Non-fasting Lipid Profile

Getting to the Heart of the Matter!

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Historical Basis for Fasting Lipids

- The initial classifications of hyperlipidemia proposed in 1967 were genetic and required *fasting triglycerides (TG)*.

- The Friedewald formula was subsequently introduced to allow calculation of a LDL-C level using *fasting data*. It was assumed that the increase in TG that occurs after eating a fatty meal has been thought to greatly affect the calculation of LDL-C using the Friedewald equation.

- In addition, the first 2 NCEP guidelines, released in 1988 and 1993, focused on primary and secondary prevention of CHD and established specific LDL-C goals. The third NCEP report (ATP III) broadened the focus by using 10-year CHD risk estimation, but still relied on specific LDL-C goals to set treatment thresholds. These guidelines therefore reinforced the use of *fasting lipids*.

However, there is lack of evidence that fasting is superior to non-fasting when evaluating the lipid profile for cardiovascular risk assessment.
Most individuals consume several meals during the day and some consume snacks between meals; the postprandial state therefore predominates over a 24 h period.

Nonetheless, in clinical practice, the lipid profile is conventionally measured in blood plasma or serum obtained after fasting for at least 8hr, and therefore may not reflect the daily average plasma lipid and lipoprotein concentrations and associated risk of cardiovascular disease.
In 2009, the Danish Society for Clinical Biochemistry recommended that routine lipid profiles be measured in non-fasting blood samples with the option of doing a repeat test if TG were above 4 mmol/L (350 mg/dL), and this has been standard clinical practice in Denmark since then.

TG increased up to 0.2 mmol/L after normal food intake in individuals with and without diabetes, whereas the postprandial reductions in LDL-C observed in both populations likely were caused by hemodilution due to fluid intake. No statistically significant differences in postprandial apolipoprotein B concentrations were found.
Plasma Lipids and Lipoproteins Change Only Modestly in Response to Habitual Food Intake

<table>
<thead>
<tr>
<th>Study population</th>
<th>Random non-fasting compared with fasting concentrations</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Triglycerides</td>
</tr>
<tr>
<td>Mora et al. (2008)</td>
<td>↑ 0.2 mmol/L</td>
</tr>
<tr>
<td>Langsted et al. (2008)</td>
<td>↑ 0.3 mmol/L</td>
</tr>
<tr>
<td>Steiner et al. 2011</td>
<td>↑ 0.1 mmol/L</td>
</tr>
<tr>
<td>Langsted and Nordestgaard (2011)</td>
<td>↑ 0.2 mmol/L</td>
</tr>
<tr>
<td></td>
<td>↑ 18 mg/dL</td>
</tr>
<tr>
<td>Sidhu and Naugler (2012)</td>
<td>↑ 0.3 mmol/L</td>
</tr>
<tr>
<td></td>
<td>↑ 26 mg/dL</td>
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</table>
Recommendation: Fasting blood sample is "preferred" for lipid testing rather than mandatory, depending on the clinical scenario, although a non-fasting blood sample could be used. For practical purposes, the traditional reliance on fasting lipids to answer most questions may no longer be necessary.
Endorsed non-fasting lipid testing in the primary prevention setting.

In people with a triglyceride concentration between 10 and 20 mmol/litre:

- repeat the triglyceride measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and
- review for potential secondary causes of hyperlipidaemia and
- seek specialist advice if the triglyceride concentration remains above 10 mmol/litre. [new 2014]
Among 5538 patients with both a non-fasting and a fasting TG measurement, concentrations were very similar fasting and non-fasting measures overall as well as when stratified by TG concentrations and the presence or absence of diabetes.
Population-based Studies and Statin Trials that have Employed Non-fasting Plasma Lipid Profiles to Assess CVD Risk and Trial Outcomes

