VOLUME 06
ISSUE 01

CLINICAL PRACTICE UPDATE IN
ENDOCRINOLOGY & DIABETES

Dyslipidemia

Robert Schlosser
MD, FRCPC

The 2009 Canadian guidelines for the diagnosis and treatment of dyslipidemia and the prevention of cardiovascular disease in the adult were published in the October 2009 issue of the Canadian Journal of Cardiology[1]. They provide the latest evidence-based recommendations and standards for identifying patients at risk, lipid modification and CVD prevention.

The recommended screening strategy for adult patients is a full lipid profile every 1 to 3 years. This strategy encompasses men aged 40 or over and women aged 50 or over, but also a patient of any age with the traditional risk factors listed above or evidence of atherosclerosis in any vascular bed. Several other medical conditions suggest the need for early screening, including HIV infection treated with antiretroviral therapy, erectile dysfunction, chronic renal disease, and autoimmune disorders associated with chronic inflammation, such as rheumatoid arthritis, systemic lupus and psoriasis.

The Framingham Risk Score (FRS) has been utilized for many years as a reliable risk calculator. It provides a reasonable estimate of the 10-year risk of a major CV event for a large portion of the Canadian population. However, the FRS does not account for family history of premature coronary artery disease which increases risk 1.7-fold in women and 2.0-fold in men.

Also pertinent is that risk evolves with time. In fact, patient age is the single most powerful driver of CV risk. Accordingly, a patient's risk for CVD should be reassessed every 3 to 5 years.

The 2009 guidelines acknowledge the limitations of the Framingham Risk Score for coronary artery disease. The consensus panel now recommends the modified FRS for total CVD (includes stroke), which is in line with the recommendations put forth by the Canadian Hypertension Education Program (CHEP) and the Canadian Diabetes Association (CDA). The panel also suggests the Reynolds Risk Score as an alternative tool that takes into account both hsCRP and family history.

CVD Risk for Women

POINTS	AGE	HDL-C mmol/L	Total Choles	SBP Not Treated	SBP Treated	SMOKER	DiABETIC
-3				<120			
-2		>1.6					
-1		1.3-1.6			<120		
0	30-34	1.2-1.3	<4.1	120-129		NO	NO
1		0.9-1.2	4.1-5.2	130-139			
2	35-39	<0.9		140-149	120-129		
3			5.2-6.2		130-139	YES	
4	40-44		6.2-7.2	150-159			YES
5	45-49		<7.2	>160	140-149		
6					150-159		
7	50-54				160+		
8	55-59						
9	60-64						
10	65-69						
11	70-74						
12	75+						

TOTAL POINTS

POINTS ALLOTTED

CVD Risk for Men

POINTS	AGE	HDL-C mmol/L	Total Choles	SBP Not Treated	SBP Treated	SMOKER	DiABETIC
-2		>1.6		<120			
-1		1.3-1.6				NO	NO
0	30-34	1.2-1.3	<4.1	120-129	<120		
1		0.9-1.2	4.1-5.2	130-139			
2	35-39	<0.9	5.2-6.2	140-149	120-129		
3			6.2-7.2	160+	130-139		YES
4			<7.2		140-159	YES	
5	40-44				160+		
6							
7	45-49						
8	50-54						
9							
10	55-59						
11	60-64						
12							
13	65-69						
14	70-74						
15	75+						

TOTAL POINTS

POINTS ALLOTTED

CVD Risk for Women

POINTS	RISK	POINTS	RISK	POINTS	RISK
-2 or less	<1%	6	3.3%	14	11.7%
-1	1.0%	7	3.9%	15	13.7%
0	1.2%	8	4.5%	16	15.9%
1	1.5%	9	5.3%	17	18.5%
2	1.7%	10	6.3%	18	21.5%
3	2.0%	11	7.3%	19	24.8%
4	2.4%	12	8.6%	20	27.7%
5	2.8%	13	10.0%	21+	>30%

The 2009 lipid guidelines retain the high, moderate and low-risk categories according to the modified Framingham Risk Score. High-risk patients are defined by having a calculated 10-year risk of at least 20% or established atherosclerotic disease or diabetes (most patients) and generally require immediate treatment (lifestyle behaviors and drug therapy). Treatment should be considered for moderate-risk patients (FRS 10-year risk 10-19%) who fit certain criteria such as: LDL-C > 3.5 mmol/L, TC/HDL-C ratio > 5 or hsCRP > 2 mg/L for men > 50 and women > 60 years of age.

