Reducing Cardiovascular Events in High-Risk Patients

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Although the age-adjusted incidence of acute CV events such as MI, stroke and CV sudden death has diminished over the past 30 years, CVD remains the most frequent cause of death. Prevention of CVD overall is a societal responsibility with an urgent need to improve healthy lifestyles including promoting smoking cessation, increased physical exertion and a healthy diet. However, the identification and initiation of preventative strategies in high-risk individuals remains the responsibility of the physician.

Identification of high-risk patients (Figure 1)

The presence of symptomatic, atherosclerotic vascular disease in any territory is associated with an increased risk for MI, stroke and CV death. The detection of silent atherosclerotic disease by carotid artery ultrasound, coronary CT angiogram or lower-limb ankle brachial index also justifies a high-risk classification. Diabetes and chronic kidney disease are both associated with a high risk for coronary and cerebrovascular disease. Patients with Type 2 diabetes should be considered high risk if they are male > 40-years-of-age or female > 50-years-of-age. The presence of microvascular disease, especially proteinuria, places the younger patient or the patient with Type 1 diabetes at high vascular risk.[1-2]

For the individual with neither vascular disease nor diabetes, the use of risk tables such as Framingham or the Systematic Coronary Risk Evaluation (SCORE) provide an estimate of the 10-year prognosis. There are limitations with the Framingham risk tables. They were devised in a North American Caucasian population and likely underestimate risk in many other ethnic groups, especially those of South Asian origin. Today, one of the greatest risk factors for CVD is insulin resistance associated with abdominal obesity and metabolic syndrome, which the tables only partly assess. It has been recommended that a patient with an intermediate Framingham 10-year risk (10% to 20%) who has features of metabolic syndrome should be reclassified as high-risk. The risk tables

Meet Justin

Justin, 45, is an accountant. He comes for a routine medical examination. His father had a MI at age 52.

Justin stopped smoking 2 years ago.

- Weight: 102 kg
- BMI: 29
- Waist circumference: 105 cm
- BP: 145/85 mmHg
- Lab total cholesterol (TC): 4.5 mmol/L
- HDL-C: 0.85 mmol/L
- LDL-C: 3.2 mmol/L
- Triglycerides: 2.5
- TC/HDL-C: 5.3
- Creatinine: 120
- Estimated glomerular filtration rate: 55 ml/min
- Fasting glucose: 5.9 mmol/L

Justin has an intermediate Framingham risk score with a 14% risk of heart disease in the next 10 years. An average man of the same age has a risk of 11%.

However, Justin also has a family history of premature coronary disease, metabolic syndrome and renal insufficiency. These additional risk factors increase the 10 year risk to high risk.

For more on Justin, turn to page 17.

