Lipid Levels in the Post-Acute Coronary Syndrome Setting

Destabilizing Another Myth?*

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For many years, the proclamation that coronary heart disease (CHD) was not attributable to traditional risk factors in up to 50% of cases (1,2) was finally submerged after careful and detailed re-analysis (3,4). In this issue of the Journal, Pitt et al. (5) take aim at another long-held notion: that clinically significant alterations in lipids occur after an acute coronary syndrome (ACS), thereby precluding meaningful interpretation until well beyond hospital discharge.

Modifications of serum lipids after ACS have been recognized for at least 50 years (6). They include reductions in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) in the range of 10% to 20%, with reciprocal increases in triglycerides approximating 20% to 30%. These changes were believed to commence approximately 24 h after presentation and to last up to several months (7–11). Several mechanisms accounting for these changes include the acute phase response (12,13) associated with up-regulation of low-density lipoprotein (LDL) receptor activity (14) and reduction in several pivotal high-density lipoprotein (HDL) regulatory proteins (15). In addition, stress-induced myocardial injury and necrosis facilitates adrenergic mediated adipocyte lipolysis leading to free fatty acid mobilization, enhanced hepatic very-low-density lipoprotein (VLDL) secretion, triglyceride (TG) elevation, and alteration in LDL and HDL particle composition (16,17). In-hospital therapy and lifestyle changes are additional contributors to post-ACS lipid changes. For example, heparinization results in reduced concentrations of TG and LDL-C owing to lipoprotein lipase (LPL)–mediated hydrolysis of TG–rich lipoproteins and facilitated uptake of cholesterol by the LDL receptor (18). Conversely, nonselective beta-blockers may reduce HDL-C and increase TG by unopposed alpha-adrenergic–mediated suppression of hormone-sensitive lipase (19). Additional contributors to lipid alterations include nonspecific postural effects (20) and reductions in saturated fat intake that may reduce LDL-C and HDL-C levels (21). Based on these acute changes, the American College of Cardiology/American Heart Association (ACC/AHA) have supported a Class I recommendation for a fasting lipid profile analysis to be obtained within 24 h of admission for ACS (22).

The study by Pitt et al. (5) suggests that lipid levels remain relatively stable during the initial 96 h after ACS based on data from the LUNAR (Limiting UNderTreatment of lipids in ACS with Rosuvastatin) study, a prospective trial comparing the efficacy of LDL-C lowering with 2 different statins (rosuvastatin and atorvastatin) after hospitalization for ACS. As part of the trial, lipid and lipoprotein levels were assessed on 3 different occasions during the first 4 hospital days. Although fasting blood samples were not mandated on the admission baseline test, subsequent samples collected on days 2 and 4 were in the fasting state. Five hundred seven patients were evaluated, representing more than twice the number of participants from the earlier studies combined (7–11), and for which direct LDL-C measurements and fasting TG levels were available. Overall, the results indicated a similar trend of reduced TC, LDL-C, and HDL-C between baseline and the day 2 sample. However, these changes were small (2% to 5%) and short-lived, with rebound increases observed by day 4. From a clinical standpoint, these data provide reassurance that lipid levels remain relatively stable within the first 96 h after ACS. Unfortunately, what cannot be deduced from the present study or its predecessors is the magnitude of LDL-C reduction compared with the pre-ACS free-living state.

Because the most profound alterations in lipids and lipoproteins are proportional to the extent and severity of myocardial ischemia (9), clinical trials such as LUNAR that generally exclude complicated patients (e.g., Killip class III/IV, ventricular dysrhythmia) are also likely to underestimate the potentially greater lipid alterations that may have otherwise resulted with their inclusion. To this end, it is also not surprising that older studies, especially those performed in the pre-thrombolytic and pre-PCI era (6–10), were associated with bigger lipid effects after ACS compared with more recent studies that, in addition to the LUNAR study, showed smaller changes in post-ACS lipids and/or quicker reversion to baseline levels (14,23–24).

How should clinicians apply the results of the present study to their practice? All patients presenting with ACS deserve lipid and lipoprotein evaluation in the hospital. This decision is not predicated on whether to institute in-patient lipid-lowering therapy, as previously reflected by evidence-based data supporting intensive LDL-C reduction post-ACS (25). Rather it serves to reinforce the importance of initiating lifestyle and therapeutic measures in-hospital to

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maximize secondary prevention efforts that include an LDL-C target of <70 mg/dl (26). The demonstration of lipid stability extending well into the post-ACS period thereby lengthens the window of opportunity to address these levels before hospital discharge and impress on the associated survival benefits related to adherence of proven therapies (27).

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