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*Cardiovascular disease (CVD) is a leading cause of morbidity and mortality for both men and women. Among individuals with coronary heart disease (CHD), there are gender differences in clinical epidemiology, prevalence of risk factors, clinical presentation, and quality and outcomes of care. Older adults and older women in particular are at risk for underdiagnosis and suboptimal management of CHD and its risk factors. Adherence to clinical practice guidelines for diagnosis and management of CHD can improve outcomes of care for older men and women with CHD and narrow gender disparities in clinical outcomes.*

*Key words: cardiovascular disease, gender, older adults, quality of care, women's health, coronary heart disease*

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## Introduction

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality for both men and women in Canada, accounting for nearly 40% of all deaths.<sup>1</sup> While mortality rates from CVD have been falling, the prevalence of CVD is expected to rise over the next 25 years as a result of population aging, increased longevity among individuals with CVD, and adverse changes in health behaviours. Among individuals with coronary heart disease (CHD), there are important gender differences in clinical epidemiology, prevalence of risk factors, clinical presentation, and quality and outcomes of care.

The onset of coronary artery disease (CHD) in women lags behind men by about 10 years due to the protective effect of estrogen prior to menopause. More serious outcomes such as myocardial infarction and sudden death may manifest among women as much as 20 years later than in men. Although the prevalence of CHD among women before menopause is lower than that in men, this difference narrows by the seventh decade, and at age 80 prevalence of CHD is nearly equal for women and men.<sup>2</sup> Gender differences in outcomes for heart disease can be explained in part by the fact that women with CHD tend to be older, have more comorbidities, and worse risk profiles than men with CHD. In addi-

tion, physical disability is an independent predictor of CHD mortality, and women with CVD are more likely to report physical disabilities.<sup>3,4</sup> Finally, psychosocial factors affect health outcomes, and older women are more likely to be poor, live alone, and lack social support, all of which increase their risk for suboptimal outcomes and impede health care access.

## Clinical Presentation and Diagnosis: Challenges Related to Aging and Gender

Asymptomatic and undiagnosed CHD is common among older adults, the majority of whom are women, due to their high prevalence of silent myocardial ischemia and "atypical" symptoms. By the seventh decade nearly 70% of individuals have CHD in anatomic studies. In the National Heart, Lung, and Blood Institute-funded Cardiovascular Health Study of risk factors for cardiovascular disease in adults 65 years or older, 38% of older women and 23% of older men who had ECG evidence of a prior myocardial infarction reported no history of myocardial infarction (MI). Six-year mortality rates were similar between those with diagnosed and undiagnosed MI.<sup>5</sup> When symptomatic, women are more likely to present with angina as their first manifestation of CHD, and men are more likely to have an MI as their initial presentation. However, this difference narrows with age, with markedly smaller gender differences in initial presentation after the age of 75.

Increased attention to symptoms associated with CHD among older adults can improve the recognition of CHD in this population. Only about 50% of aging individuals present with classic symptoms for CHD such as chest pain, and when chest pain is present it may be vague, poorly localized, and have atypical characteristics.<sup>6</sup> Exertional dyspnea and fatigue are common presenting symptoms among older men

## Gender and Coronary Heart Disease

and women with CHD. Other manifestations of myocardial ischemia in older adults include syncope, nausea, anorexia, confusion, and dyspnea at rest. Because of reduced activities due to comorbidities such as arthritis and claudication, ischemic symptoms associated with exercise may be less frequent and symptoms may occur at rest or after meals. Women report symptoms more often during daily activities and mental stress than during exercise.<sup>7</sup> Angina may also be precipitated by comorbid conditions such as anemia and thyroid disease, which are prevalent in older women.<sup>2</sup>

Older women may be at particularly high risk for underdiagnosis of CHD due to both age and gender biases in diagnosis.<sup>8,9</sup> A number of studies have found that women are less often referred for diagnostic studies when presenting with symptoms of CHD. In a study of primary care doctors in the U.K. and U.S., Arber *et al.* found that patient gender significantly influenced doctors' diagnostic activities, as women were asked fewer questions, received fewer examinations, and had fewer diagnostic tests ordered for CHD than men with similar presentations.<sup>10</sup> According to American Heart Association/ American College of Cardiology (AHA/ACC) guidelines women benefit equally from risk stratification with commonly used noninvasive cardiac tests as do men when pretest probability is taken into account.<sup>11</sup> In acute coronary syndromes indications for invasive and noninvasive testing are the same for men and women.

