

Cardiovascular risk assessment: Identification of individuals at increased risk

Patients with diabetes, kidney disease, and chronic obstructive pulmonary disease should all be considered at increased risk for cardiovascular disease and should receive risk-modifying therapy.

ABSTRACT: Cardiovascular disease is a common clinical entity that accounts for significant morbidity and mortality in British Columbia. Strategies to decrease the impact of cardiovascular disease focus on risk stratification and targeted intervention. Today risk stratification largely relies on the Framingham risk score. Because this measure fails to accurately quantify risk in certain subpopulations, including patients with diabetes or renal insufficiency, clinicians should consider an aggressive approach to cardiovascular disease prevention for patients with these and other risk equivalents, regardless of the patient's Framingham risk score. By intervening early in those with established peripheral or cerebral vascular disease, diabetes, chronic kidney disease, or chronic obstructive pulmonary disease, we can significantly decrease the morbidity of cardiovascular disease in BC.

In 2004, cardiovascular disease (CVD) accounted for approximately 30% of all Canadian deaths, with an age-standardized mortality of approximately 162 per 100 000 population.¹ In 1999, CVD accounted for 36% of all deaths in British Columbia alone.² Along with an excess of premature mortality, CVD results in a significant burden of morbidity and health care cost. In 1998, CVD was the most expensive disease in British Columbia, accounting for 11.6% of the total costs of illness. More than half of these costs were related to premature mortality, loss of productivity, and long-term disability.³

CVD rates vary by age, gender, ethnicity, and socioeconomic and risk factor status, hence the benefit of primary prevention lies in targeted intervention. Although the majority of CVD deaths occur in lower risk individuals, it would not be practical from a cost or humanistic perspective to offer therapy to all low-risk patients, so in these cases accurate risk factor identification and global risk assessment can have a primary beneficial effect.

The current guidelines (2002) from the American College of Cardiology/American Heart Association

(ACC/AHA) recommend screening for the presence of cardiovascular risk factors beginning at age 20.⁴ Major risk indicators such as fasting serum lipid and fasting blood glucose levels should be measured at least every 5 years (and every 2 years if risk factors for hyperlipidemia and diabetes are present). Smoking status, blood pressure, pulse, body mass index, waist circumference, diet, alcohol intake, and physical activity should be assessed at every routine evaluation (at least every 2 years). Family history of premature CVD should be regularly updated.

Global cardiovascular risk evaluation should be undertaken at least every 5 years, beginning at age 40 or earlier if more than two risk factors are present. An estimate of 10-year risk is achieved most practically by obtaining a Framingham risk score (FRS) or using the European Society of Cardiology (ESC) SCORE system.

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In general terms, these cardiovascular risk assessment tools rely on established risk factors such as age, sex, tobacco use, blood pressure, total cholesterol, HDL cholesterol (and in some cases, LDL cholesterol), and diabetes to estimate a 10-year CVD risk. The FRS is based on American study subjects and as a result is the favored North American assessment tool. The ESC SCORE was created to better reflect risk in the European population.

As well as being designed for different populations, these two systems differ in terms of measured outcome. The ESC SCORE estimates the 10-year risk of atherosclerotic death, including outcomes such as MI, aortic dissection, and stroke. As such, it underestimates the total (fatal and nonfatal) event rate by a factor of approximately 2. Using the ESC model, patients are deemed to be at increased risk if they have a 10-year mortality rate of 5% or a 10-year event rate of 10%.⁵ The FRS calculates and estimates risk of a diagnosis of coronary artery disease (CAD) or a clinical event.⁶ In the Framingham model, patients with a 10-year risk of greater than 20% can be considered at a level

of risk similar to a patient with established CVD.⁶

Risk equivalents

While risk assessment scores are accurate and validated in many circumstances, they can be less effective with people who are not of Northern European heritage. The scores are also less reliable for patients with a family history of premature CAD, patients with a single severe risk factor (e.g., arterial hypertension), and patients with diabetes or renal insufficiency.⁷ Patients with these established risk equivalents should be considered at high risk for CVD and managed accordingly.

