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www.reachmd.com
info@reachmd.com
(866) 423-7849

Triglycerides and Residual Risk in Secondary Cardiovascular Prevention: Lessons From UCC-SMART

Mr. Quigley:

You're listening to *Heart Matters* on ReachMD, and this is an *AudioAbstract*. I'm Ryan Quigley, and today, we'll be exploring findings on the often overlooked role of triglycerides in secondary cardiovascular prevention.

Even when LDL cholesterol is tightly controlled, cardiovascular risk doesn't go away. Many patients who hit their LDL-C targets still go on to experience heart attacks, strokes, or cardiovascular deaths. This gap—often called residual risk—has led researchers to look beyond LDL and ask what other lipids might be driving outcomes.

Triglycerides and the remnant lipoproteins they reflect have long been suspected. But just how strong is that link in patients who have already been treated to guideline-recommended lipid targets?

The UCC-SMART cohort offers one of the most robust datasets to explore this. More than 9,000 adults with established cardiovascular disease were followed for a median of nine years. Baseline triglyceride levels were measured and tracked against outcomes like recurrent cardiovascular events, cardiovascular mortality, and all-cause mortality.

The results were striking in their consistency. For every doubling of triglyceride levels, the risk of recurrent cardiovascular events increased by about 11 percent. The risk of cardiovascular death climbed by 15 percent, and the risk of death from any cause was higher as well.

Notably, these relationships didn't depend on whether patients had already reached LDL-C or non-HDL-C targets, or on the intensity of their lipid-lowering therapy. Even in people with what we consider "good numbers" by current standards, triglycerides stood out as an independent predictor of worse outcomes.

So why does this matter? It highlights that triglycerides aren't just passive bystanders—they may actually play an active role in progression of atherosclerosis and recurrent events. For clinicians, this reinforces the need to pay closer attention to triglyceride-rich lipoproteins in secondary prevention.

Lifestyle interventions like weight loss, increased physical activity, and limited alcohol consumption remain first-line strategies. But this data also fuels the growing interest in emerging therapies that target triglyceride-rich particles. Agents like pemafibrate, APOC3 inhibitors, and ANGPTL3 inhibitors are now being studied to see if lowering triglycerides translates into fewer events.

Of course, limitations temper the conclusions. This was an observational analysis, so causality can't be confirmed. Additionally, triglycerides were measured only once at baseline, leaving uncertainty around how fluctuations over time affect risk. And because the cohort was largely white and European, we don't know whether the same risk associations hold in more diverse populations.

Still, the study provides one of the clearest pictures yet: in people with established cardiovascular disease, triglycerides remain a strong signal of risk even after LDL cholesterol is controlled. Tackling residual risk will likely require strategies that go beyond LDL lowering, with triglyceride-rich lipoproteins now squarely in the spotlight.

In day-to-day practice, this means we shouldn't dismiss triglyceride levels as routine lab noise—instead, we can use them to guide conversations with patients about ongoing risk and reinforce the importance of comprehensive management beyond LDL cholesterol alone.

This has been an *AudioAbstract* for *Heart Matters*, and I'm Ryan Quigley. To access this and other episodes in our series, visit

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