Population-based studies totalling >300,000 non-fasting individuals

- Tromsø Heart Study
- Norwegian National Health Service
- Northwick Park Heart Study
- British Population Studies
- European Prospective Investigation of Cancer–Norfolk
- Copenhagen General Population Study
- The global 52-country case-control INTERHEART study

Population-based studies totalling >300,000 non-fasting individuals

- Apolipoprotein-related Mortality Risk
- Copenhagen City Heart Study
- Women’s Health Study
- Nurses’ Health Study
- Physicians’ Health Study
- National Health and Nutrition Examination Survey III
- Circulatory Risk in Communities Study

Statin trials totalling 43,000 non-fasting individuals

- Heart Protection Study
- Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm
- Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine
Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points—a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine

**Key recommendations**

- Fasting is not required routinely for assessing the plasma lipid profile.
- When non-fasting plasma triglyceride concentration >5 mmol/L (440 mg/dL), consideration should be given to repeating the lipid profile in the fasting state.
- Laboratory reports should flag abnormal values based on desirable concentration cut-points.
- Life-threatening or extremely high concentrations should trigger an immediate referral to a lipid clinic or to a physician with special interest in lipids.
Maximal difference between random non-fasting lipids (1-6 hours after a meal) and fasting lipids is not clinically significant

Nordestgaard BG. European Heart Journal (2016) 37, 1944–1958
Which screening tests are recommended for the detection of cardiovascular risk?

**Fasting Lipid Profile** Use a fasting lipid profile to ensure the most precise lipid assessment; this should include total cholesterol, LDL-C, TG, and non-HDL-C (**Grade C; BEL 4, upgraded due to cost-effectiveness**).

Lipids, including TG, can be measured in the non-fasting state if fasting determinations are impractical (**Grade D**).
Advantages of Non-fasting Lipid Profile

- Patients who have not fasted do not have to make another appointment to have their blood drawn
- By not requiring an overnight fast, the crowd of patients showing up in the morning for a blood test is lessened
- Physicians are spared from having to track down repeat tests
- Non-fasting lipid profiles predict increased risk of cardiovascular events
When is Non-fasting Sample preferred?

- During initial lipid profile test in any patient – With current guidelines, LDL-C values may not be needed for some clinical scenarios but rather total cholesterol and HDL-C are needed, both of which vary little between the fasting and non-fasting state. Therefore, in the estimation of initial risk among the primary prevention patients who are not on lipid-lowering therapy, non-fasting lipid measurements would be acceptable.

- For a cardiovascular risk assessment – American Heart Association suggests that providers could use non-fasting TG >200 mg/dl to identify hypertriglyceridemic states. In most cases, when an elevated result is observed, then a repeat fasting TG can be measured in 2-4 weeks.

- In the cases when extreme TG levels are observed, for example ~1000 mg/dl, there is no need for repeat of fasting lipids prior to treatment.

- For a patient admitted with acute coronary syndrome.

When is Non-fasting Sample preferred?

- Assessment of metabolic parameters which define metabolic syndrome can assist the provider and patient to initiate changes, in particular lifestyle changes, which reduce risk of diabetes and CVD. Non-fasting measures including TG >200 mg/dl and a low HDL (40 mg/dl in men or <50 mg/dl in women), in the setting of a HbA1c >5.6% would be consistent with traditional metabolic criteria and thus allow for therapeutic interventions to begin.

- In children.
- In the elderly.
- In patients on stable drug therapy.
- In patients who prefer non-fasting lipid profile.
- In diabetic patients (due to hypoglycemic risk).
When should Fasting Lipid Profile be done?

- If a patient has non-fasting TG >5 mmol/L (440 mg/dL)

- Patients with known hypertriglyceridemia (and is being followed in lipid clinic) – An LDL-C >190 mg/dl is the most common result during screening and follow-up of patients with a family history of genetic (familial) hyperlipidemia and/or premature ASCVD wherein fasting measure is recommended.

