2012 Update of the Canadian Cardiovascular Society Dyslipidemia Guidelines

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Smith's Case

Mr. Smith is a 49-year-old, asymptomatic man with no history of vascular disease. He is a lifetime nonsmoker and has no family history of premature vascular disease. He has no inflammatory conditions and is on no medications. His blood pressure is 145/90 mmHg, BMI is 28, and waist circumference is 92 cm. His glucose is 5.5, total cholesterol 5.6 mmol/L, LDL-C is 3.3 mmol/L, HDL-C is 0.9 mmol/L and triglycerides are 3.0 mmol/L. His eGFR is > 60ml/min/1.73m.^{2} His FRS is 13% and, thus, classified as intermediate risk.

Based on the current guidelines, in addition to lifestyle modification, should he be considered for statin therapy?

There are several key changes in the 2012 Update of the Canadian Cardiovascular Society Dyslipidemia guidelines that will be highlighted. The primary panel concentrated the update on the following: **1)** risk assessment, **2)** secondary testing, **3)** lifestyle and behaviour modification and **4)** statin intolerance.[1]

Risk Assessment

The decision to measure a lipid profile needs to be coupled with CV risk assessment. Men ≥ 40 years and women ≥ 50 years of age (or post-menopausal) should be screened. Subjects with higher risk features, including traditional risk factors and inflammatory conditions, should be screened regardless of age. The Framingham risk score (FRS) has been recommended to classify subjects as low (< 10%), intermediate (10 to 19%), or high (≥ 20% per 10 years) risk (see Table 1). New in the guidelines is the recommendation to double the FRS per cent risk in subjects who have a family history of premature vascular disease (< 55 years for first-degree male relatives, < 65 years for females).

The decision to treat with statins will be based on the risk assessment and the level of low density lipoprotein cholesterol (LDL-C). Another change this year recognizes that nonHDL-cholesterol (nonHDL-C) (total cholesterol minus HDL-C), like apolipoprotein B (apoB is an alternate marker of atherogenic risk.[2] It is strongly associated with CV outcomes, can be calculated from the standard lipid panel without additional testing, and is valid in a nonfasting state or when LDL-C is not calculated due to high triglyceride levels.

In general, low-risk individuals will not be treated with statins. High-risk subjects that include those with an FRS ≥ 20% and many with diabetes, high-risk hypertension, and chronic kidney disease (new recommendation) should be considered for statin therapy. Intermediate risk subjects should be considered for statin therapy if **a)** LDL-C is ≥ 3.5 mmol/L, **b)** apoB ≥ 1.2 g/L or nonHDL-C ≥ 4.3 mmol/L, or **c)** a secondary test suggests a higher risk.

Secondary Testing

The vast majority of subjects can be risk stratified using a FRS history and lipid biochemistry. A secondary test should only be utilized in subjects who do not qualify for statin therapy but would consider it if a secondary test suggested an increased risk. These should be used after an extensive discussion between the health care

Table 1: Target Levels

Risk Level	When to Initiate Therapy	Primary Target LDL-C	Alternate Target
High	• Consider treatment in all cases (Strong, High)	• ≤ 2 mmol/L or 50% decrease in LDL-C (Strong/High)	• ApoB ≤ 0.8 g/L (Strong/Moderate)
Intermediate	• LDL-C ≥ 3.5 mmol/L (Strong, Moderate) • Consider if Apo B ≥ 1.2 g/L or NonHDL-C ≥ 4.3 mmol/L (Conditional Moderate)	• ≤ 2 mmol/L or 50% decrease in LDL-C (Strong, High)	• ApoB ≤ o.8 mg/L NonHDL-C ≤ 2.6 mmol/L • (Conditional Moderate)
Low*	• LDL-C ≥ 5.0 mmol/L • Familial hypercholesterolemia (Strong, Moderate)	• 50% reduction in LDL-C (Strong, Moderate)	

** For those in the 6 to 9% group, consider yearly calculation of FRS and discussion about the risk-to-benefit ratio of pharmacotherapy at lower levels of LDL-C*

provider and patient has taken place. In addition, we have not recommended multiple tests, as these strategies have not been tested in trials. Many markers could have been included; however, the new guidelines limited discussion to **1)** biochemical markers, including lipoprotein(a), hs-CRP, HbA1c, and urine albumin/creatinine ratio, and noninvasive testing, including exercise stress test, ankle-brachial index, carotid US, and coronary calcium scoring. Clinicians should choose tests based on the clinical scenario, local expertise, and availability.

