Impact of calculated LDL-c on residual cardiovascular risk assessment

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Introduction:The residual risk observed in atherosclerotic cardiovascular disease (ASCVD) has been largely attributed to remnant cholesterol (RC), defined as the cholesterol component of triglyceride-rich lipoproteins

Purpose: To evaluate the impact of using measured (mLDL-C) versus calculated LDL-C (cLDL-C) on the accuracy of remnant cholesterol (RC) estimation and to determine its implications for more precise cardiovascular risk assessment in clinical practice.

Methods: We compared RC values derived from directly measured LDL-C (mRC) versus calculated (cRC) in patients with a cardiovascular risk factor. mLDL–C was measured by direct enzymatic method compared to cLDL-C calculated by using application MD calc with Friedwald equation. RC was obtained by subtracting LDL-C and HDL-C from total cholesterol (TC).

Results: A total of 738 lipid profiles were analyzed over a four-month period. Among males (n = 330), the mean mRC was 1.28 ± 1.18 mmol/L, significantly higher than the mean cRC of 0.72 ± 0.35 mmol/L (paired t (329) = 7.8, $p < 0.0001$). The mean difference of 0.56 mmol/L (95% CI 0.42–0.70) corresponded to a 44% underestimation by cRC and a moderate effect size (Cohen's d = 0.43). In females (n = 408), mean mRC was 1.18 ± 0.75 mmol/L compared with cRC 0.56 ± 0.20 mmol/L (paired t (407) = 14.45, $p < 0.0001$), with a mean difference of 0.62 mmol/L (95% CI 0.53–0.71), reflecting a 53% underestimation and a large effect size (Cohen's d = 0.72). These results demonstrate systematic and clinically relevant discrepancies between measured and calculated RC, indicating that cRC substantially underestimates remnant cholesterol levels—and consequently residual cardiovascular risk in both sexes.

Conclusion: cRC underestimates mRC, especially in females, suggesting that cRC may not fully capture residual atherogenic risk. This emphasizes the clinical value of directly measuring remnant cholesterol for more accurate cardiovascular risk assessment, particularly in patients with higher levels of triglycerides, diabetes or cardiovascular disease, where calculated values may be unreliable.