sup>\*2</sup>**<sup>1</sup>*Prof & HOD , Department of Biochemistry, SBMCH, Chromepet, Chennai, INDIA.*<sup>2</sup>*Post graduate , Department of Biochemistry, SBMCH, Chromepet, Chennai, INDIA.***ABSTRACT**

Advanced Lipid Profile testing is a combination of laboratory investigations which provides a more direct and detailed lipid subfraction measurements. Some studies have claimed that this additional information on lipids could improve the ability to predict the risk assessment of cardiovascular disease from 40% (existing biochemical investigations) to more than 90% (advanced lipid profile testing ). Some of these tests include LDL phenotyping , Vertical auto profile test , Nuclear magnetic resonance test, Lipoprotein(a), Lipoprotein-associated phospholipase A2. These additional biomarkers may offer a way to further evaluate the residual risk and could become secondary treatment targets to further lower risk.

**KEYWORDS :** LDL phenotyping , VAP, NMR, GGE, Lp-PLA2.**DR.RATHI ROOPAVATHY.J**

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## INTRODUCTION

Advanced Lipid Profile, an array of more sophisticated tests provides better assessment of cardiovascular risk than the routine biochemical tests. Many guideline protocols assessing cardiovascular risk for the patients by physicians from United States, Europe and Middle East countries include LDL-cholesterol and non-HDL cholesterol. At present the treatment guidelines does not consider about the residual risk that remains the reason for mortality even after normalisation of LDL-cholesterol and non-HDL cholesterol. Some of the tests in advanced lipid profile include LDL phenotyping, Vertical auto profile test, and Nuclear magnetic resonance test. These tests bridges the gap of the residual risk and thereby can improve the ability to predict the risk of cardiovascular disease from about 40% to more than 90%. These additional biomarkers may offer a way to further evaluate the residual risk and could become secondary treatment targets to further lower risk for cardiovascular diseases.

### LITERATURE REVIEW

#### ADVANCED LIPID PROFILE TESTING

##### LDL PHENOTYPING

LDL phenotyping identifies multiple subfractions of LDL. The two patterns of LDL are large buoyant LDL and Small dense LDL. Small dense LDL is more atherogenic, binds

poorly to the receptor and their clearance is delayed. So they are associated with increased triglycerides level (RoheimPS,AsztalosBF et.al) . Some studies on LDL particle size have concluded that small dense LDL particals predict CHD risk. LDL-phenotyping is used when patient on treatment is at their LDL goal but pattern B subfraction persists, thereby more aggressive risk lowering therapy may be considered<sup>1</sup>

#### VERTICAL AUTO PROFILE (VAP) TEST

Vertical auto profile (VAP) testing determines the cholesterol content of all the lipoprotein particles in blood .The principle is that the lipoprotein classes are separated according to their density by using vertical spin density gradient ultra centrifugation. Following seperation, an enzymatic reagent reacts with the cholesterol in the sample to form a colored product which can be detected and measured. VAP cholesterol test commercially marketed by Atherotech. VAP test directly measures VLDL, IDL, LDL and HDL-C concentration and a number of lipoprotein subfractions. Newer VAP (VAP-II) includes direct measurements of Lp (a) and IDL cholesterol, there are studies showing that VAP method can be a more accurate method than the usual lipid panel<sup>2</sup>.(Kulkarni KR, Garber DW ).

Table 1

**VAP components (Kulkarni KR et al., Quantification of cholesterol in all lipoprotein classes by VAP-II method. J lipid Res 1994; 35(1) : 159-168)**

NCEP ATP III Guidelines	VAP Cholesterol Test	Routine Cholesterol Profile
Total Cholesterol	YES	YES
HDL	YES	YES
LDL	YES (directly measured, using "gold standard" ultracentrifugation)	YES (calculated)
Triglycerides	YES	YES
Non-HDL Cholesterol (LDL + VLDL)	YES	NO
Metabolic Syndrome	YES	NO
Lp(a)	YES	NO
LDL Pattern Size	YES	NO
Atherogenic Remnant Lipids (IDL + VLDL)	YES	NO

### **NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY**

NMR spectroscopy gives direct measurements of LDL particle number and size of LDL particles ( LDL – P ) . It is based on the observation that different size particles produce different methyl lipid NMR signal. It also measures HDL and VLDL subclasses . There are studies showing correlation of LDL-P with coronary artery disease progression and prediction of cardiovascular disease risk<sup>3</sup>. It can be used when LDL-cholesterol concentration in the therapeutic range but still contains excessive number of LDL particles that may correlate with increased risk .

### **GGE - GRADIENT GEL ELECTROPHORESIS**

Gradient gel electrophoresis is a more practical method of lipoprotein subclass analysis and it is Commercially available through University of California by Berkeley heartlab<sup>4</sup> . LDL-S3 GGE (LDL – segmented gradient gel electrophoresis ) , It identifies seven subclasses of LDL-cholesterol . It measures more subclasses than techniques that report pattern A/B phenotypes . Subclasses IIIa,IIIb,IVb make up the small dense LDL particles .In addition apo B levels are measured , but more studies needs to be done to evaluate its role in further reducing the cardiovascular risk. This can be used when the percent and amount of small dense LDL needs to be accurately measured for assessing residual risk.

### **LIPOPROTEIN (A)**

Lp(a) particles are similar to LDL consisting of a cholesterol-rich core, with an apoB-100 protein attached . However, Lp(a) uniquely differs to LDL in that it also has an apo(a) protein attached via a disulfide bond .Lp(a) levels may be associated with higher coronary heart disease risk<sup>5</sup> . The size of the apo(a) protein is genetically determined and varies widely hence, levels of Lp(a) can vary up to 1000-fold between individuals . The methods for measurement of Lp(a) includes

Immunoturbidimetry and ELISA. Plasma levels rise shortly after birth up to a consistent level within several months, typical plasma levels of Lp(a) are similar in men and women: one in five (20%) have levels above 50 mg/dL<sup>6</sup>. Lp(a) was proposed to act as the main scavenger for oxidized phospholipids in human circulation and to mediate clearance of the proinflammatory and proatherogenic adducts via cleavage through lipoprotein-associated phospholipase A2 (Lp-PLA2). Lp(a) level can be used when the patient treated with LDL lowering therapy and could not achieve the expected reduction.

### **LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 (LP-PLA2)**

Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme produced by inflammatory cells, co-travels with circulating low-density lipoprotein (LDL), and hydrolyzes oxidized phospholipids in LDL. The Lp-PLA2 test should be performed on a serum or EDTA plasma sample by immunoassay.Lp-PLA2 levels (mass or activity) are higher in those in whom future cardiovascular events develop (univariate analysis). The Lp-PLA2 test may be performed on individuals at intermediate or high risk for developing coronary heart disease who are any age with at least two major risk factors .

### **CONCLUSION**

Advanced lipid testing should especially be beneficial for patients with multiple cardiometabolic risk factors or high risk individuals for whom more aggressive therapy is warranted.It provides more accurate risk information than the existing biochemical tests and so improves patient management. Though these markers appear promising , their effects on risk reduction and improving mortality has not yet been proven to provide clinically significant benefit which needs further studies for validation.

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