An important change is that for both high-risk and moderate-risk patients, the LDL-C goal is < 2 mmol/L OR at least a 50% reduction from baseline. Low-risk patients (FRS < 10%) for whom lipid-lowering therapy is deemed appropriate should seek to lower their LDL-C by at least 50% from baseline.

CVD Risk for Men

POINTS	RISK	POINTS	RISK	POINTS	RISK
-3 or less	<1%	5	3.9%	13	15.6%
-2	1.1%	6	4.7%	14	18.4%
-1	1.4%	7	5.6%	15	21.6%
0	1.6%	8	6.7%	16	25.3%
1	1.9%	9	7.9%	17	29.4%
2	2.3%	10	9.4%	18+	>30%
3	2.8%	11	11.2%		
4	3.3%	12	13.3%		

2009 Dyslipidemia Recommendation summary table:

Risk Assessment	Initiate/Consider Treatment If Any of the Following	Primary Target: LDL-C	Class, Level
HIGH CAD PAD Atherosclerosis Most diabetic pts FRS ≥ 20% RRS ≥ 20%	Consider treatment in all patients	LDL-C < 2 mmol/L or ≥ 50% ↓ LDL-C Primary **Alternate** Target: Apo B < 0.80 g/L	Class I, Level A
MODERATE FRS 10%–19%	• LDL-C > 3.5 mmol/L • TC/HDL-C > 5.0 • hsCRP > 2 mg/L* - in men > 50, women > 60 • Family history and/or hsCRP modulates risk (RRS)		Class IIa, Level A
LOW FRS < 10%	• LDL-C > 5.0 mmol/L	≥ 50% ↓ LDL-C	Class IIa, Level A

A hsCRP level should not be measured in high risk individuals since treatment is already indicated on the basis of clinical risk. This test is typically only required in men > 50 years and in women > 60 years who are at moderate risk for CVD (by FRS) and whose level of LDL-C is < 3.5 mmol/L, because these individuals—if they also have elevated hsCRP—have been shown to benefit from statin therapy in the JUPITER study[2]. The lower of 2 hsCRP values taken at least 2 weeks apart in the absence of acute inflammatory illness should be used.

The JUPITER study demonstrated that moderate-risk patients > age 50 (men) or > age 60 (women) with no history of CVD or diabetes and baseline CRP > 2mg/L who were treated with rosuvastatin 20mg/day were significantly less likely to experience the primary composite CV endpoint as well as mortality. At the time of the JUPITER study termination (median follow-up 1.9 years), 142 first major CV events had occurred in the rosuvastatin group and 251 in the placebo group. This represented a 44% relative risk reduction and an absolute risk reduction of 1.2% (HR: 0.56; 95% CI: 0.46 to 0.69; p<0.00001). The number needed to treat (NNT) was 95. If projected out to 5 years, the NNT would be 25.

In a recent retrospective substudy[3], application of the 2009 Canadian lipid guidelines was examined in the JUPITER trial population consisting of 6091 participants with baseline estimated 10-year Framingham risks of 5% to 10% and 7340 participants with baseline estimated Framingham risk of 11% to 20%. In these 2 "intermediate risk" subgroups, relative risk reductions consistent with the overall trial treatment effect were observed: 49% risk reduction with FRS 10-20% (5 year NNT estimate = 18) and 45% risk reduction with FRS 5-10% (5 year NNT estimate = 40). Use of the Reynolds Risk Score to stratify the study population gave similar results.

A meta-analysis by Robinson et al[4] examined the relationship between percent relative reduction of LDL-C and the resulting absolute reduction of nonfatal MI and CHD mortality. There appears to be a linear relationship between % LDL-C reduction and reduction of CHD events (approximately 1% CVD risk reduction for every 1% LDL-C reduction) irrespective of the method of cholesterol reduction, although statin trials show the most benefit presumably due to their more potent LDL-C reducing efficacy. Therefore, a 50% reduction in LDL-C is recommended as an alternative target.

Most patients will be able to achieve their LDL-C target with statin monotherapy. Some may require combination therapy – a statin plus a cholesterol absorption inhibitor (ezetimibe) or bile acid binder (cholestyramine, colestipol); or a statin plus niacin or a fibrate. These combinations are generally safe and can decrease LDL-C by an additional 10% to 30%. Data is still lacking on the clinical benefits of combination therapy, but clinical endpoint trials are now in progress. In the recently published ACCORD-LIPID trial[5], combination therapy with fenofibrate and simvastatin failed to reduce the risk of cardiovascular events, in patients with type 2 diabetes who were at high risk. However, there was a suggestion of benefit observed among patients with higher triglyceride and lower HDL-cholesterol levels.