- Patients with pancreatitis OR Is recovering from hypertriglyceridemic pancreatitis OR is starting medications that cause severe hypertriglyceridemia should have a fasting lipid profile checked to assess for a TG level >500 mg/dl. Patients at risk for hypertriglyceridemia include those with HIV treated with ART, patients treated with long-term steroids, patients with a family history of hypertriglyceridemia or visceral adiposity who are starting oral contraceptive or HRT, and women who are planning to get pregnant.

- For patients currently treated with lipid-lowering therapies, assessment of factors including diet, physical activity, smoking status, blood pressure, and glucose are important modifiable components of CVD risk, beyond LDL levels. Moderate- and high-intensity statin therapy generally results in a relative risk reduction of 20% per 1 mmol/L (39 mg/dl) of LDL lowering. Comparison of LDL levels pre- and post-statin therapy can estimate the relative risk reduction obtained; thus, a fasting measure can be recommended.

When should Fasting Lipid Profile be done?

- A fasting lipid profile among treated patients provides prognostic value with regard to risk for statin-induced diabetes, as a TG level <150 mg/dl is associated with a lower risk of diabetes. Prognostic value is also present with lower treated LDL with regard to acute coronary syndrome incidence.

- Adherence to therapy is important for all treated patients. Providing patients with a review of the trends over time in their lipid profile allows for a discussion of the risk reduction afforded with lower LDL and non-HDL levels. Even among those in whom the clinician does not have pretreatment values, assessment of fasting lipids can allow for detection of changes related to adherence for statins and/or lifestyle factors. Thus, a fasting measure is recommended.

- If additional laboratory tests are requested that require fasting or morning samples (eg, fasting glucose or therapeutic drug monitoring)
Necessity of Fasting for Lipid Measurements

Summary of Clinical Scenarios and Fasting Requirements

<table>
<thead>
<tr>
<th>Clinical Scenarios</th>
<th>Necessity of Fasting</th>
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<tbody>
<tr>
<td>• Estimating initial risk in an untreated primary prevention patient</td>
<td>Non-Fasting Acceptable</td>
</tr>
<tr>
<td>• Screening and following patients with family history of genetic hyperlipidemia or premature ASCVD</td>
<td>Fasting Required*</td>
</tr>
<tr>
<td>• Clarifying the diagnosis of metabolic syndrome</td>
<td>Non-Fasting Acceptable</td>
</tr>
<tr>
<td>• Estimating residual risk for a treated patient</td>
<td>Fasting Preferred</td>
</tr>
<tr>
<td>• Assessing patients with or at risk for pancreatitis</td>
<td>Fasting Preferred†</td>
</tr>
<tr>
<td>• Diagnosing hypertriglyceridemia</td>
<td>Fasting Preferred</td>
</tr>
</tbody>
</table>

Practical Algorithm for Screening for Elevated Triglycerides

Screen with Nonfasting Triglycerides

- <200
  - Follow-up as required
- ≥200
  - Fasting lipoprotein panel

Optimal
- <100
Normal
- <150
Borderline
- 150-199
High
- 200-499
Very High
- ≥500

