Comprehensive Cardiovascular Profile 2.0

Advanced Cardiac Markers with Lipid Fractionation

Support Guide

"About three-quarters of the population of the USA older than 30 years has some lesion related to atherosclerosis in the arterial tree. This lesion gets worse almost every day in all these people and will eventually result in closure of a vital artery in half of them, causing their death."[1]

William P. Castelli, MD
Director, Framingham Heart Study

OVERVIEW

Preventing heart disease requires much more than simply screening for high cholesterol in the blood. *"Although this approach has been useful, it fails to identify almost one-half of the 1.3 million individuals who develop MI* [myocardial infarction] *in the US each year who have either normal or only moderately increased serum cholesterol concentrations,"* researchers have pointed out.[2]

What's more, an estimated 80% of patients who develop coronary artery disease have cholesterol levels (as measured by standard lipid profiles) comparable to those in healthy individuals.[3] And nearly half of all cases of premature coronary artery disease are missed when using only current standard guidelines for cholesterol testing.[4]

Even among patients who have been identified with high cholesterol, a significant number of individuals do not respond to routine lipid reduction strategies, or, they go on to experience a cardiac event despite drops in cholesterol.[5]

This cumulative evidence clearly underscores the urgency of assessing patients with more advanced cardiovascular risk markers than those included in standard lipid panels.

Comprehensive Cardiovascular Profile 2.0

The **Comprehensive Cardiovascular Profile 2.0** provides a state-of-the-art assessment of cardiovascular risk and treatment response. By utilizing new lipid fractionation technology, this assessment significantly increases a physician's ability to detect atherogenic lipoprotein profiles, even in patients with normal cholesterol levels.

This advanced profile:

- Provides a full array of the latest significant risk factors for cardiovascular disease, stroke, Alzheimer's disease, and other vascular-related disorders.
- Alerts to early signs of Metabolic Syndrome and Type 2 diabetes, an increasingly prevalent cause of patient morbidity and mortality
- Measures highly atherogenic cholesterol fractions linked to four-fold higher cardiovascular risk and accelerated arterial plaque progression (even when total LDL is normal).[6]
- Monitors therapy to lower cholesterol particle density and increase size, a strategy shown to hasten regression of arterial plaques.[7,8]
- More accurately predicts patient response to lipid-altering and risk reduction treatments, allowing more precise, cost-effective interventions.[5]
- Evaluates dynamics of nutrient metabolism, blood regulation, inflammation and other important independent risk factors underlying the synergistic progression of cardiovascular disease.

The advanced markers on this test have been shown to identify more than 84% of patients with subclinical coronary atherosclerosis—nearly 30% more than the number of patients detected by standard lipid profiles based on National Cholesterol Education Guidelines.[9]

Marker	Interpretation	Therapeutics
Total cholesterol	Carried in the blood by lipoprotein particles. Influenced by diet and genetics. Problematic only at levels > 200 mg/dl. Various subfractions have a powerful impact on cardiovascular disease processes.	**Pharmaceutical:** May be reduced by pharmacologic therapy aimed at LDL (see below) ↓ **Dietary/Lifestyle:** Increased fiber intake, policosanol[21], cholestin (red yeast extract)[10,11] ↓
High Density Lipoprotein (HDL)	Protective factor that can offset other risk factors at levels > 60mg/dl.[12] Two main subfractions clarify potential risk reduction realized from "good" cholesterol levels.	See below for specific therapeutic effects on HDL fractions
HDL2 (most protective)	Affords greater protection from ischemic heart disease than HDL3 fraction.[13] Lower levels associated with insulin resistance and Metabolic Syndrome (Syndrome X).[14]	**Pharmaceutical:** Niacin (crystalline or possibly inositol hexaniacinate)[15] Fibric acids (if triglycerides are high)[16] ↑ **Dietary/Lifestyle:** Aerobic exercise, omega-3 fats (EPA, DHA),[17,18] moderate ETOH use (red wine) Allium sp.[19] (garlic, onions, shallots) ↑

Marker	Interpretation	Therapeutics
HDL3 (less protective)	May actually be associated with increased risk of coronary disease.[20]	**Dietary/Lifestyle:** Fish oil may decrease HDL3 while increasing HDL2 [21] ↓
Low Density Lipoprotein (LDL)	Linked with increased incidence of myocardial infarction, stroke, and all cause-mortality. Primary target of therapy to reduce coronary heart disease risk. Three main fractions of "bad" cholesterol (IDL, LDL, and Lp(a)) provide insight into "hidden" cardiovascular risk, especially in individuals with normal LDL levels.	**Pharmaceutical:** Statins, niacin, and the bile sequestrants[22,23,24] ↓ **Dietary/Lifestyle:** Low-fat, low-cholesterol diet (eg, AHA Phase I and II diets)[25] policosanol,[26] Commiphora (myrrh)[27] ↓
Intermediate Density Lipoprotein (IDL)	Triglyceride-rich particle can indicate insulin resistance, the Metabolic Syndrome (Syndrome X),[28] and increased carotid-wall thickening. [29] May correlate with changes in cardiac lesions.[30,31]	**Pharmaceutical:** Low dose niacin and/or low-dose statin [32] ↓ **Dietary/Lifestyle:** Possibly red yeast extract, policosanol ↓
LDL Density Pattern	Indicates proportion of small, dense LDL particles (Pattern B) as opposed to large, buoyant LDL particles (Pattern A). Strongest physiologic risk factor in coronary artery disease and the best predictor of arteriographic progression.[5] Pattern B associated with a four-fold higher risk relative to Pattern A, even with normal LDL levels.[6] Pattern B also associated with diabetes,[33] insulin resistance,[34] and polycystic ovary disease.[35] Therapy to promote lower LDL density and greater LDL size appears to aid regression of arterial plaque.[36]	**Pharmaceutical:** Niacin (inositol hexaniacinate), estrogen[37], alpha-blockers, statins, fibrates (gemfibrozil), colestipol 5 to shift toward→ Pattern A NOTE: Beta-blockers, diuretics, insulin may shift toward → Pattern B [38,39] **Dietary/Lifestyle:** Exercise/weight loss, nutrients for improved insulin-sensitivity (eg, chromium, zinc, magnesium), DHA[40] with antioxidants to shift toward → Pattern A
Lipoprotein(a) (Lp(a))	Influenced by heredity. Linked to earlier, more severe coronary artery disease, myocardial infarction, more rapid progression of coronary atherosclerosis, and higher risk of thromboses.[5,41] Acts synergistically with LDL and other risk factors to increase cardiac risk.[42]	**Pharmaceutical:** Niacin,[43] fibrate,[44] estrogen (for women)[5] ↓ **Dietary/Lifestyle:** Vegetable-based foods), Vitamin C (ascorbate), L-lysine, L-carnitine,[45] N-acetyl cysteine ↓
Very Low Density Lipoprotein (VLDL)	Triglyceride-carrying lipid. Includes two types: buoyant (VLDL1,2) and dense, cholesterol-laden particles (VLDL3). VLDL3 (dense) subfraction stimulates foam cell activity and plaque formation and correlates with atherosclerosis and coronary artery disease progression.[46-48]	**Pharmaceutical:** Fibrates,[49] niacin[50] ↓ **Dietary/Lifestyle:** EPA/DHA supplementation,[51-53]low-fat, limited- carbohydrate diet (according to NCEP ATP III guidelines) ↓