Patient-level factors may also attribute to gender differences in diagnosis. Women may be less aware of their risk for CHD. Compared to men, women have been reported to be less likely to attribute their symptoms to cardiac-related

causes or seek timely medical attention for these symptoms. The Heart and Stroke Foundation National Omnibus Survey of 2003 found that 60% of Canadian women felt breast cancer was the leading cause of death, whereas only 17% identified heart disease as the major cause of mortality.<sup>12</sup>

## Gender, Cardiovascular Risk, and Prevention

Contrary to previous belief, the overwhelming majority of CHD can be attributed to conventional risk factors, which are the same for men and women.<sup>13,14</sup> However, there are gender differences in the prevalence and relative contribution of these risk factors to the development of CHD (Table 1, Figure 1). Khot *et al.* found that among individuals with CHD the rate of smoking was higher in men than in women, but the prevalence of diabetes, hyperlipidemia, and hypertension were higher in women than in men.<sup>13</sup> Women were more likely to have multiple CHD risk factors. In analyses stratified by age these gender differences were also present in the geriatric population. In this study, 80–90% of patients with CHD had at least one of these four major risk factors.

The INTERHEART Study, a case-control study of individuals from 52 countries, found that nine cardiovascular risk factors—lipid abnormalities, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, physical inactivity, low fruit and vegetable intake, and alcohol (moderate alcohol use was protective—accounted for 90% of the attributable risk for acute myocardial infarction (AMI) in men and 94% in women.<sup>14</sup> Among both men and women age 65 and older these nine risk factors accounted for 88% of AMI risk. The population attributable risk (PAR) of these risk factors for AMI varied by gender for some risk factors but not for others. For example, abnormal lipids contributed equally to cardiovascular disease in both men (49.5%) and women (47.1%), as did abdominal obesity (19.7% vs. 18.7% respectively). However, the PAR for smoking was greater in men (42.7% vs. 14.8%), while the PARs for psychosocial risk factors (28.8% vs. 45.2%) and hypertension (14.9% vs. 29.0%) were greater in women.