Diabetes

As of 2004, approximately 1.3 million Canadians, or 4.9% of the population age 12 or older, had been diagnosed with diabetes.⁸ A study by Leiter and colleagues suggests that another 2% of the Canadian population has overt but undiagnosed diabetes, and a further 3.5% has undiagnosed glucose intolerance.⁹

The presence of diabetes is a strong predictor of CAD, with rates of

MI comparable to that of patients who have already had an MI.¹⁰ In the diabetic population, CVD accounts for 16% of all primary care visits, 67% to 75% of all hospitalization days, and is the cause of death in 50% to 80% of patients, with mortality rates almost twice that of the age-matched general population.¹¹⁻¹³ Contrast this with the rate of death directly attributable to diabetes, a mere fraction of the cardiovascular mortality rate in this population (Figure 1).¹²

This excess rate of CVD is partly explained by the “ticking clock” hypothesis.¹⁰ It is postulated that a prolonged period of subclinical insulin resistance, elevated blood glucose, and metabolic abnormalities exists for up to 10 years before the development of type 2 diabetes and leads to the occurrence of microvascular and macrovascular disease. At the time of diabetes diagnosis, 27% of patients already have established nephropathy, 22% have established retinopathy, and up to 50% have established CVD.¹³⁻¹⁶

So what can be done about this increased risk? The first step involves recognizing that these patients are at high risk for the development of CVD

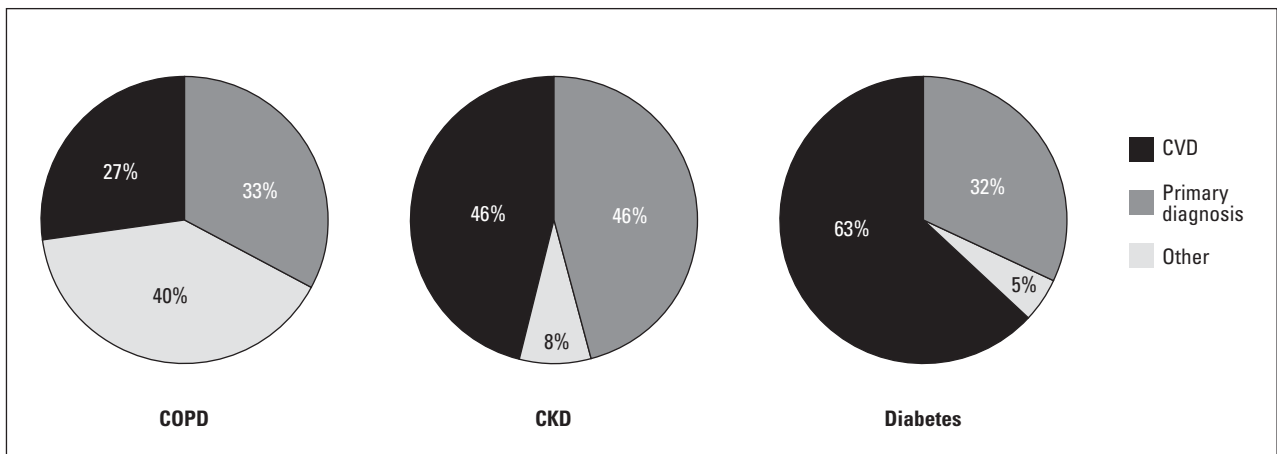


Figure 1. Causes of death for patients with a primary diagnosis of either chronic obstructive pulmonary disease, chronic kidney disease, or diabetes. Rates of death directly attributable to cardiovascular disease are compared with those attributable to the primary diagnosis and other causes of mortality.

and that once CVD does develop these patients have a poorer prognosis than those without concurrent CVD.¹⁰ The second step involves initiating appropriate therapies. Many trials with common cardiovascular medications have shown these agents to have beneficial effects on cardiovascular

lent by the AHA.²³ For every stage of CKD, CVD is the leading cause of death, with an exponential increase in cardiovascular mortality as renal function declines.^{23,24} In fact, the large majority of CKD patients are much more likely to die of CVD before they require renal replacement therapy.²³

derive benefit from these therapies, often to a similar extent as those with preserved renal function.^{23,25}