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Marker	Interpretation	Therapeutics
High-sensitivity C-Reactive Protein (hs-CRP)	Acute-phase reactant for systemic inflammation, tissue damage, and immune activation. Rises in response to antigenic burden from infectious organisms (including C. pneumoniae).[54,55] Strong independent risk marker for cardiovascular disease and powerful predictor of future first coronary event in apparently healthy men and women.[1,56,57]	**Pharmaceutical:** Aspirin,[58]pravastatin ↓ **Dietary/Lifestyle:** Anti-inflammatory and anti-infectious therapies, including garlic, omega-3 fats (EPA/DHA),[59] pycnogenols, carotenoids,[60,61] exercise, smoking cessation, weight loss, Vitamin E,[62] bioflavonoids,[63,64] Ginkgo biloba,[65] improved glycemic regulation and blood pressure control1↓
Homocysteine (Hcy)	Cardiovascular risk arising from nutrient deficiency, Vitamin B dysmetabolism, and genetic predisposition. High levels correlated with poorer endothelial integrity, vascular dysfunction, and atherosclerotic lesions.[66]Implicated in myocardial infarction, diabetes, senile dementia, depression, and other degenerative conditions.[67]	**Pharmaceutical:** Prescription modifications (niacin, colestipol can raise Hcy5 ↑) **Dietary/Lifestyle:** Vitamin B12, folate, B6, betaine, serine, omega-3 oil (EPA & DHA), lifestyle modifications ↓ Coffee, tobacco use ↑
Fibrinogen	Marker for hyper-coagulation and thrombotic events, important for identifying subclinical atherosclerosis.[68] Independent risk factor; also interacts synergistically with lipids to increase risk.[69,70] Associated with acute inflammatory process. Affected by lifestyle factors.[71] May correlate with the small-dense LDL pattern.[72]	**Pharmaceutical:** Niacin,[73] fibrates[74] ↓ **Dietary/Lifestyle:** Vitamins E and C, monounsaturated and omega-3 fats (olive oil, EPA, DHA, GLA),75 Allium sp. (garlic, onion, shallots), licorice, ginger, smoking cessation,[71] Mediterranean diet with red wine,[76] dietary fiber[77] ↓
Triglycerides	Significant independent marker associated with Metabolic Syndrome (Syndrome X) and insulin resistance; high levels can increase cardiovascular risk by nearly two-fold and Metabolic Syndrome risk by nearly four-fold.[78,79]	**Pharmaceutical:** Lovastatin, gemfibrozil, probucol, fibrates, niacin ↓ **Dietary/Lifestyle:** Omega-3 fats (EPA/DHA) with antioxidants, Allium sp. (garlic, onion, shallots), reduced carbohydrates and hydrogenated oils, increased soluble fiber, alcohol restriction,[80] chromium, vanadium, exercise, weight loss ↓

* Addition of EPA/DHA (fish oil) may increase oxidation of LDL; therefore, it is recommended that antioxidants be added to the regimen whenever fish oils are used.[81]

Appendix

Drugs Affecting Lipoprotein Metabolism

Drug Class	Agents	Lipid/Lipoprotein Effects
HMG CoA reductase inhibitors (statins)	Lovastatin Pravastatin Simvastatin Fluvastatin Atorvastatin	**LDL** ↓ 18-55% **HDL** ↑ 5-15% **TG** ↓ 7-30%
Bile acid Sequestrants	Cholestyramine Colestipol Colesevelam	**LDL** ↓ 15-30% **HDL** ↑ 3-5% **TG** No change or increase
Nicotinic acid	Immediate release *(crystalline)* Nicotinic acid, extended release Nicotinic acid *(Niaspan ®)*, sustained release Nicotinic acid	**LDL** ↓ 5-25% **HDL** ↑ 15-35% **TG** ↓ 20-50%
Fibric acids	Gemfibrozil Fenofibrate Clofibrate	**LDL** ↓ 5-20% (may be increased in patients with high TG) **HDL** ↑ 10-20% **TG** ↓ 20-50%

National Cholesterol Education Program, ATP III Guidelines

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