COMMENTARY

Nonfasting lipid testing: the new standard for cardiovascular risk assessment

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Hypercholesterolemia is the strongest modifiable risk factor for coronary heart disease,[1] and measurement of plasma lipid levels is an integral part of overall cardiovascular risk assessment. Physicians and patients are used to having lipid profiles measured when the patient has fasted because of the assumption that fasting lipid profiles avoid substantial variability in the results caused by eating. However, recent evidence has shown that nonfasting lipid testing is more suitable, and nonfasting testing for baseline and follow-up complete lipid profiles, including low-density–lipoprotein (LDL) cholesterol and triglycerides, is now recommended by the Canadian Cardiovascular Society[2] and the College of Family Physicians of Canada[3] guidelines for lipid testing. Nonfasting lipid testing is more comfortable and convenient for patients, and can increase the timeliness and safety of lipid screening. We discuss the evidence behind the recent recommendations and how the results of such tests should be interpreted by physicians.

KEY POINTS

- Large population studies have shown that total cholesterol and high-density–lipoprotein (HDL) cholesterol do not vary and low-density–lipoprotein (LDL) cholesterol and triglycerides vary slightly after eating.
- Use of non-HDL cholesterol in a nonfasting plasma sample captures the atherogenic effect of remnant lipoproteins and is a better indicator of cardiovascular risk than LDL cholesterol.
- Nonfasting testing for baseline and follow-up complete lipid profiles, including LDL cholesterol and triglycerides, is recommended by the Canadian Cardiovascular Society and the College of Family Physicians of Canada guidelines for lipids.
- Removing the need to have the patient fast for testing of lipid profiles increases the convenience, safety, and timeliness of screening and follow-up testing, is appreciated by patients and may entirely remove the need for fasting prior to testing.

Large population studies performed in Copenhagen and Calgary over the last decade showed that serum lipid levels after eating show minor variation, with triglyceride levels increasing by only 20%, at most, postprandially.[4,5] Low-density–lipoprotein cholesterol can actually be lowered by as much as 10% after eating,[4,5] possibly because of replacement of some cholesterol on LDL by triglycerides. Other lipid fractions, including total cholesterol, high-density–lipoprotein (HDL) cholesterol and apolipoprotein B100, do not change substantially after eating.[4,5]

Other high-quality studies have shown that nonfasting lipid levels predict risk for coronary heart disease and stroke better than fasting lipid levels.[6,7] One study suggested that this is due to the added atherogenic effect of cholesterol in remnant lipoproteins, including intermediate density lipoproteins and chylomicron remnants, which cross the vascular endothelium like LDL and become trapped in the artery wall, contributing to plaque formation.[7] Remnant cholesterol is captured along with LDL cholesterol in the non-HDL cholesterol level regardless of the time since eating.[8] A 2012 meta-analysis found that non-HDL cholesterol is a better predictor of cardiovascular disease risk than LDL cholesterol;[9] therefore, non-HDL cholesterol has been recommended as an alternate target to LDL cholesterol since the publication of that study.[8] Reporting non-HDL cholesterol comes with no additional cost because it is simply the difference of total cholesterol minus HDL cholesterol; it should be provided by clinical laboratories on all lipid profile reports in Canada.

Based on the Copenhagen General Population and City Heart Studies, nonfasting lipid testing has been adopted as the norm in Denmark since 2009.[4] In Canada, reporting of the nonfasting complete lipid profile, including LDL cholesterol and triglyceride levels, was adopted in Alberta in 2014 and has been recommended by the College of Family Physicians of Canada lipid guideline since 2015.[3] In 2016, the Canadian Cardiovascular Society lipid guideline panel recommended the use of nonfasting profiles for both baseline and follow-up lipid testing (strong recommendation, high-quality evidence).[2] Physicians can still request fasting for testing of lipid profiles, but the intent of the recommendation is that nonfasting lipid testing becomes the norm.

Nonfasting lipid testing is being adopted gradually by clinical laboratories in all Canadian provinces and territories, such that any patient who presents for lipid testing without fasting should have LDL cholesterol and triglycerides reported along with total cholesterol, HDL cholesterol and non-HDL cholesterol. Patients can present at any time after eating, and there is also no requirement to abstain from alcohol before testing. The 2016 Canadian Cardiovascular Society lipid guideline also recommended that fasting continue to be required for lipid profiles in any patient with

a history of triglyceride levels greater than 4.5 mmol/L (about 2% of the population), because these patients were excluded from population-based studies of nonfasting lipid panels.[2,4,5]

The modified laboratory requisition for lipid testing in British Columbia will, as of January 2019, indicate that fasting is not required for any full or partial lipid profile unless requested by the physician (e.g., in patients with a history of triglyceride levels greater than 4.5 mmol/L). An audit of the laboratory information system used by the Vancouver Coastal Health region showed that 15% of outpatient lipid profiles were performed in patients who had not fasted greater than 10 hours and that no lipid tests were cancelled because of nonfasting (internal audit, unpublished data, 2018), suggesting partial concordance with the new guidelines.

In addition to better prediction of coronary disease and stroke risk, nonfasting lipid testing removes the need for patients to present to the laboratory in the morning before eating or drinking, possibly to wait a long time while fasting. This may improve time to screening because patients can go for testing at any time of day, including immediately after visiting their physician. It also removes the risks associated with fasting in patients who are diabetic[10] or frail. Nonfasting lipid testing does not affect risk stratification using the Framingham risk score, which uses total and HDL cholesterol, and has been shown not to be altered substantially by eating. Nonfasting lipid testing may also remove entirely the need for patients to fast for routine blood work, because glycated hemoglobin, which can be performed at any time, is now an acceptable sole test for the diagnosis and monitoring of type 2 diabetes mellitus.[11]

Clinicians may opt to focus on non-HDL cholesterol when assessing nonfasting lipids, because the nonfasted state affects the level of LDL cholesterol more than the level of non-HDL cholesterol, and non-HDL cholesterol has a greater predictive value than LDL cholesterol. The 2016 Canadian Cardiovascular Society lipid guideline recommends targeting a non-HDL cholesterol level of less than 2.6 mmol/L in patients at moderate or high risk as an alternative to targeting an LDL cholesterol level of less than 2.0 mmol/L.[2] As per the guidelines mentioned previously,[2,3] in the event that nonfasting triglycerides are greater than 4.5 mmol/L, the lipid profile should be repeated after fasting.

The shift to performing lipid profiles without fasting may feel strange initially to physicians and patients. However, clear evidence that lipids do not vary substantially after eating, inclusion of the risk associated with postprandial remnant lipoproteins in the test for non-HDL cholesterol, a better assessment of cardiovascular risk when using nonfasting compared with fasting levels, and the many practical advantages of not requiring a patient to fast to perform lipid testing, mean that this is a guideline change your patients do and will appreciate.

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