In summary, the 2009 Canadian Lipid Guidelines represent a significant evolutionary step in the management of patients with dyslipidemia. The main changes include more precise estimation of global cardiovascular risk, as well as simplified but still aggressive targets for high and moderate risk patients, incorporating the most recent clinical trial evidence.

References

1. Genest J et al. 2009 Canadian Cardiovascular Society: Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult. Can J Cardiol 2009;25(10):567–79

2. Ridker P et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008;359:2195–207.

3. Ridker PM et al, Rosuvastatin for primary prevention among individuals with elevated high-sensitivity C-reactive protein and 5% to 10% and 10% to 20% 10-year risk in the JUPITER trial. Circ Cardiovasc Qual Outcomes. 2010;3:5 447-452

4. Robinson JG, Smith B, Maheshwari N, et al. Pleiotropic effects of statins: benefit beyond cholesterol reduction? A meta-regression analysis. J Am Coll Cardiol 2005; 46(10):1855-62.

5. The ACCORD Study Group. Effects of Combination Lipid Therapy in Type 2 Diabetes Melitus.N Engl J Med 2010; 362:1563-1574

a closer look at the Mediterranean Diet for patients with Dyslipidemia

What is the Mediterranean diet?

Based on the traditional dietary patterns of Southern Italy, Crete and most of Greece this diet emphasizes large consumption of vegetables, fresh fruits, legumes, unrefined cereals, the use of olive oil as the predominant source of fat, yogurt and cheese, fish, poultry, nuts and small amounts if any of red meat. Red wine is also included in moderation. Patients who are currently treating their dyslipidemia with medication could also benefit from the adoption of a Mediterranean style diet. Some studies illustrated a further 20-30% reduction of LDL following inclusion of a reduced fat Mediterranean diet to their current medication regime.

MEATS AND ALTERNATIVES

- Choose fatty fish rich in omega-3 (3oz) 2/week (salmon, mackerel, trout, sardines, herring), other fishes
- Add legumes to soups, salads, and side dishes
- Remove skin from poultry
- Maximum 4 eggs/wk (no restriction for egg whites)

DAIRY

- Select cheeses with <20% M.F
- Choose skim or 1% milk and yogurts < 2% M.F

FATS

- Choose extra-virgin olive oil 4-6 tsp/day
- Avoid butter and hydrogenated margarines
- Choose nuts as a snack (1/4 cup)

ALCOHOL

- Limit/avoid if triglycerides are high
- Men 2 drinks/day, women 1 drink/day (4oz red wine)

Example of Mediterranean Diet

DAY ONE

breakfast:
3/4 cup of plain yogurt (<2%M.F.)
1 cup of berries
2 tbsp of sliced almonds

snack:
1 pear or 1 nectarine

lunch:
1 cup of sliced tomatoes, cucumbers
1 oz (30g) feta cheese (< 20% M.F)
1 tsp of olive oil, lemon juice and pepper to taste
1 slices of whole wheat bread
3 chopped sardines
4 olives
1 cups of lentil soup (with spinach, onions, carrots, celery)
1 apple or 1 orange or 15 grapes

snack:
1 cup of carrots and celery
1/4 cup of hummus

supper:
4 oz (120g) of salmon grilled with garlic, basil
1 tsp of olive oil
1 cup grilled vegetables (peppers, onions, mushrooms)
1 medium potato sliced and grilled
1 tsp of olive oil
3/4 cup of yogurt (<2% M.F)

DAY TWO

breakfast:
2 slices of whole wheat bread
1 egg
1 tsp of olive oil
1 cup of sliced tomatoes and cucumbers

snack:
3/4 cup yogurt

lunch:
1 cup of cooked whole wheat pasta
4 oz chicken breast grilled cut into strips
1 cup of broccoli, cauliflower, onions, and garlic
1/4 cup of olives
1 tsp of olive oil
1/2 cup of artichoke hearts
1/2 cup of tomatoes
15-20 grapes or 1 cup of melon

snack:
1/4 cup of walnuts

supper:
1 cup of legumes (chickpeas, red kidney beans, navy beans) cooked with tomatoes, celery and spices
3 oz fish grilled with garlic and olive oil
1 ½ cup of green salad (romaine lettuce, endives, etc)
1 tsp olive oil, lemon juice and pepper to taste
½ cup of yogurt (<2% M.F)
½ cup of berries

Supported by educational grants from members of the pharmaceutical industry.