La Editorials: Controversies in Family Medicine

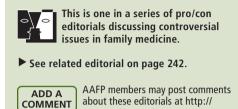
Should We Treat Moderately Elevated Triglycerides?

No: Reducing Moderately Elevated Triglycerides Is Not Proven to Improve Patient Outcomes

TYLER CYMET, DO, American Association of Colleges of Osteopathic Medicine, Chevy Chase, Maryland

Despite much research, the effect of triglycerides on the vascular system of otherwise healthy persons remains unclear.^{1,2} The overproduction or impaired removal of triglycerides from the bloodstream is associated with coronary heart disease (CHD), but has not been shown to directly cause CHD.1,2 Originally, low-density lipoprotein (LDL) cholesterol was implicated in heart disease through epidemiologic and genetic observations in humans and animal models. The involvement of LDL has now been confirmed by the repeated demonstration that LDLlowering statins reduce cardiovascular events and mortality, especially in patients with established heart disease.3 However, there is no similar evidence showing that treating patients with moderately elevated triglyceride levels will prevent CHD.4

Although statins, fibrates, niacin, and fish oil are all used to lower triglyceride levels, statin therapy for elevated LDL levels has been most effective in the primary and secondary prevention of CHD, particularly in high-risk groups, including patients with diabetes mellitus.5 However, evidence showing that aggressively lowering moderately elevated triglycerides as a distinct therapeutic target for improving patientoriented outcomes is lacking. Older trials using clofibrate (not available in the United States) and gemfibrozil (Lopid) reported moderate reductions in a combined end point of coronary events, but no change in all-cause mortality in the Helsinki Heart Study and significantly increased all-cause mortality in the World Health Organization trial.6,7



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More recently, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial randomized more than 5,000 highrisk patients with diabetes to fenofibrate (Tricor) plus simvastatin (Zocor) or simvastatin alone and followed them for nearly five years.8 There was no difference in allcause mortality or cardiovascular events. Although a post hoc analysis identified a trend among patients with low high-density lipoprotein and high triglyceride levels, this did not achieve statistical significance. In addition, there was no association with triglyceride levels alone, and the large number of subgroup analyses could mean that this was a coincidental finding.8 These findings are consistent with those of the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, which randomized 9,795 patients with diabetes to fenofibrate or placebo and found no difference in the combined coronary event outcomes and a clinically unimportant difference in all cardiovascular events (13 versus 14 percent, P = .04, number needed to treat for five years = 100).9 Furthermore, there was a nonsignificant increase in all-cause mortality in patients randomized to fenofibrate.9

The National Cholesterol Education Program Adult Treatment Panel III guidelines have identified LDL cholesterol as the primary target for primary and secondary prevention of vascular disease, and lowering LDL levels as the goal of cholesterollowering therapy.¹⁰ In a patient with a target

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LDL level, there is no additional benefit in treating moderately elevated triglyceride levels. Recent data have shown that there may not even be a benefit in measuring triglyceride levels. Total cholesterol, high-density lipoprotein, and fasting or nonfasting apolipoprotein measurements are adequate to assess a person's risk of CHD. 2

Although evidence shows that lowering triglyceride levels provides little benefit in primary prevention, the evidence is more encouraging for secondary or tertiary prevention (i.e., preventing a first coronary event after asymptomatic CHD—atherosclerosis—has developed, or preventing a subsequent coronary event or complication after the first one has occurred). A study on mortality after coronary artery bypass grafting in patients who had high triglyceride levels showed that they had a greater mortality rate than those who did not have high triglyceride levels.¹³ Several trials have shown reductions in subsequent coronary events when fibrates and niacin were used for secondary prevention, including significant reductions in cardiovascular mortality.10

In summary, moderately elevated triglyceride levels have not been established as an independent risk factor for CHD. More importantly, the lowering of moderately elevated triglyceride levels with drug therapy has not been shown to decrease the rate of CHD for primary prevention in otherwise healthy individuals.

Address correspondence to Tyler Cymet, DO, at tcymet@ aacom.org. Reprints are not available from the author.

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