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events and overall mortality. Aspirin is universally recommended for primary and secondary prevention of CVD in diabetic patients.¹⁷ Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have been shown to improve cardiovascular outcomes in diabetic patients with or without hypertension in multiple large trials.¹⁸⁻²⁰ Similarly, significant benefits have been shown for primary and secondary prevention of CVD with statins in all diabetic patients, regardless of their LDL cholesterol levels.²¹ Despite the knowledge of the almost universal beneficial effect, recent studies have shown that these medications are “systematically underused for patients with diabetes, even among those with established atherosclerotic disease.”²²

Chronic kidney disease

Like diabetes, chronic kidney disease (CKD) is a common problem and one that affects an estimated 2 million Canadians. CKD has also been identified as a cardiovascular risk equiva-

Part of this excess risk is explained by the high burden of traditional risk factors present in the CKD population.²³ However, the altered metabolic milieu of CKD also brings a significant burden of novel risk factors that have been associated with increased cardiovascular risk. Specifically, CKD patients have excessively high rates of anemia, inflammation, mineral metabolism abnormalities, and hemodynamic overload.²³ Despite controlling for these standard risk factors, CKD remains a powerful predictor for future cardiovascular events, prompting the AHA to recommend that patients with CKD should be “considered in the highest-risk group.”²³

Despite their high risk, CKD patients are less likely to receive aggressive risk factor modification with therapies that are proven to be beneficial in patients with normal renal function.²⁵ Specifically, prescription rates of ASA, beta blockers (BB), statins, and ACEIs appear to be inversely related to renal function despite the fact that patients with CKD of all stages do

Emerging risk equivalent: COPD

A recent analysis of the mortality in the GOLD study confirmed that patients with mild to moderate COPD are “more likely... to be hospitalized with or die from CV causes” than they are from COPD itself.^{26,27} Like CKD, part of this risk may be due to a commonality of risk factors, but after adjusting for age, gender, and CV risk factors, the prevalence of CVD still increased with COPD severity, leading to claims that COPD itself is an “independent risk factor for CVD.”^{26,28} Recently there has emerged the concept of a common “chronic systemic inflammatory syndrome” that underlies such disparate diagnoses as heart failure (HF), CAD, hypertension, diabetes, as well as COPD.^{27,29} If true, it would be expected that targeted intervention should exert beneficial effects in the COPD population and reduce clinically significant endpoints.

COPD patients, like patients with diabetes and CKD, have benefited from therapy with statins, ACEIs, and beta blockers. A recent Canadian study demonstrated that the combination of statins and either ACEIs or ARBs resulted in a significant reduction in pulmonary as well as cardiovascular outcomes (COPD hospitalization, MI, overall mortality).³⁰ The authors concluded that a dual “cardiopulmonary protective” effect may exist for these medications, explaining their beneficial effect on COPD patient mortality. Similarly, a mortality benefit has been shown for beta blockers in patients with COPD and concomitant CVD.^{31,32} Traditionally the concerns about pulmonary tolerability have led to the avoidance of this class of medication in patients with respiratory diseases. However, two

studies from 2002 directly addressed this issue. A large meta-analysis by Salpeter and colleagues concluded that “cardioselective beta-blockers do not produce clinically significant adverse respiratory effects in patients with mild to moderate reactive airway disease” or chronic airway obstruction and they “should not be withheld from patients.”³¹ Similarly Kotlyar and colleagues showed that carvedilol was safe in patients with heart failure and COPD, and that this group of patients achieved substantial cardiac benefits from the treatment.³²

Conclusions

CVD is a common clinical entity that was responsible for 30% of all Canadian deaths in 2004.¹ In comparison, the sum of the total annual Canadian mortality directly attributable to diabetes, CKD, and COPD only approximates 40% of the annual cardiovascular mortality (see Figure 2).

Although the majority of CVD deaths occur in lower risk individuals, it would not be practical to offer therapy to all patients. As the benefit of preventive therapy lies in targeted intervention, we should concentrate on risk stratification and more effective disease prevention and modification.