Driver SL. J Am Coll Cardiol 2016;67:1227-1234
<table>
<thead>
<tr>
<th>Guideline or statement</th>
<th>Year</th>
<th>CVD risk assessment or before starting lipid lowering therapy</th>
<th>During lipid lowering therapy</th>
<th>Non-fasting triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Atherosclerosis Society/European Federation for Laboratory Medicine (2)</td>
<td>2016</td>
<td>Fasting lipids are not routinely required</td>
<td>Fasting is not required if patients are on stable drug therapy</td>
<td>For triglycerides &gt;400 mg/dL (5 mmol/L), fasting may be considered; refer to a specialist</td>
</tr>
<tr>
<td>National Clinical Guideline Center (NICE) and Joint British Societies Guidelines (3)</td>
<td>2014</td>
<td>A fasting sample is not needed</td>
<td>Consider an annual non-fasting non-HDL cholesterol</td>
<td>Non-fasting triglycerides ≥175 mg/dL (2 mmol/L) is elevated</td>
</tr>
<tr>
<td>American College of Cardiology/American Heart Association Guidelines (4)</td>
<td>2013</td>
<td>A fasting sample is preferred (but not mandatory)</td>
<td>Fasting lipids to assess per cent reduction in LDL cholesterol and adequate response to statin therapy</td>
<td>For triglycerides &gt;200 mg/dL (880 mg/dL), refer to a specialist</td>
</tr>
<tr>
<td>Canadian Cardiovascular Society Guidelines (5)</td>
<td>2012</td>
<td>Non-HDL cholesterol has the advantage of being applicable in a non-fasting state</td>
<td>LDL cholesterol is the primary target of therapy</td>
<td>For triglycerides between 10 and 20 mmol/L (880 to 1,770 mg/dL), repeat fasting</td>
</tr>
<tr>
<td>European Society of Cardiology/European Atherosclerosis Society (6)</td>
<td>2011</td>
<td>If possible (for triglyceride and LDL cholesterol), blood sampling should be made after fasting 12 hours</td>
<td>(Fasting) LDL cholesterol is treatment target</td>
<td>Elevated non-fasting triglycerides ≥200 mg/dL should be repeated fasting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total and HDL cholesterol can be determined in non-fasting samples</td>
<td>(Fasting or non-fasting) Non-HDL cholesterol is secondary target in people with diabetes, metabolic syndrome, combined hyperlipidemias, or chronic kidney disease</td>
<td>If ≥500 mg/dL, screen for secondary causes</td>
</tr>
<tr>
<td>Canadian Hypertension Education Program Guidelines (7)</td>
<td>2016</td>
<td>A fasting sample is no longer required, non-fasting is equally appropriate.</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

The recommended laboratory report for non-fasting abnormal values based on desirable concentration cut-points are:

- triglycerides $\geq 175$ mg/dl
- total cholesterol $\geq 190$ mg/dl
- LDL-C $\geq 115$ mg/dl
- non-HDL-C $\geq 155$ mg/dl
- Lp(a) $\geq 50$ mg/dl
- apo B $\geq 100$ mg/dl
- HDL-C $\leq 40$ mg/dl
- apo A-1 $\leq 125$ mg/dl

The non-HDL cholesterol calculation does not rely on a triglyceride value, so there is no need to fast.

Furthermore, the non-HDL cholesterol value reflects all of the major lipoproteins linked with a higher risk of cardiovascular disease.

Non-HDL cholesterol level goal should be 30 mg/dL higher than the LDL cholesterol level goal e.g. if aim is for an LDL cholesterol of 100 mg/dL, then the goal for non-HDL should be 130 mg/dL.

Key Messages

- There's going to be a gradual trend to see more and more non-fasting lipid tests, but it's going to require education of our patients to not come in after a very high-fat meal the day of testing.

- A non-fasting sample could be used if the patient has just eaten a meal with less than 15 g of fat.

- The international writing committee of experts from eight European countries, Australia, and the US add the caveats that clinicians should consider repeating a non-fasting lipid profile test with a fasting test if plasma TG are above 5 mmol/L (440 mg/dL), and importantly, they should immediately refer a patient with life-threatening or extremely high concentrations of TG or LDL-C to a lipid clinic or a physician who specializes in lipid disorders.

- Laboratory reports should flag abnormally high non-fasting lipid values.

https://www.medscape.com/viewarticle/862837#vp_2
**Test Done at SRL**

<table>
<thead>
<tr>
<th>TEST</th>
<th>METHOD</th>
<th>CODE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Profile-Non-fasting (Total cholesterol, LDL cholesterol, HDL cholesterol, Non HDL cholesterol)</td>
<td>Biochemistry</td>
<td>1209ADNF</td>
</tr>
</tbody>
</table>
Thank You