

Break the fast?

Update on patient preparation for cholesterol testing

Christopher Naugler MD FRCPC Davinder Sidhu MD

Abstract

Objective To provide an update on the clinical usefulness of nonfasting versus fasting lipid testing to improve patient compliance, patient safety, and clinical assessment in cholesterol testing.

Quality of evidence Recommendations are identified as supported by good, fair, and poor (conflicting or insufficient) evidence, according to the classifications adopted by the Canadian Task Force on Preventive Health Care.

Main message Screening for dyslipidemia as a risk factor for coronary artery disease and management of lipid-lowering medications are key parts of primary care. Recent evidence has questioned the fasting requirement for lipid testing. In population-based studies, total cholesterol, high-density lipoprotein cholesterol, and non-low-density

lipoprotein cholesterol all varied by an average of 2% with fasting status. For routine screening, nonfasting cholesterol measurement is now a reasonable alternative to a fasting cholesterol measurement. For patients with diabetes, the fasting requirement might be an important safety issue because of problems with hypoglycemia. For the monitoring of triglyceride and low-density lipoprotein cholesterol levels in patients taking lipid-lowering medications, fasting becomes more important.

Conclusion Fasting for routine lipid level determinations is largely unnecessary and unlikely to affect patient clinical risk stratification, while nonfasting measurement might improve patient compliance and safety.

Screening for dyslipidemia as a risk factor for coronary artery disease and the management of lipid-lowering medications are key parts of primary care. The traditional recommendation has been to measure lipid subclass levels after a minimum 8-hour fast (level II and III, fair and poor consensus evidence).^{1,2} The 2012 Canadian Cardiovascular Society guidelines continue to recommend fasting specimen collection because measurement of low-density lipoprotein cholesterol (LDL-C) is recommended as a primary indicator of the need for therapy and as the primary target during therapy (level III).³

However, 2 lines of evidence suggest that fasting for cholesterol testing might be unnecessary for most patients in routine screening in which most medical decision making and risk assessment are based on total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels. The first comes from a recent population-level study examining more than 200 000 patients, which showed that eating before a cholesterol test appeared to affect the HDL-C and total cholesterol by around 2% (level II),⁴ an amount unlikely to be clinically significant for most individuals. Second, the Framingham risk score calculation is based on using non-LDL-C (HDL-C and total cholesterol), thus the composite risk score is not significantly affected by nonfasting lipid results (level II).⁵

This update is intended to review the current literature relating to fasting versus nonfasting measurement of lipid markers in

EDITOR'S KEY POINTS

- Guidelines continue to recommend a minimum 8-hour fast before measurement of lipid levels, but convincing evidence for this recommendation is lacking and emerging evidence suggests that fasting might not be necessary for most patients presenting for routine clinic visits.
- The incremental gain in information from a fasting profile probably does not offset the gains in patient compliance and safety and in efficient use of health care resources that come with nonfasting measurement.
- Based on emerging evidence, the authors suggest that it is reasonable to begin with a nonfasting lipid profile for risk assessment, decisions about initiating treatment, and monitoring the effects of treatment. For patients with very high triglyceride levels and for monitoring triglyceride and low-density lipoprotein cholesterol levels in patients taking lipid-lowering medications, fasting becomes more important.



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cholesterol testing and to make recommendations as to the clinical usefulness of nonfasting lipid profiles.

Quality of evidence

The search for all relevant peer-reviewed articles was conducted using the Ovid MEDLINE and PubMed databases. For each of the reviewed articles, the level of evidence (I, II, and III) was established using the research design classification criteria of the Canadian Task Force on Preventive Health Care. Where applicable, guideline grades of recommendations are identified as supported by good, fair, or poor (conflicting or insufficient) consensus evidence, according to the classifications adopted by the Canadian Task Force on Preventive Health Care.⁶

Main message

For most individuals, a nonfasting cholesterol level will vary little from a fasting level (level I, good consensus,⁷ and level II^{4,8}), and the association with predicting cardiovascular events is maintained with nonfasting lipid levels (level II⁹ and level I¹⁰), suggesting that measurement of nonfasting lipid subclasses might be an acceptable alternative in routine cholesterol screening. Further, some nonfasting lipid subclasses have proven to be better predictors of cardiovascular events and clinical outcomes in randomized trials and in specific populations (level II⁹ and level I^{11,12}); possibly this is because most people are in the nonfasting or postprandial state for most of a 24-hour cycle, and nonfasting values of lipid subclasses might provide a more representative assessment of individual metabolic status (level II).¹³ Further, the usefulness of nonfasting markers might include identification of postprandial lipid or lipoprotein clearance metabolic abnormalities that have been associated with insulin resistance (level II)¹⁴ and might identify individuals for further screening and supplementary testing (level II)¹⁵ or those who could benefit from closer monitoring or more stringent treatment goals.

