This ratio helps assess cardiovascular risk by comparing total cholesterol to HDL levels.

Cholesterol-related risks have predominantly been linked to individual lipid measurements, including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and non-high density lipoprotein cholesterol (non-HDL-C).[1] For the primary prevention of atherosclerotic cardiovascular disease (ASCVD), the 2018 guidelines from the American Heart Association (AHA), American College of Cardiology (ACC), and other societies recommend that individuals aged 40 to 75, who do not have diabetes and possess LDL-C levels between 1.81 and 4.89 mmol/L, undergo an initial assessment of absolute ASCVD risk utilizing the Pooled Cohorts Equations. Following this assessment, the evaluation of clinical "risk enhancing factors" and, if applicable, coronary artery calcium may provide further risk stratification.[2,3]

In contrast, other medical organizations, such as the National Lipid Association (NLA), International Atherosclerosis Society, and the European Society of Cardiology (ESC) in conjunction with the European Atherosclerosis Society (EAS), advocate for specific LDL-C and non-HDL-C targets based on risk categories. However, the complexity of cholesterol-related risk encompasses various elements, including cholesterol particle concentration, reverse cholesterol transport, and triglyceride-rich lipoproteins (TRL), among others.[4,5,6]

The ratio of TC to HDL-C (TC/HDL-C), which can be derived from the standard lipid profile at no additional cost and is closely associated with LDL particle (LDL-P) numbers, has been identified as a significant cardiovascular risk indicator in multiple studies. Recently, our research indicated that discordance between TC/HDL-C and LDL-C or non-HDL-C is prevalent among 1.3 million individuals.[7] The TC/HDL-C ratio was found to reclassify atheroma progression and major adverse cardiovascular event (MACE) rates in secondary prevention patients when it differed from LDL-C, non-HDL-C, and Apo-B levels. Despite this, while Apo-B is recognized as a "risk enhancing factor" in the 2018 AHA/ACC/Multi-Society Cholesterol Guidelines, the TC/HDL-C ratio does not receive similar acknowledgment.[8,9] Utilizing data from the Atherosclerosis Risk in Communities (ARIC) Study, a community-based prospective cohort primarily consisting of biracial middle-aged adults monitored for more than 20 years, we examined the influence of the TC/HDL-C ratio on assessing the risk of atherosclerotic cardiovascular disease (ASCVD) in cases where it was discordant with LDL-C and non-HDL-C levels, specifically among ARIC participants who were free of ASCVD at the outset.[10,11,12]

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