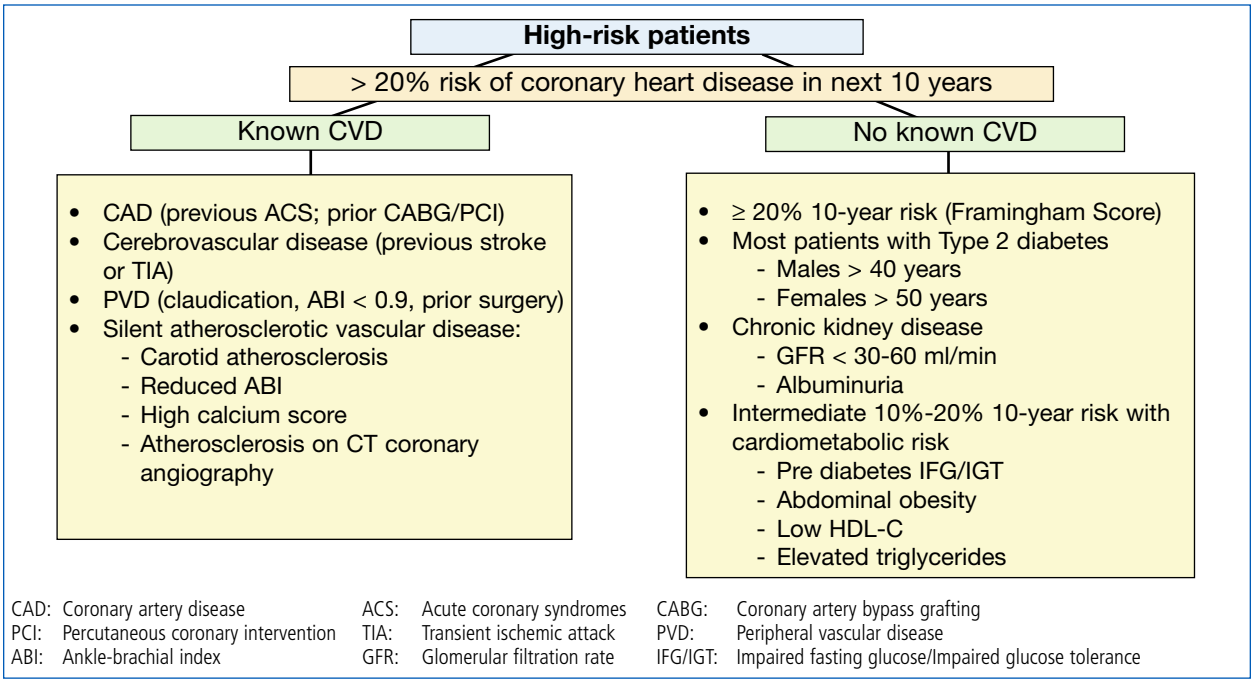

Figure 1. Identification of patients at high-risk for CV events.

also underestimate risk in younger individuals with risk factors such as elevated cholesterol and diabetes, who have a high lifetime risk for CVD. In addition, as absolute risk increases with age, arbitrary cutoffs for intervention may lead to overtreatment in the elderly. Demonstrating evidence of relative high-risk, compared to people of the same age without risk factors, may not only motivate the patient to make lifestyle changes, but also provide justification for pharmacological treatment (*e.g.*, lipid reduction) at an earlier age.

The influence of family history on outcomes is also not considered in most risk tables. Studies have shown that the risk associated with family history of early coronary heart disease (in first-degree relatives, male < 55 years and female < 65 years) is one-half to twofold and is independent of the classical risk factors. Consequently, a patient in the moderate Framingham risk range (10-year risk of 10% to 20%) should probably be considered as high risk if he/she has a first-degree relative with premature coronary heart disease.

Identification and management of patients at high risk for CV disease is a huge challenge (Table 1). Firstly, patients with overt CV disease and most with Type 2 diabetes should be targeted for multifactorial risk reduction. Secondly, a proportion of patients without CVD or diabetes should be screened for CV risk with a lipid profile, blood glucose and urine protein followed by a Framingham risk score. It is suggested that patients with hypertension and those with a family history of premature CVD are groups with a greater incidence of high CV risk, and a good starting point to evaluate risk in patients with no history of CVD.

Management of high CV risk

Patients at high risk for CVD usually require both lifestyle modification and pharmacological treatment to reduce the incidence of vascular complications of stroke, MI and CV death. Lifestyle modification (Table 2) is the most effective strategy to prevent diabetes and CV disease. However, lifestyle modification, especially weight reduction, is not often successfully achieved. To be successful the patient must be motivated and have realistic goals. Patient counselling is crucial if success is to be achieved.

Pharmacological treatment for BP, lipids, glycemic control, as well as medications to modulate the renin angiotensin system and platelet activity

Table 1

Who should we assess for total CV risk?

- All patients with hypertension
- Those with known elevated cholesterol
- Middle-aged smokers
- Those with a family history of premature CVD

History:	Family history, smoking, exercise, diet
Exam:	Weight, height, BMI, waist circumference
Lab:	Fasting glucose, lipid profile, creatinine Urine protein/creatinine ECG
Risk evaluation:	Framingham table, or SCORE chart

SCORE: Systematic Coronary Risk Evaluation.

should be applied (Table 3). For patients with a modest elevation of BP, the addition of an ACE inhibitor or ARB provides both vascular protection and the benefits of BP reduction. Other patients with higher baseline BPs are likely to require several antihypertensive agents to achieve desired targets.