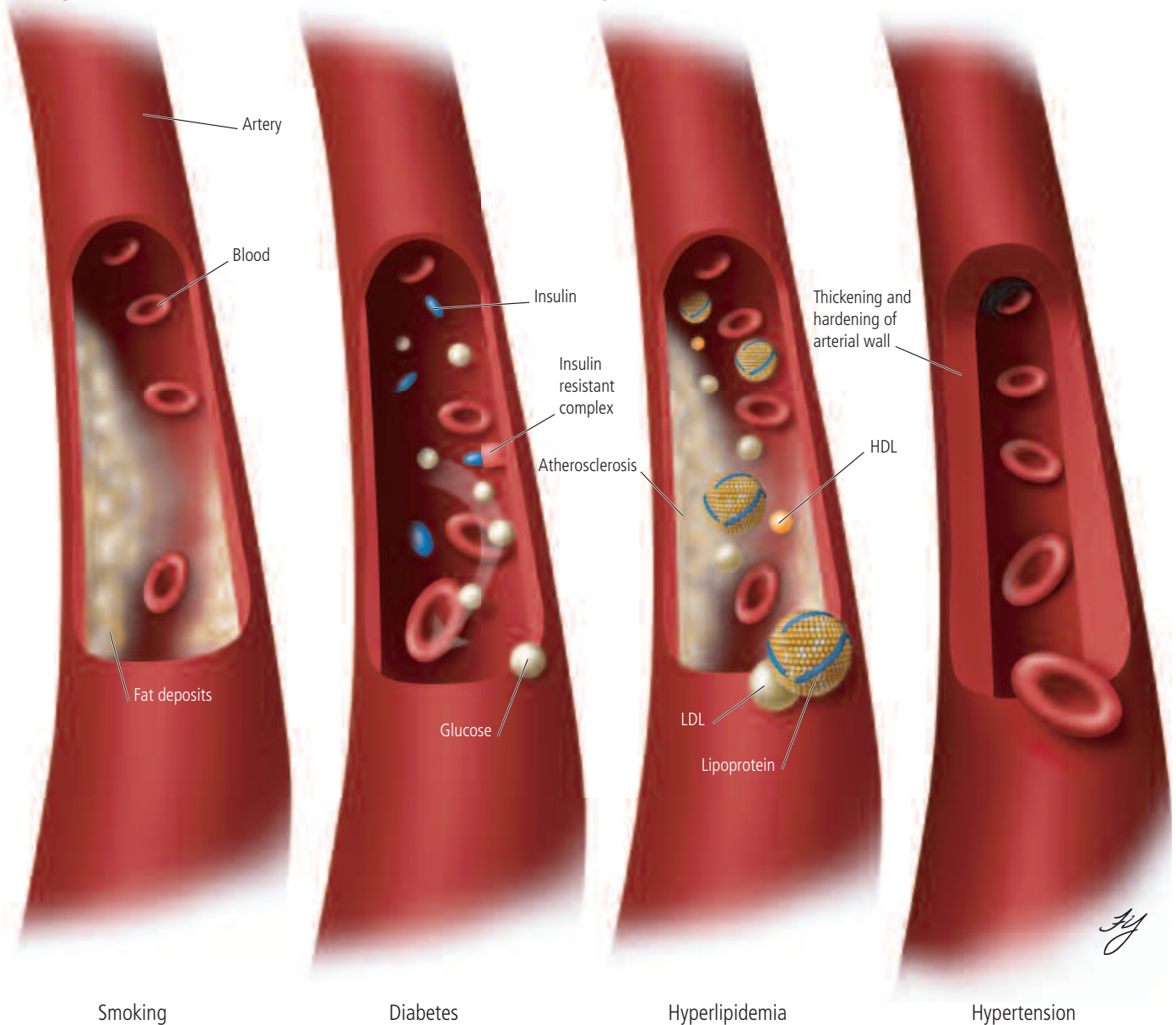
A population-based study in Canada found a high prevalence of modifiable CVD risk factors in the population, with geographic and gender variation in risk factor prevalence.<sup>1</sup> Older adults and women are at risk for suboptimal management of CHD risk factors. A study of older patients with cardiovascular disease and diabetes found not only underuse of lipid-lowering therapy, but that use of this therapy declined with both increasing age and increasing cardiovascular risk.<sup>15</sup> Mosca *et al.* found that gender differences in risk factor management could largely be explained by physicians underestimating risk for women at intermediate risk for CVD according to Framingham risk scores.<sup>16</sup> When risk was correctly assessed there were no gender differences in risk factor management. Online resources for assessing 10-year Framingham risk scores for CVD can be found at the NHLBI website at [www.nhlbi.nih.gov/about/framingham/riskabs.htm](http://www.nhlbi.nih.gov/about/framingham/riskabs.htm).

**Table 1:** Sex Differences in Risk Factors for Coronary Heart Disease

Risk Factors	Women (%)	Men (%)	Women 65–74 (%)	Men 65–74 (%)	Women 75+ (%)	Men 75+ (%)
Smoking	30	42	19	23	8	12
Diabetes	23	15	25	19	22	18
Hyperlipidemia	40	34	42	30	29	20
Hypertension	56	38	60	45	60	43
No. of Risk factors (0–4)						
0	15	19	16	25	23	36
1	37	43	36	42	42	41
2	33	28	35	26	28	19
3	13	9	12	7	7	4
4	1	1	1	1	0	0

Source: Adapted from Khot *et al.*, 2003.<sup>13</sup>

Figure 1: Gender Differences in Risk Factors for Coronary Heart Disease



Smoking can cause an increase in blood pressure and heart rate. Prolonged pressure on vessel walls can result in vascular strain, hardening, and tears. Smoking also leads to fat deposit accumulation on the arterial walls, slowing down blood flow and potentially leading to a myocardial infarction, cancer, low oxygen flow to limbs, emphysema, and low sex drive. The rate of smoking tends to be higher in men versus women.