Nonfasting lipid measurement should particularly be considered for those with diabetes or others at risk of fasting-induced hypoglycemia due to medications or physiologic derangements in glucose metabolism (level III).¹⁶ In patients taking insulin, especially basal insulin the night before, or those taking long-acting sulfonylureas, compensatory release of glucose from the liver during fasting might be impaired by the lingering effects of the antidiabetic medications. This is particularly more likely to occur in patients with long-standing diabetes who are at increased risk of having impaired glucagon secretion, and in patients with autonomic neuropathy who are at risk of impaired epinephrine release (level II).¹⁶ While patients with diabetes might in particular benefit from nonfasting specimen collection, those without diabetes might also suffer from hypoglycemia after prolonged fasting and could benefit. The potential

serious harm to patients should be of particular interest to risk managers, laboratories, and clinicians. The shift toward nonfasting blood testing in other screening examinations in high-risk groups is also reflected in recent changes in type 2 diabetes screening recommendations: shifting to nonfasting hemoglobin A_{1c} screening in individuals at moderate to high risk of diabetes as an alternative to fasting glucose measurement (level III).¹⁷

From a logistical perspective, random nonfasting specimen collection is more convenient for patients and is beneficial to laboratory collection sites because of the reduction in demand for early-morning collections. Reduced wait times and elimination of return visits to clinics for collection of fasting specimens might also improve patient compliance with routine screening, avoid unnecessary delays, and allow for more timely counseling of patients (level III).¹⁸ The province of Alberta has recently adopted a policy whereby if patients present to laboratories for lipid testing in a nonfasting state, the test is performed anyway and the results along with the number of hours the patient fasted are transmitted back to the ordering clinician. The clinician can then decide if a repeat lipid determination in a fasting state is necessary.

The improved precision of fasting lipid profiles might be useful for determining whether to treat dyslipidemia in some borderline patients (level I).¹⁹ However, recent guidelines emphasize total risk as a main driver of the need to treat; the modest degree of imprecision generated by the minimal variation in the total cholesterol and HDL-C levels is likely tolerable. This is reflected in the 2012 Canadian Cardiovascular Society guidelines, which support the use of nonfasting lipid results with the introduction of non-HDL-C (total cholesterol minus HDL-C) as an alternate target in medium- and high-risk patients receiving therapy. Non-HDL-C is not significantly different in the fasting and nonfasting states (level III).³ A growing body of evidence from observational studies and statin clinical trials suggests that nonfasting or fasting blood draws can be used for cardiovascular risk assessment and therapeutic decisions, especially when lipid subfractions other than LDL-C (eg, the total cholesterol to HDL-C ratio or non-HDL-C) are emphasized (level III).²⁰ Randomized clinical trials have increasingly used nonfasting lipid testing, showing that when monitoring the response to initiating treatment with a statin, the stability of total cholesterol and HDL-C values makes non-HDL-C levels measured randomly a viable way to track a patient's response to therapy (level I).^{21,22}

Finally, it is important to note that LDL-C levels are generally calculated (via the Friedewald equation) instead of being measured directly. The Friedewald equation is not accurate when triglyceride levels are higher than 4.52 mmol/L (400 mg/dL), and so LDL-C levels are generally not reported if the triglyceride levels are above this value. Data from our own laboratory

show that for fasting individuals, 98.6% will have triglyceride levels that allow for the calculation of LDL-C, while for nonfasting individuals this percentage decreases to 97.2% (unpublished data). Thus, testing lipid levels in a nonfasting state will result in a slight increase in individuals for whom an LDL-C level cannot be calculated. The options for these individuals are to repeat testing in a fasting state or use an alternative measure (eg, non-HDL-C or apolipoprotein B) that does not vary with fasting state. Some laboratories might also be able to perform a direct LDL-C determination that does not rely on the Friedewald equation.

Given the growing evidence for the acceptability of nonfasting lipid determinations, laboratories should be encouraged to report lipid panels in either fasting or nonfasting states. When reporting on patients in a nonfasting state, the number of hours of fasting should be reported back to the ordering clinician. In many jurisdictions this will involve changes in laboratory policy. Ideally, the decision to fast or not to fast is left in the hands of the clinician and patient, and laboratories should process lipid samples regardless of the patient fasting state.

Conclusion

At best, fasting for bloodwork might represent an inconvenient and unpleasant experience for patients. At worst, it might pose a serious patient safety issue, an obstacle to accurate diagnostic and prognostic risk assessment, and an impediment to efficient clinic and laboratory work flow. The incremental gain in information for a fasting profile is particularly small for total cholesterol and HDL-C values and likely does not offset the logistic impositions placed on patients, laboratories, and clinicians' ability to provide timely counseling to patients. Convincing evidence for the superiority of fasting lipid testing is lacking, and it is reasonable to consider nonfasting determination of lipid subclasses in most individuals who present for routine clinic visits. In practice, you can begin with a nonfasting lipid profile for risk assessment, decisions about initiating treatment, and monitoring the effects of treatment. For individuals presenting with very high triglyceride levels and for monitoring triglyceride and LDL-C levels in patients taking lipid-lowering medications, fasting becomes more important.

Fasting for routine lipid level determinations is largely unnecessary and unlikely to affect patient clinical risk stratification, while nonfasting testing is likely to improve patient compliance and safety and allow for more efficient use of health care resources. Using this new approach, most lipid profiles can be obtained in the nonfasting state, increasing convenience for patients and clinicians and decreasing the burden on laboratories, with little to no adverse effect on clinical decision making. 

Dr Naugler is a family physician, a general pathologist, and Division Head of General Pathology at the University of Calgary in Alberta. **Dr Sidhu** is a lawyer

and senior resident in the General Pathology residency training program at the University of Calgary.

Contributors

Drs Naugler and **Sidhu** contributed to the literature search, analysis, and interpretation, and preparing the manuscript for submission.

Competing interests

None declared

Correspondence

Dr Christopher Naugler, University of Calgary, Pathology and Laboratory Medicine, C414, 9-3535 Research Rd, Calgary, AB T2N 2K8; e-mail christopher.naugler@cls.ab.ca

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