



Notes and Quotes

Cardiovascular risk prediction in people with HIV: looking beyond low-density lipoprotein cholesterol

Aiming for a robust, sustained reduction in low-density lipoprotein cholesterol (LDL-C) levels is central to decreasing the risk for major adverse cardiovascular events [1]. But achieving guideline-recommended LDL-C targets may not be enough to stave off adverse outcomes, as other atherogenic lipoprotein particles may drive residual risk for atherosclerotic cardiovascular disease (ASCVD) [2].

For individuals living with HIV, atherogenesis follows a complex trajectory that may not be meaningfully captured by the evolution of LDL-C levels alone. Research has shown that traditional risk calculators underestimate ASCVD risk in people with HIV (PWH), largely because HIV-specific factors may increase cardiovascular risk independently of LDL-C levels [3]. Assessing the levels of other atherogenic particles during routine lipid evaluation may improve cardiovascular risk stratification, particularly for patients who are deemed to have a low-to-intermediate risk of cardiovascular events based on LDL-C criteria. Recent clinical findings have suggested that increased plasma triglyceride (TG) levels and decreased high-density lipoprotein cholesterol (HDL-C) levels, which have been linked to metabolic syndrome and cardiovascular disease [2], may play a role in predicting the risk for ASCVD in this population.

A retrospective analysis of a large cohort of PWH recently showed that an elevated TG/HDL-C ratio was a stronger and more consistent predictor of cardiovascular events than LDL-C levels, even among individuals with LDL-C values that typically predict a low-to-intermediate ASCVD risk [4]. The analysis, initially presented at the 75th Annual Scientific Session of the American College of Cardiology (ACC 2026), included more than 10 000 adults with HIV on stable antiretroviral therapy (ART), whose fasting lipid levels were recorded in the TriNetX database between 2015 and 2025. People with hypertension, diabetes, chronic kidney disease, familial hypercholesterolemia, or preexisting cardiovascular disease were excluded, as were those who had detectable HIV RNA ≥ 20 copies/ml.

“Metabolic dysfunction is common among people with HIV due to chronic immune activation, insulin resistance, and alterations in glucose metabolism, as well as some

ARTs such as integrase inhibitors,” lead author Kathleen Ebersol, DO, noted during a presentation at ACC 2026. “LDL-C is the cornerstone lipid biomarker in algorithms used for cardiovascular risk in the general population, but the TG/HDL-C ratio, which reflects atherogenic dyslipidemia and insulin resistance, may better capture residual risk in people with HIV.”

Ebersol and colleagues at the Penn State Health Milton S. Hershey Medical Center, in Hershey, Pennsylvania analyzed the TG/HDL-C ratio as a predictor of composite cardiovascular outcomes that included ischemic heart disease, myocardial infarction, heart failure, stroke, and all-cause death in PWH with low (LDL-C of 69 mg/dl or lower), intermediate (70–129 mg/dl), and high (130 mg/dl or higher) LDL-C levels. The analysis revealed that high TG/HDL-C ratios (TG 150–400 mg/dl and HDL-C ≤ 49 mg/dl) were associated with greater odds of adverse outcomes in individuals with low and intermediate LDL-C levels compared with low TG/HDL-C ratios (TG ≤ 149 mg/dl and HDL-C ≥ 50 mg/dl). A similar trend was observed in PWH with high LDL-C levels, but this association did not reach statistical significance. Low TG/HDL-C ratios were associated with the lowest rates of adverse cardiovascular events across all LDL-C categories [4]. The researchers concluded that the TG/HDL-C ratio may capture residual cardiovascular risk that is not reflected in the LDL-C levels and may emerge as a valuable adjunct marker for risk stratification, particularly for the aging adults with HIV.

“We focus so much on LDL-C,” Ebersol remarked. “But we want to ultimately have a broader look at risk factors, especially in [specific] populations, whether those are people with HIV or women. It becomes increasingly important to prevent long-term cardiovascular morbidity as the population with HIV ages. Looking at triglyceride and HDL-C levels when we get our lipid panel can be as important as [assessing] LDL-C, as well as other [atherogenic particles] such as lipoprotein(a) and apolipoprotein B, in order to treat our patients thoroughly.” Ebersol added that analyzing the evolution of TG/HDL-C ratios over time could refine the prediction of risk for adverse cardiovascular events that may be underestimated if clinicians rely solely on the clinical snapshots obtained through single assessments. Moreover, the speaker said, future prospective studies may help determine whether screening and therapeutic interventions targeting TG/HDL-C levels can ultimately improve cardiovascular outcomes in individuals with HIV.

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As cardiovascular risk prediction for PWH continues to evolve, comprehensive clinical assessments that incorporate factors like the TG/HDL-C ratio, biomarkers of low-grade systemic inflammation, and residual viremia may better capture the risk for adverse cardiovascular outcomes related to chronic inflammation and metabolic dysfunction in this population.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

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