Cholesterol modification with a statin agent has the largest pharmacological contribution to risk reduction. All high-risk patients, irrespective of baseline cholesterol should be considered for statin therapy. The therapeutic goals are to lower LDL-C by 50%, as well as reducing LDL-C to below 2 mmol/l.[3] These targets may be hard to achieve in high-risk patients. The addition of other agents such as ezetimibe or bile acid sequestrants to statins may further lower LDL-C and achieve the therapeutic target. A secondary goal is to reduce the ratio of total cholesterol to HDL-C to < 4. This goal can be achieved with increased dose of statins or by the addition of niacin or a fibrate. For the very high-risk patient with diabetes and coronary heart disease with HDL-C < 0.8 to 0.9, the use of niacin to increase HDL-C should be considered.

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Table 2

Lifestyle modification

- Smoking cessation
  - Group therapy
  - Pharmacological
- Weight control
  - Realistic goal: 5%-10% weight loss
- Increased physical activity
  - 30 minutes moderate activity daily
- Diet
  - Weight loss
  - Low salt
  - Heart healthy choices

A multifactorial strategy for risk reduction is likely to achieve improved outcomes. The STENO 2 trial[4] randomized patients with diabetes and microalbuminuria to either a vigorous risk-reduction strategy (targets total cholesterol < 4.5, BP < 130 to 140/80 to 85 mmHg, A1C < 6.5, as well as treatment with ASA and ACE inhibitor) in a specialized clinic, or to the patient's normal care. Over the four-year course of the randomized study, the patients receiving the aggressive management had a 50% relative lowering of CV events compared to those receiving usual care. When patients were followed for an additional four years,[5] there was a 20% absolute reduction of total mortality for the patients randomized to the multifactorial strategy. Consequently the strategy of improving all risk factors in high-risk patients is likely to have an important impact on survival and the prevention of MI and stroke.

Implementation of CVD risk reduction strategies

Current evidence indicates that management of CV risk factors in high-risk patients is far from optimal.[6] Only half of patients with diabetes receive statins and only half of high-risk patients receiving treatment have LDL-C < 2.5 mmol/L. Target BP control is only achieved in 30% of high-risk patients and glycemic targets are achieved in < 30% of patients with diabetes. Furthermore, there are many high-risk

Table 3
Pharmacological reduction of CV risk: thresholds and goals

	Initiate treatment	Therapeutic goals
BP	Diabetes > 130/80 Others > 140/90	< 130/80 < 140/90
Glycemic	Fasting blood sugar (FBS) > 7 mmol/L	A1C < 7% FBS 4 mmol/L-7 mmol/L
Cholesterol (statin treatment)	All high-risk irrespective of baseline LDL-C	LDL-C < 2.0 mmol/L and reduced by > 50%
ACE inhibitor or ARB	All established CVD and diabetes with other risk factors or target organ damage	Target dose in trials
ASA	All	81 mg q.d.

Justin's case cont'd...

Justin needs to have maximal vascular protective measures to reduce his short term and lifelong CV risk. Lifestyle changes recommended include weight loss, increased physical activity and a heart healthy diet. Pharmacological measures should include a statin to reduce LDL cholesterol 50% to < 2mmol/L, ASA and an ACE inhibitor or an ARB.

patients that are not recognized as such and consequently receive either suboptimal or no treatment.

CV risk management involves making changes for life. Consequently, physicians must respect patients' beliefs, values and choices, even if they do not agree. Changes and treatment must be realistic—lifestyle changes should be attainable and pharmacological treatment should be associated with minimal adverse effects and be affordable. The patient should be involved in management, with encouragement for self-measurement of BP, weight and blood sugar. Furthermore, patients should be aware of laboratory results and the goals of treatment.

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Take-home message

1. Many individuals have the same risk for CV events as those with prior MI or stroke
2. People at high risk for CV events need to be identified
3. A good place to start is with hypertensive individuals and those with a family history of premature CVD
4. Evaluation by Framingham tables may underestimate risk especially with family history of premature CVD, metabolic syndrome, diabetes and chronic kidney disease
5. Lifestyle changes with smoking cessation, weight loss and increased physical activity is recommended for all risk levels
6. Pharmacological measures such as lipid lowering, ASA and ACE inhibitors/ARBs are important for all high-risk patients. BP control and glycemic control are used as necessary to achieve targets

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