Individuals with diabetes, such as type II diabetes, can have a resistance to insulin. Resistance to insulin results in a low uptake of glucose into surrounding cells for energy. An increase in blood glucose levels can lead to complications with the heart, eyes, and kidneys. The prevalence of diabetes tends to be higher in women versus men.

Hyperlipidemia is an elevation of lipids in the blood stream. Low-density lipoproteins (LDL) and other non-high-density lipoproteins accumulate cholesterol within the walls of the arteries, slowing down blood flow and increasing blood pressure. High-density lipoproteins (HDL) help to retrieve the cholesterol from the arterial wall and return it to the liver. However, if LDL levels are too high or HDL levels are too low, there is an increased chance for atherosclerosis (narrowing of the vessel wall due to plaque deposit accumulation). Women have a higher prevalence of hyperlipidemia than men.

Hypertension is a condition in which an individual suffers from high blood pressure. The arterial wall may thicken in response to the constant pressure. Potential consequences of hypertension include heart attacks, heart failure, strokes, aneurysms, and atherosclerosis. Hypertension tends to be a higher risk for women versus men.

## Gender and Coronary Heart Disease

Table 2 summarizes evidence-based guidelines developed by the ACC/AHA for the prevention of CVD in women. Based upon risk stratification using Framingham risk scores, they were developed to help close the gender gap in cardiovascular risk factor management.<sup>16</sup> The recommen-

**Table 2:** Priorities for Prevention in Practice According to Framingham Risk Group

### High-risk women (>20% risk)

#### Class I recommendations:

- Smoking cessation
- Physical activity/cardiac rehabilitation
- Diet therapy
- Weight maintenance/reduction
- Blood pressure control
- Lipid control/statin therapy
- Acetylsalicylic acid therapy
- Beta-blocker therapy
- ACE inhibitor therapy (ARBs if contraindicated)
- Glycemic control in diabetics

#### Class IIa recommendation:

- Evaluate/treat for depression

#### Class IIb recommendations:

- Omega 3 fatty-acid supplementation
- Folic acid supplementation

### Intermediate-risk women (10% to 20% risk)

#### Class I recommendations:

- Smoking cessation
- Physical activity
- Heart-healthy diet
- Weight maintenance/reduction
- Blood pressure control
- Lipid control

#### Class IIa recommendations:

- Acetylsalicylic acid therapy

### Lower-risk women (<10% risk)

#### Class I recommendations:

- Smoking cessation
- Physical activity
- Heart-healthy diet
- Weight maintenance/reduction
- Treat individual CVD risk factors as indicated

Source: Mosca L, et al., 2004.<sup>16</sup>

dations include lifestyle interventions (smoking cessation, physical activity, diet), treatment of major risk factors (blood pressure, diabetes, hyperlipidemia), and the utilization of preventive drug interventions (antiplatelet therapy).

## Improving Quality and Outcomes of Care

In multiple studies women have been found to have worse outcomes after acute cardiac events and cardiac procedures in unadjusted analyses. However, when evidence-based interventions are used appropriately in women and confounding factors such as age and comorbidities are controlled for these differences are often small or nonexistent. There is opportunity to improve CHD outcomes among women by addressing the underuse of diagnostic tests and interventions, together with increased attention to risk factor modification and management of comorbid conditions.