Lifestyle Modification

Individuals in all risk categories should be encouraged to adopt healthy eating habits to lower risk. Favourable effects on risk can be expected with a diet that promotes a healthy weight. Specific recommendations included the Mediterranean, Dietary Approaches to Stop Hypertension, and Portfolio diets. It is also recommended that 150 min/week of moderate-intensity exercise be incorporated into one's routine. Smoking cessation and alcohol consumption in moderation (< 30 g/day) are also key elements.

Smith's Case Continued

Mr. Smith has an LDL-C that is below the threshold for intermediate risk (≥ 3.5 mmol/L); however, his nonHDL-C is 5.5 - 0.9 = 4.6 mmol/L. This is above the ≥ 4.3 mmol/L cut-off that warrants consideration for statin therapy. As such, secondary testing would not be required. Mr. Smith will embark on lifestyle modification and started on statin therapy.

Statins

In individuals that require pharmacotherapy, statins are first-line therapy based on a wealth of randomized trial data.[3] The relative risk reduction (approximately 22% per 1 mmol/L reduction in LDL-C) is fairly independent of baseline risk. Thus, the expected clinical benefit is higher in subjects at higher risk, and we should be more persistent in keeping those subjects on therapy. At least 10% of subjects will have some difficulty with statin therapy, usually in the form of muscle aches. A standardized approach to managing these side effects is important.[4] To date, no supplements have been shown to decrease statin-induced myalgias.

Frequently Asked Questions

1. I am not in the practice of calculating FRS. Is it really that important to do?

a. There are many tools to help measure FRS, including online solutions, and this can usually be done within a minute or so. Since treatment decisions require an evaluation of the risk level and treatment may be life-long, it is time well spent.

2. Once I initiate someone on statin therapy what blood work is required in follow-up?

a. A baseline alanine transaminase (ALT) should be measured prior to starting treatment. Subsequently, routine measurement of ALT or creatine kinase is not required unless there is a clinical reason to do so. Once at target, yearly measurement of the lipid profile is all that is required.

3. How important is it for patients to fast prior to lipid determination?

a. For the majority of patients, fasting doesn't alter LDL-C more than a few per cent, but this may be important for subjects with post-prandial dyslipidemia. As such, we have still recommended a 12 hour fast. For subjects in whom fasting is not accomplished, nonHDL-C or apolipoprotein B are accurate risk markers and can be used.

4. When do I consider using lipid-lowering drugs other than statins?

a. Nonstatin lipid modulating agents should be considered in subjects who can not tolerate moderate dose statins or who do not achieve goal LDL-C levels and are at high risk. The data for combination therapy and CV risk reduction has not been established (except for the SHARP study). The level of persistence with low dose statins, alternate agents, or combination therapy should be directly related to the clinical scenario and underlying risk.

5. My patients like to use co-enzyme Q10 or vitamin D to prevent muscle aches on statins. Is there any evidence to support this?

a. No, the data to date do not suggest that these supplements are of benefit for the prevention or treatment of statin-induced muscle aches.

Take-home Message

1. The decision to measure a lipid profile should be accompanied by a FRS to assess CV risk.
2. LDL-C remains the primary treatment target. NonHDL-C has been added to apolipoprotein B as an alternate target.
3. The use of secondary testing should be used sparingly and only when it will lead to a change in treatment decision.
4. Lifestyle modification in diet and exercise is the cornerstone of risk reduction.
5. Statins are first-line therapy and an approach to statin side effects is important in the overall management of CV risk.

Summary

The 2012 dyslipidemia guidelines stressed the need for a systematic risk assessment at the time of measurement of a lipid profile. The importance of nonHDL-C, chronic kidney disease as a high-risk feature, lifestyle modification, and statin therapy was emphasized. The goal is to identify subjects who will benefit from therapy, reducing the burden of CV morbidity and mortality in Canada.

References

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