Endorsement of Routine Non-Fasting Lipid Panels

<table>
<thead>
<tr>
<th>Year</th>
<th>Society</th>
<th>Non-Fasting Triglycerides cutoff*</th>
<th>Risk Assessment (Prior to Therapy)</th>
<th>Lipid Assessment on Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>European Atherosclerosis Society and European Federation for Laboratory Medicine</td>
<td>&gt;400 mg/dL</td>
<td>Non-fasting lipid panel is appropriate.</td>
<td>Non-fasting lipid panel is acceptable.</td>
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<tr>
<td>2014</td>
<td>National Clinical Guideline Center and Joint British Societies</td>
<td>&gt;400 mg/dL</td>
<td>Non-fasting lipid panel is appropriate.</td>
<td>Non-fasting lipid panel is acceptable.</td>
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<tr>
<td>2013</td>
<td>American College of Cardiology / American Heart Association</td>
<td>&gt;200 mg/dL</td>
<td>Fasting lipid panel is preferred but not required.</td>
<td>Fasting lipid panel recommended prior to statin initiation. Non-fasting is acceptable on treatment follow-up.</td>
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</tbody>
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* Repeat measure of triglycerides using fasting sample is recommended following elevated non-fasting triglycerides.

fries, and a milkshake, there will be a significant increase in measured triglycerides. For these reasons, the American Heart Association recommends that any non-fasting triglycerides >200 mg/dL be followed up with a fasting lipid panel (14). Clinicians and laboratorians could also partner to deal with this issue by targeting patients for fasting who have a history of hypertriglyceridemia or through patient education. Requesting that patients avoid fatty meals a few hours prior to a blood draw is a very different request than a complete fast for 8-12 hours.

Non-Fasting Triglycerides and Risk of Heart Disease

Interestingly, while the association between fasting triglycerides and risk of heart disease is minimal, growing evidence suggests that non-fasting triglyceride concentrations confer significant risk. One study followed 26,509 U.S. women over 12 years for myocardial infarction, ischemic stroke, coronary revascularization, or cardiac death. The risk of having an adverse cardiac event was double (hazard ratio (HR) 1.98 [95% confidence interval (CI) 1.21-3.25]) for women in the highest tertile of non-fasting triglycerides (≥171 mg/dL) after adjusting for age, blood pressure, smoking, and blood cholesterol. In contrast, the investigators found no additional risk for women in the highest tertile of fasting triglycerides (HR 1.09 [95% CI 0.85-1.41]) (15).

Another study of 1,337 patients with type 2 diabetes mellitus found a significant increase in cardiac events among patients with elevated non-fasting triglycerides (16). Multiple studies have reported similar findings for non-fasting triglycerides (8, 10, 17-19).

What About Estimated LDL-C?

Even if the fasting influence on triglycerides is debatably minimal, an 800-pound gorilla remains in the room. Triglycerides are part of the Friedewald equation. Any increase in triglycerides will result in a decrease in the reported LDL-C.

Several large studies have set aside the fasting rule and estimated LDL-C by the Friedewald formula in non-fasting blood samples (1, 8, 20, 21). Figure 1 shows that Friedewald estimated LDL-C and measured LDL-C are not significantly different when tested in non-fasting samples from a general population study (n=470) (1). In one cohort of 586,481 patients with median triglyceride concentrations of 125 mg/dL (interquartile range (IQR) 87-182), the median ultracentrifugemeasured LDL-C was 115 mg/dL (IQR 91-142), while the median Friedewald estimated LDL-C was 112 mg/dL (IQR 87-139) (11).

Another study comparing fasting and non-fasting LDL-C (estimated by the Friedewald formula in both cases) among 209,180 community outpatients showed an average decrease of 4 mg/dL LDL-C due to non-fasting (22).

Two factors help minimize the impact of fasting on estimated LDL-C. First, as explained above, the typical increase in triglycerides is less than previously assumed. Second, estimated LDL-C is only reduced by 1 mg/dL for every 5 mg/dL increase in triglycerides. Since most patients have at most a non-fasting increase of 25 mg/dL triglycerides, then LDL-C estimates are only expected to vary by 5 mg/dL.

The Clinical Significance of Decreased Non-Fasting LDL-C

Clinicians use LDL-C to establish a patient’s risk of cardiovascular disease and to monitor the impact of therapeutic interventions. The primary tools used to assess a patient’s risk of cardiovascular disease are the Framingham Score, the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equation, the Reynolds score, and European Systematic Coronary Risk Evaluation Score. All of these calculations incorporate age, sex, blood pressure, smoking status, total cholesterol, and HDL-C. None formally include triglycerides or LDL-C. The endorsed means of risk assessment are completely independent of a patient’s fasting status.

Data from 8,270 patients enrolled in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) confirm the rationale for excluding these measures. In ASCOT, investigators found greater than 95% concordance between fasting and non-fasting lipids using the 2013 ACC/AHA Pooled Cohorts equation (23). Incidentally, this study found that non-fasting LDL-C was a stronger indicator of