Recognizing the problem

As of 1 July 2007 the population of British Columbia was estimated to be 4 380 256.³³ Using current prevalence estimates, we can expect that approximately 440 000 British Columbians have COPD, 440 000 have diabetes, and nearly 701 000 have CKD. While there will be significant overlap among these groups of patients, it is clear that a significant number of British Columbians, perhaps as many as 1 million, may have already developed CVD that is not yet clinically apparent. As outlined above, the prevalence of CVD

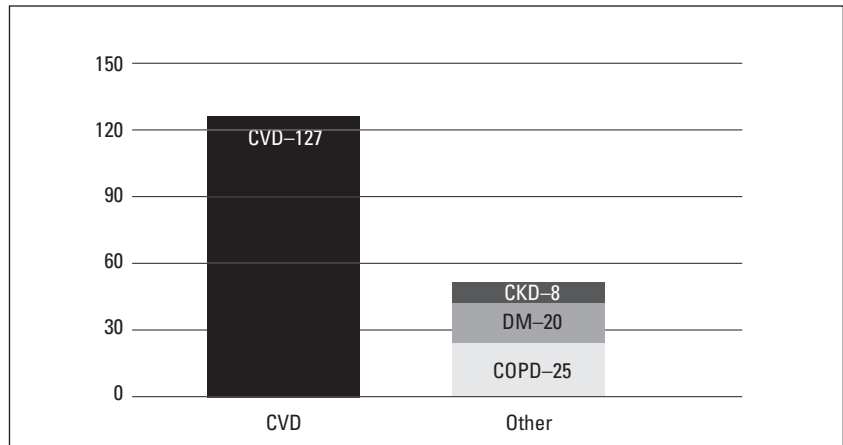


Figure 2. Total Canadian mortality in 2004 from cardiovascular disease or selected risk equivalents: chronic kidney disease, diabetes mellitus, and chronic obstructive pulmonary disease.

in these populations is disproportionately high (Figure 3), with up to 80% of patients with diabetes or CKD dying a cardiovascular death. While it is difficult to provide exact numbers, if these patients are added to those already diagnosed with established CVD (i.e., patients with CAD, peripheral vascular disease, or stroke) there may be as many as 1.5 million people, or up to one-third of the BC population, who require aggressive lifestyle and pharmacologic intervention.

Expanding the CDM program

BC physicians must become leaders in risk stratification and intervention. The fact that family physicians in British Columbia are now paid for using the FRS to assess cardiovascular risk is a step in the right direction. However, the relative undertreatment of CVD requires that this process be taken further. For those patients without a risk equivalent it is reasonable to continue with extensive risk evaluation using the FRS as outlined above

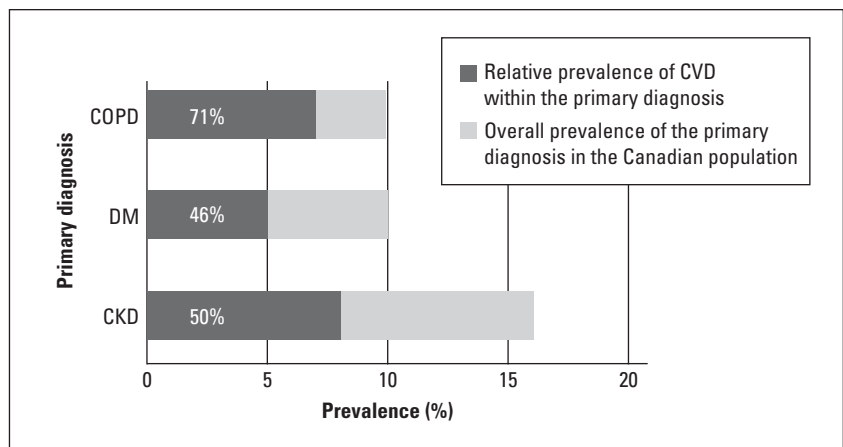


Figure 3. Prevalence of COPD, DM, and CKD in the Canadian population, showing the relative prevalence of CVD within those groups.

and in the 2002 ACC/AHA guidelines, but for those patients with a known CVD risk equivalent, such as diabetes, CKD, or COPD, it is reasonable to forgo formal risk stratification with the FRS and simply initiate therapy

For those patients with a known CVD risk equivalent, such as diabetes, CKD, or COPD, it is reasonable to forgo formal risk stratification with the FRS and simply initiate therapy to current secondary prevention targets.

to current secondary prevention targets. Patients with diabetes and CKD, and most probably COPD, should be added to the CDM program established by the BC Ministry of Health and the British Columbia Medical Association. By ensuring that more patients at risk receive appropriate disease-modifying therapies we can reduce the burden of CVD in British Columbia. The time to act is now.

Competing interests

None declared.

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