Transcript Details
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Subcutaneous Lp(a)-Lowering Therapies: Understanding the Evidence

Announcer:
This is *Heart Matters* on ReachMD. On this episode, Dr. M. Melih Dogan will discuss his recent research on the efficacy and safety of subcutaneous lipoprotein(a)-lowering therapies. Dr. Dogan is a Postdoctoral Researcher at East Carolina University Heart Institute, and he spoke about this topic at the 2026 European Society of Cardiology Congress in Munich. Let's hear from him now.

Dr. Dogan:
What we did was a systematic review and meta-analysis. We searched four major databases through April 2025 and identified seven randomized control trials totaling 1,181 patients. Those studies are comparing subcutaneous Lp(a)-lowering agents against placebo. For the statistical analysis part, we ran the random-effects inverse-variance model, and we rated certainty of evidence using GRADE.

The primary outcome is the clearest finding. The effect on Lp(a) is large and consistent. Every single trial showed a significant reduction with a pooled mean difference of 66 percent and a confidence interval from 51 to 82 percent. Heterogeneity was high—around 89 percent—which likely reflects the differences in agent potency and dosing. So, basically, the magnitude of effect varied, but the direction didn't change. The agents also reduced LDL cholesterol by about 14 percent, and apolipoprotein B by about 13 percent.

However, this effect weakened when we excluded the studies at high risk of bias, especially for the LDL effect. When it comes to mortality, the effect was not significant, with a risk ratio of 0.77. However, to show an effect on a rare outcome like mortality, you need larger trials with long follow-up, and most of the studies are currently in phase 2. So we are waiting for bigger, phase 3 trials to be able to assess outcomes like major cardiovascular events and mortality.

For the safety picture, it was reassuring, because overall adverse events, serious adverse events, and discontinuation due to adverse events were all neutral, with no signal of harm.

But when we assessed the quality of evidence using GRADE, certainty was very low for nearly every outcome. When we say very low certainty, we are not saying the drugs don't work. We are rating the quality of evidence, not the size of the effect. Those are two separate things, and conflating them is the most common error people make when they've read a paper like ours.

Announcer:
That was Dr. M. Melih Dogan talking about the efficacy, safety, and current evidence supporting subcutaneous lipoprotein(a)-lowering therapies. To access this and other episodes in this series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

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