

The Clinical Relevance of Plasma Cholesterol Ratios

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It is well established that elevated plasma total cholesterol (TC), LDL-cholesterol (LDL-c), and triglyceride (TG), and low HDL-cholesterol (HDL-c) concentrations are associated with increased risk of cardiovascular disease (CVD). However it is the ratios, rather than one individual value, that may be more indicative of CVD risk. Many studies have examined these ratios and their association with cardiovascular outcomes in an attempt to determine the “optimal” tool for risk assessment [1]. Each of these ratios, and their clinical validity, are discussed below.

In the United States, the recommendation for minimizing CVD risk is to maintain a plasma TC concentration < 200 mg/dL, while optimal HDL-c concentration is > 60 mg/dL for both men and women, equating to an ideal TC:HDL-c ratio of 3.33 or less. A ratio of 5.0 or greater is associated with a 2-times increased risk for a cardiovascular event in non-diabetic individuals [2]. The TC:HDL-c ratio is highly correlated with other CVD risk factors, including carotid intima media thickness (IMT) [3], high BMI [4], and metabolic syndrome [5]. Therefore, the TC:HDL-c ratio is widely accepted as a good predictor of CVD risk.

Perhaps the most commonly assessed ratio is the LDL-c:HDL-c ratio. An optimal LDL-c:HDL-c ratio is < 2.5 [6]. The LDL-c:HDL-c ratio has been established as an accurate predictor of CVD risk, and is often monitored in lipid-lowering studies to assess efficacy and risk reduction. An increase in LDL-c:HDL-c ratio was seen along with increased IMT over time [7]. Recently, however, assessment of LDL-c:HDL-c has been suggested to be less appropriate because it does not account for VLDL and TG concentrations, both of which contribute to plasma TC. The Quebec Cardiovascular Study found the TC:HDL-c ratio to more accurately predict CVD risk, particularly in men [8]. Analysis of plasma lipid data from the Helsinki Heart Study also found that elevated TG, along with the LDL-c:HDL-c ratio, was most strongly associated with increased CVD risk [6], suggesting a preference for the TC:HDL-c ratio.

Because of the observed association between elevated plasma TG and CVD risk, interest has shifted to the TG:HDL-c ratio. In a study of men and women who recently experienced myocardial infarction (MI), plasma TG and TC were positively associated [9], supporting the usefulness of the TG:HDL-c ratio. Furthermore, the TG:HDL-c ratio was a strong predictor of MI [9]. Other studies also reveal an association between an elevated TG:HDL-c ratio and insulin resistance, as well as risk for a cardiac event. In a large observational study, insulin resistance contributed more than unfavorable LDL-c:HDL-c or TC:HDL-c ratios to CVD risk. Because a high TG:HDL-c ratio is often observed in insulin resistance, this ratio was significantly correlated to CVD risk. Numerous other studies support this association. The TG:HDL-c ratio was also highly correlated with visceral adiposity [10] and a diagnosis of metabolic syndrome [5], both of which place individuals at a higher risk for CVD. A TG:HDL-c ratio of > 3.5 for men and > 2.5 for women is associated with increased CVD risk. However, this ratio is not equally predictive across all ethnicities [10]. A second disadvantage of this ratio is the large individual variation in fasting plasma TG [11], suggesting a high degree of variability. Therefore, multiple measurements to determine an average ratio may necessary to accurately determine CVD risk via the TG:HDL-c ratio.

Nevertheless, the present body of evidence supports a significant association between plasma TG and CVD risk, as well as an association between a high TG:HDL-c ratio and insulin resistance, suggesting that the TC:HDL-c or TG:HDL-c ratios may be the preferred assessment tools for determination of CVD risk in most populations.

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