

Dyslipidemia: What to Look For

Dyslipidemia is a condition characterized by abnormal concentrations of lipids or lipoproteins in the blood. In this review, Dr. Frohlich examines the relationship that exists between dyslipidemia and cardiovascular risk for MI, while providing readers with an overview of the latest treatment options and their effects.

Jiri Frohlich, MD, FRCPC

A number of clinical trials¹⁻⁶ and a recent meta-analysis⁷ all find the concept “lower is better” for LDL-cholesterol (LDL-C) to be valid. Based on these findings, the US Adult Treatment Panel III⁸ decided to recommend even lower LDL-C targets, namely 1.8 mmol/L for “very high risk” patients. “Very high risk” patients include those with established coronary heart disease (CHD) and multiple major-risk factors, such as:

- diabetes,
- hypertension,
- smoking, or
- other poorly controlled risk factors,
- metabolic syndrome and
- all patients with acute coronary syndrome.

The benefit of treating patients with diabetes and older individuals has also been re-emphasized.

The US Adult Treatment Panel III has decided to recommend even lower LDL-C targets, namely 1.8 mmol/L for “very high risk” patients.

Cardiovascular risk factors

In the hierarchy of the major cardiovascular (CV) risk factors, elevated serum apolipoprotein B (apoB), which correlates with the number of LDL particles and low apolipoprotein AI (apoAI), which reflects the number of HDL particles, were at the top of nine CV risk factors in the recently published INTERHEART study.⁹ High apoB/apoAI ratio accounted for almost half of the risk of MI in patients of all ethnic backgrounds studied. Other factors (in decreasing order of importance) included:

- smoking,
- diabetes,
- hypertension,
- abdominal obesity,
- psychosocial factors,
- low daily intake of fruits and vegetables,
- lack of exercise and
- alcohol intake.

These nine common risk factors accounted for 90% to 96% of risk for MI.

In the past, the likelihood of CV mortality was greatly increased in patients with CHD and now, for the first time in the recent Treating to New Targets (TNT) Study,¹ non-CV mortality was greater than CV mortality in this cohort of participants with CHD. With the use of high-dose statins, β -blockers, angiotensin-converting

enzyme inhibitors and anti-coagulants, the CV mortality decreased dramatically from an average of 7% during other clinical trials to slightly above 2% in the TNT study.

Predictors of dyslipidemia

Predictors of outcomes were studied in a number of trials. These included apoB and apoAI, along with c-reactive protein.

ApoB and apoAI

Interestingly, apoB, associated with LDL and Lp(a) particles, had a better predictive value in patients receiving treatment than LDL-C alone. In particular, when the increase in apoB is associated with higher levels of triglycerides (typically > 1.7 mmol/L), the risk increases, as does the proportion of the smaller, denser LDL particles. Also, this combination of high apoB and high triglycerides is found in patients with more serious dyslipidemia, namely the broad category of familial-combined dyslipidemia, rather than in the less atherogenic familial hypertriglyceridemia, where apoB is low-normal in the presence of increased triglycerides. The exception to this is Type III disease, dysbetalipoproteinemia, where apoB is low or normal in the presence of usually markedly increased serum cholesterol and triglycerides.

About the author...

Dr. Frohlich is a Professor at the University of British Columbia, Department of Pathology and Laboratory Medicine and the Academic Director at St. Paul's Hospital, Healthy Heart Program, Vancouver, British Columbia.

C-reactive protein

High sensitivity C-reactive protein (hsCRP) has been touted as an excellent predictor of CV events, independent of traditional risk factors. In some studies, hsCRP added to Framingham Risk Score and significantly modified it. In addition, it is interesting to note that statin treatment decreases CRP levels and that statin benefits are greater in patients with higher baseline CRP levels.

However, several recent studies indicate that CRP may not have an additive value to that of the traditional lipid and non-lipid CV risk factors.

Treating dyslipidemia

After the proper diagnosis of a primary disorder has been made, the benefits of treating of dyslipidemia has been proven beyond a reasonable doubt. It is certainly cost-effective in high-risk patients and the benefit of statins may extend to help treat other disorders, such as:

- cancer,
- Alzheimer's disease and
- osteoporosis.

The mechanisms of beneficial effects of statins are both lipid-dependent and possibly also lipid-independent (pleiotropic effects, [e.g., a reduction in stroke has now been explained by these]).

sanofi aventis
Because health matters

ALTACE 10mg
ramipril

Angiotensin converting enzyme inhibitor
Product Monograph available upon request.

sanofi-aventis Canada Inc.
Laval, Quebec H7L 4A8
CDN.RAM.06.02.02E

Dyslipidemia

The major complications of statin therapy are myopathy and rarely rhabdomyolysis, which may be fatal. The solution is to use a less potent statin at a lower dose, combined with cholesterol absorption inhibitors, such as ezetimibe or resins. This combination therapy is currently underused.


Treatment complications

The major complications of statin therapy are myopathy and rarely rhabdomyolysis, which may be fatal. The solution is to use a less potent statin at a lower dose, combined with cholesterol absorption inhibitors, such as ezetimibe or resins. This combination therapy is currently underused.

In small surrogate endpoint studies, treatment with a combination of niacin and statin resulted in, on average, a 70% reduction in CV events compared to the usual 30% to 40% reduction obtained with statins in relatively short term trials. Confirmation of this concept awaits the results of “hard end-point” outcome studies, such as the Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes trial.

Final thoughts

Ongoing trials will examine the benefit of even lower targets for LDL-C, namely those below 1.0 mmol/L. It is likely that, in the future, an even greater reduction in LDL-C, combined with an increase in HDL-C will result in much more

dramatic CV benefits. Thus, newer medications that combine cholesteryl ester transfer protein inhibitors with statins may bring a dramatic change to our management of patients with CV disease. 

References

1. LaRosa JC, Grundy SM, Waters DD, et al: Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005; 352(14):1425-35.
2. Cannon CP, Braunwald E, McCabe CH, et al: Intensive vs. moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004; 350(15):1495-504.
3. Sever PS, Poulter NR, Dahlof B, et al: Reduction in cardiovascular events with atorvastatin in 2,532 patients with type 2 diabetes: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA). *Diabetes Care* 2005; 28(5):1151-7.
4. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: A randomized placebo-controlled trial. *Lancet* 2003; 361(9374):2005-16.
5. Packard CJ, Ford I, Robertson M, et al: Plasma lipoproteins and apolipoproteins as predictors of cardiovascular risk and treatment benefit in the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER). *Circulation* 2005; 112(20):3058-65.
6. Baigent C, Keech A, Kearney PM, et al: Efficacy and safety of cholesterol lowering treatment. *Lancet* 2005; 366(9493):1267-78.
7. Executive Summary of the Third Report of the National Cholesterol Education (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285(19):2486-97.
8. Yusuf S, Hawken S, Ounpuu S, et al: Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet* 2004; 364(9438): 937-52.