To Fast or Not to Fast?

Comments on the Consensus Statement From the European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine

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The European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine recently published a consensus statement promoting the routine use of nonfasting blood samples for the assessment of plasma lipid profiles. That statement follows the consensus recommendation that has been implemented in Denmark since 2009 and in the United Kingdom since 2014, whereas in the United States, the most recent 2013 American College of Cardiology/American Heart Association guideline does not require fasting blood samples for estimation of atherosclerotic cardiovascular disease (ASCVD) risk, but the guideline recommends a fasting lipid panel to calculate low-density lipoprotein cholesterol (LDL-C) before initiating statin treatment, and for individuals with non–high-density lipoprotein cholesterol levels (non–HDL-C) of 220 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0259) or triglyceride (TG) levels of 500 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0113). The rationale for the European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine stance is ease of collection and greater compliance in patient preparation for lipid testing. Non–fasting cholesterol levels (total cholesterol, non–HDL-C, and LDL-C) are comparable to fasting cholesterol levels in postprandial state on the assessment of cardiovascular disease risk by citing studies in which various nonfasting lipid parameters were monitored relative to clinical outcomes. The conclusion here was that nonfasting lipid testing may actually be superior to fasting lipid profiles for predicting cardiovascular disease. Finally, the consensus statement recommends that the abnormal lipid values obtained from nonfasting samples should be flagged based on desirable lipid cutoffs published by accepted guidelines and consensus statements.

Nonfasting Lipid Panel in the Assessment of Cardiovascular Risk

Currently, worldwide, many laboratories follow the policy of an overnight fast for a minimum of 8 hours before obtaining samples for testing the lipid profile. There are indeed several advantages to obtaining a nonfasting lipid profile. It is easier in the outpatient setting and would likely improve compliance in special populations, such as people with diabetes, pregnant women, and children, if fasting were not required. Although nonfasting tests are convenient for population screening of dyslipidemias, there have been no studies, to our knowledge, that examine in a detailed fashion fasting versus postprandial lipid profiles, their accuracies, and the cost effectiveness of switching to nonfasting lipid profiles. Whether nonfasting lipid measurements can replace the fasting lipid tests in routine clinical practice has been debated intensely. The American College of Cardiology/American Heart Association panel reviewed several studies and noted that a nonfasting lipid panel does not appear to alter assessment of cardiovascular risk.

The questions that arise from the European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine consensus statement include the 3 questions discussed in the following paragraphs.

What Are the Lipid Parameters That Fasting Has a Minimal Impact On?

A standard lipid profile includes total cholesterol, TG, HDL-C, and calculated LDL-C levels, based on the Friedewald formula, in the absence of TG levels of 400 mg/dL or greater. Total cholesterol and HDL-C concentrations show little variation after habitual meals, although the accuracy of the automated, direct HDL-C assay is subject to interference from hypertriglyceridemia. However, TG and calculated LDL-C concentrations are directly dependent on

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the fat and carbohydrate content in a meal. The Friedewald equation, which was based strictly on fasting lipid values, has shown to underestimate LDL-C levels when TG levels are 150 mg/dL or more, particularly in patients with LDL-C levels less than 70 mg/dL. Because the LDL-C result is the major component for decision making regarding statin therapy, even small inaccuracy in the LDL-C calculation may misclassify a patient into a differently intensified treatment group. In the setting of a nonfasting TG/lipid panel, either a directly measured LDL-C or an apolipoprotein B result can be used to overcome the limitations of the calculated LDL-C.

The beauty of fasting lipid testing is the minimal variation from day to day. Although the maximal mean changes in TG level at 1 to 6 hours after habitual meals have been documented as +26 mg/dL, these numbers do not completely capture the random variation in the postprandial state. The day-to-day biologic variations in fasting lipid levels have been documented, whereas little corresponding data are available for nonfasting lipids. To our knowledge, there are no studies detailing the differences caused by a low fat and/or carbohydrate diet versus the diet of someone consuming a high fat and/or carbohydrate meal on the day of the lipid profile testing.

In What Clinical Settings Is Fasting Not Mandatory for Lipid Profile Testing?

It has always been a challenge for clinicians to ensure that patients fast for more than 8 hours before a lipid profile test and/or to interpret the results when a patient’s fasting status is uncertain. For most patients with lipid profiles tested annually as part of the long-term ASCVD risk assessment, total cholesterol and HDL-C results at nonfasting status are acceptable for the pooled cohort equation. On the other hand, for patients with a diagnosis of genetic dyslipidemia or hypertriglyceridemia, who are being tested for response to treatment, mandatory fasting before the lipid test eliminates the potential difficulties in reaching a conclusion with the test result. Although nonfasting samples are a convenient screening tool, diagnosis of familial dyslipidemias will then necessitate a follow-up fasting lipid profile in addition to other laboratory measurements to define the dyslipidemia and to begin appropriate targeted therapy. This is especially true for individuals who may have familial hypertriglyceridemia. The European Atherosclerosis Society/European Federation of Clinical Chemistry and Laboratory Medicine panel also highlighted certain situations in which fasting before testing is preferred, such as when nonfasting TG levels were greater than 440 mg/dL (whereas in the United States, we follow a triglyceride cutoff level of more than 400 mg/dL), or for treatment of hypertriglyceridemia including pancreatitis.

In What Patient Populations Have We Accumulated Sufficient Evidence to Support the Interchangeability Between Fasting and Nonfasting Lipid Profile Testing?

Patients who are in constant hypertriglyceridemic states because of disease, such as type 2 diabetes or metabolic syndrome, tend to have calculated LDL-C results that underestimate their actual LDL-C levels. Therefore, the accuracy of a postprandial calculated LDL-C in these patients may be questionable. In addition, there are ethnic differences in lipid profile results, especially for triglycerides in South Asians and Latin American populations, in which a TG concentration of more than 150 mg/dL may be deleterious. There is little data regarding children, for whom postprandial plasma lipid levels may vary greatly. In a prospective study of 26330 healthy women, Mora et al examined associations of baseline lipid levels with incident cardiovascular disease (n = 754 fasting, 78.5%; n = 207 nonfasting, 21.5%) during 11 years of follow-up. In their study, except for TG levels, lipid concentrations differed minimally (<5%) for fasting versus nonfasting test results. Their study demonstrated that, although nonfasting HDL-C, TG, and apolipoprotein A1 predicted cardiovascular disease, total cholesterol, LDL-C, and non–HDL-C, as well as apolipoprotein B in the nonfasting state, were less useful in predicting cardiovascular risk.

CONCLUSIONS

In summary, nonfasting lipid profile testing offers advantages in convenience for patients and has been proven as reliable, or even superior to, fasting lipid testing in assessing ASCVD risk. Fasting is still of great help in testing for certain lipid results, certain clinical situations, and certain patient populations. This discussion calls for more data to be generated or analyzed for us to fully understand the pros and cons of choosing nonfasting versus fasting lipid profile testing in all populations. Until then, nonfasting total cholesterol and HDL-C test results are sufficient to assess initial ASCVD risk. Those patients with nonfasting non–HDL-C results of more than 220 mg/dL, which is indicative of genetic hyperlipidemia, should be evaluated with a fasting lipid profile. In addition, those patients with a nonfasting TG level of 200 mg/dL or greater will benefit from a follow-up fasting lipid profile.

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References


