

FROM THE FAMILY PRACTICE INQUIRIES NETWORK

When should we treat isolated high triglycerides?

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■ EVIDENCE-BASED ANSWER

No evidence exists that treating isolated high triglyceride levels in the absence of other risk factors prevents coronary events. Although elevated triglycerides in some studies correlates with coronary events, the association weakens when controlled for factors such as diabetes, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, body mass index, and other cardiac risk factors.

Coincident lowering of triglycerides, while treating other dyslipidemias (such as high LDL and low HDL), can contribute to decreasing coronary events (strength of recommendation [SOR]: **A**, based randomized controlled trials). Treating triglyceride levels over 500 to 1000 mg/dL may reduce the risk of pancreatitis (SOR: **C**, expert opinion).

■ EVIDENCE SUMMARY

Truly isolated hypertriglyceridemia is rare. To date, no good trials directly address the effect of reducing truly isolated hypertriglyceridemia on cardiovascular morbidity or mortality. High triglycerides are usually accompanied by other features of the “metabolic syndrome” (low HDL, high LDL, insulin resistance, diabetes, hypertension, and obesity), making it almost impossible to look at these in isolation or attribute risk to a specific component.¹

Whether high triglyceride levels pose risk in the true absence of these other metabolic factors is controversial. One meta-analysis of 17 population-based prospective studies of triglycerides and cardiovascular disease (including 57,000 patients) showed high triglyceride levels to be predictive of cardiac events, even when adjusted for HDL and other risk factors (age, total and LDL cholesterol, smoking, body mass index, and blood pressure).² After adjusting for these other risk factors, the authors found an increased risk for all cardiac endpoints (myocardial infarction, death, etc) of 14% for men and 32% for women (*Men*: relative risk [RR]=1.14; 95% confidence interval [CI], 1.05–1.28; *Women*: RR=1.37; 95% CI, 1.13–1.66).

Another meta-analysis of 3 prospective intervention trials with 15,880 enrolled subjects found that triglyceride levels did not provide any clinically meaningful information about risk beyond that provided by other cholesterol subfractions.³

In treatment trials, the most impressive risk reductions come from the groups who fit the lipid triad of low HDL, high LDL, and high triglycerides. Low levels of HDL appear to interact with hypertriglyceridemia to increase coronary risk, and all studies showing improved outcomes have simultaneously increased HDL while lowering triglycerides.⁴⁻⁶ In 3 large-scale prospective, placebo-controlled trials (the Helsinki Heart Study, a primary prevention study, and the VA-HIT and Bezafibrate Infarction Prevention trials, both secondary prevention studies), lowering triglycerides and raising HDL concurrently improved outcomes.⁵ Successful dietary and medical interventions, especially with statins and fibrates, improved overall lipid profiles—not just triglyceride levels.

Accordingly, elevated triglycerides should prompt providers to rigorously identify these other risk factors for cardiovascular morbidity and mortality, which may not be immediately obvious. In the absence of such other factors, no evidence exists to guide therapy. Expert opinion^{7,8} supported by epidemiologic evidence⁹ suggests that patients with triglyceride levels of 500 to 1000 mg/dL may have an increased risk of pancreatitis. Accordingly, providers should consider therapy to lower triglycerides to less than 500 in these patients, regardless of accompanying risk factors.

■ RECOMMENDATIONS FROM OTHERS

The American College of Physicians, the European Society of Cardiology, and the US Preventive Services Task Force do not recommend screening for hypertriglyceridemia. Clinical guidelines of the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III), American Heart Association/American College of Cardiology, and the American Diabetes Association all support LDL lowering as the primary target of therapy based on the patients risk profile.¹⁰ NCEP/ATP III has identified triglyceride levels of <150 as normal, 150–199 as borderline high, 200–499 as high, and 500 as very high.⁷

A patient with high triglycerides should prompt a search for components of the “meta-bolic syndrome” and secondary causes, including high dietary fat, high alcohol intake, drugs (steroids, beta-blockers, high-estrogen oral contraceptives), medical conditions (hypothyroidism, nephrosis, renal failure, liver disease, Cushing disease, and lupus), and rare familial dyslipidemias.^{7,10,11}

CLINICAL COMMENTARY

Elevated triglyceride level? First look at the big picture

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Observing the pendulum swings of medical knowledge over time is one of the hallmarks of the experienced family physician. As a student, I was warned of the evils of high triglycerides, only to enter a period in the 1970s and 1980s of therapeutic nihilism when triglycerides were not thought to be an independent coronary risk factor.

As outlined here, the pendulum is moving toward a more complex consideration of the effect of triglycerides on heart disease—and what we should do about it. Our patients are better served when we focus on total coronary risk rather than a specific level of triglycerides. An elevated triglyceride level leads me first to look at the glucose. I have found several poorly controlled or even new diabetic patients this way. By then following the adage to “major on the majors and minor on the minors,” I have focused on glucose and LDL control to the benefit of my patients.

REFERENCES

1. Forrester JS. Triglycerides: risk factor or fellow traveler? *Curr Opin Cardiol* 2001;16:261–264.
2. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol* 1998;81(4A):7B–12B.
3. Avins AL, Neuhaus JM. Do triglycerides provide meaningful information about heart disease risk? *Arch Intern Med* 2000;160:1937–1944.
4. Rubins HB, Robins SJ, Collins D, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med* 1999;341:410–418.
5. Secondary prevention by raising HDL cholesterol and reducing triglyceride in patients with coronary disease: the Bezafibrate Infarction Prevention (BIP) Study. *Circulation* 2000;102:21–27.
6. Effect of fenofibrate on progression of coronary-artery disease in type 2 diabetes: the Diabetes Atherosclerosis Intervention Study a randomised study. *Lancet* 2001;357:905–910.
7. Expert Panel on Detection. Evaluation and. Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486–2497.
8. Chait A, Brunzell JD. Chylomicronemia syndrome. *Adv Intern Med* 1992;37:249–273.
9. Athyros VG, Giouleme OI, Nikolaidis NL, et al. Long-term follow-up of patients with acute hypertriglyceridemia-induced pancreatitis. *J Clin Gastroenterol* 2002;34:472–475.
10. Breuer HW. Hypertriglyceridemia: a review of clinical relevance and treatment

options: focus on cerivastatin. *Curr Med Res Opin* 2001;17:60–73.

11. Malloy MJ, Kane JP. A risk factor for atherosclerosis: triglyceride-rich lipoproteins. *Adv Intern Med* 2001;47:111–136.