Novel ways for cholesterol testing to improve risk prediction

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Cholesterol testing is one important component in risk equations such as the Framingham Risk Score or the Systematic Coronary Risk Evaluation (SCORE), which are widely used to assess the risk for incident cardiovascular mortality. Low-density lipoprotein (LDL) cholesterol provides stronger prognostic information than total cholesterol values. Direct methods to measure LDL cholesterol are available but more often LDL cholesterol is calculated indirectly by the Friedewald formula from total cholesterol, high-density cholesterol, and triglyceride values. However, this formula has several limitations in subjects with low LDL cholesterol and/or high triglyceride levels. Furthermore, fasting lipid assessment is often recommended as triglyceride values are highly variable, which may be inconvenient.

Martin and collaborators recently presented a method for improved LDL cholesterol estimation using an adjustable ratio of triglyceride to very low-density lipoprotein cholesterol levels¹. The same authors now present results² from a large database of more than 1.5 million patients (one third were fasting) to show that this novel estimated LDL cholesterol is more closely related to directly measured LDL cholesterol and less affected by fasting status than LDL cholesterol derived by conventional measurements and the Friedewald formula. The advantage for this novel estimated LDL cholesterol method was strongest for patients with low LDL cholesterol and high triglycerides. These findings have several clinical implications. Cholesterol testing in non-fasting conditions is often much simpler for the patient than the request for fasting samples. The availability of more potent lipid lowering drugs and more aggressive targets for lipid lowering therapy in secondary prevention currently recommended make it more important to have accurate determinations also at lower values of LDL cholesterol. Taken together, this novel LDL cholesterol calculation provides a simpler way to obtain a more accurate lipid profile, and may improve risk stratification³.

Another interesting aspect of how the evaluation of cholesterol levels could be improved was recently published by Kim and co-workers⁴. Increased blood pressure variability and decreased heart rate variability has been recognised as markers of increased cardiovascular risk. Whether the visit-to-visit variability in cholesterol levels relates to incident cardiovascular events has, however, not been well studied. These authors analysed data on the visit-to-visit variability of total cholesterol and future cardiovascular events and death in more than 3.5 million people in South Korea with no previous history of an acute myocardial infarction or stroke, who underwent three or more health examinations from 2002 to 2007. The median follow-up was 8.3 years.

The authors showed that increased variability in total cholesterol values (assessed as standard deviation, coefficient of variation, or variability independent of the mean) in a multi-variable adjusted statistical model all related to all cause mortality, acute myocardial infarction, and stroke, independent of mean total cholesterol levels and other potentially confounding factors⁴. Although the results of this study should be viewed in the light of its potential limitations, it appears that the variability in total cholesterol, similar to blood pressure, heart rate, and other physiologic measures provides independent prognostic information. Whether this association represents causation, and if a reduction in cholesterol variability improves prognosis, remains to be shown and warrant further study⁵.

References overleaf

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REFERENCES

1. Martin SS, Blaha MJ, Elshazly MB, Toth PP, Kwiterovich PO, Blumenthal RS, Jones SR. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *JAMA*. 2013;310:2061–2068. doi: 10.1001/jama.2013.280532.
2. Sathiyakumar V, Park J, Golozar A, Lazo M, Quispe R, Guallar E, Blumenthal RS, Jones SR, Martin SS. Fasting versus nonfasting and low-density lipoprotein cholesterol accuracy. *Circulation*. 2018;137(1):10-19. doi: 10.1161/CIRCULATIONAHA.117.030677.
3. Farukhi Z, Mora S. The future of low-density lipoprotein cholesterol in an era of nonfasting lipid testing and potent low-density lipoprotein lowering. *Circulation*. 2018;137(1):20-23. doi: 10.1161/CIRCULATIONAHA.117.031857.
4. Bangalore S. Cholesterol variability: a marker for increased risk or a risk factor? *Eur Heart J*. 2017;38(48):3567-3568. doi: 10.1093/eurheartj/ehx656.
5. Kim MK, Han K, Kim HS, Park YM, Kwon HS, Yoon KH, Lee SH. Cholesterol variability and the risk of mortality, myocardial infarction, and stroke: a nationwide population-based study. *Eur Heart J*. 2017;38(48):3560-3566. doi: 10.1093/eurheartj/ehx585.