Underuse of effective interventions among women has been identified in both ambulatory and hospital settings. Suboptimal screening and treatment of vascular risk factors in women was demonstrated in a recent survey by the AHA; only 60% of high-risk women with CHD had their cholesterol checked in the last year. Men are significantly more likely to be on lipid-lowering therapy than women.<sup>17</sup> In women with known CHD, lipid-lowering therapy can reduce mortality due to CHD by 26%, nonfatal myocardial infarction by 37%, and major CHD events by 21%.<sup>18</sup>

Anand and colleagues found that high-risk women with acute coronary syndromes were less likely than men to undergo coronary angiography, angioplasty, and coronary artery bypass surgery (CABG), and while they do not have a higher incidence of cardiovascular death, recurrent MI, or stroke, they found that women had increased rates of refractory ischemia and rehospitalization postintervention.<sup>9</sup> In the Euro Heart Survey of Stable Angina among patients with stable angina, women who were assessed by a cardiologist were less likely to undergo an exercise ECG, less likely to be referred for coronary angiography, and less likely to be revascularized when coronary disease was confirmed. In addition, antiplatelet and statin therapies were prescribed less frequently in women than men and women had worse outcomes after adjusting for clinical confounders.<sup>19</sup>

Adherence to clinical practice guidelines can substantially improve outcomes of care for older men and women with CHD and narrow gender disparities in clinical outcomes. For example, the American College of Cardiology's Guidelines Applied in Practice (GAP) project for AMI care, implemented in 33 acute-care hospitals, resulted in increased use of evidence-based therapies including acetylsalicylic acid (ASA), beta-blockers, and lipid-lowering therapy and a significant reduction in 30-day (26%) and one-year (22%) mortality in patients age 65 and older who had an average age of 76.<sup>20</sup> Use of the discharge tool developed by the GAP program was independently associated with a 50% reduction in one-year mortality in women.<sup>21</sup> The American College of Cardiology

### Key Points

Although the prevalence of coronary heart disease (CHD) in women before menopause is lower than that in men, this difference narrows by the seventh decade, and at age 80 prevalence of CHD is nearly equal for women and men.

Older adults and older women in particular are at risk for underdiagnosis and suboptimal management of CHD.

Older age accounts for some of the gender differences in clinical presentation; asymptomatic disease and "atypical" symptoms are common among older adults with CHD.

Risk factors for CVD are the same for men and women but the prevalence and relative contribution of these factors to the development of coronary heart disease differs by gender. Diabetes, hypertension, and hyperlipidemia are more prevalent in women than men with CHD.

Risk factor modification and management of comorbid conditions that can contribute to poor outcomes are important to optimal management of older adults with CHD.

Adherence to clinical practice guidelines for diagnosis and management of CHD can narrow gender disparities in clinical outcomes.

and American Heart Association have issued a series of scientific statements and guidelines focussed on the prevention, management, and diagnosis of heart disease in women that provides an important resource for clinicians to reduce and eliminate gender differences in performance.<sup>22,23</sup>

While women have higher unadjusted mortality rates after CABG than men, the gender gap in postoperative mortality after CABG has narrowed over time. Differences in mortality are attributed to gender differences in age, clinical factors, and comorbidity as well as differences in clinical practice.<sup>24</sup> In Ontario women have been found to have increased risk of mortality in the first year after CABG and higher rates of readmission for congestive heart failure and unstable angina.<sup>25,26</sup>

In order to achieve further reductions in gender differences in outcomes after CABG, the Society of Thoracic Surgeons has developed Gender-Specific Practice Guidelines for Coronary Artery Bypass Surgery.<sup>24</sup> In an evidence-based review the society concluded that outcomes in women could be improved by assuring that dosages for anesthesia and sedation account for body weight and by better perioperative management of three comorbidities common in women: anemia, diabetes, and thyroid disease. They found that the use of internal mammary artery grafts is underutilized in women undergoing CABG procedures. Because the internal mammary artery confers a protective effect that is associated with a significant reduction in CABG mortality compared to surgical revascularization with venous conduits alone they recom-

mend that whenever it is technically possible, at least one internal mammary artery is used in every CABG procedure.

A prime outcome of importance to older adults with CHD is reduction of morbidity and improved quality of life. Cardiac rehabilitation can improve functional health outcomes after an acute coronary event or revascularization. Women are less likely to be referred to cardiac rehabilitation and may encounter gender-related access barriers such as transportation or competing demands from caregiving when referred. Strategies are being identified to increase the participation of women with CHD in cardiac rehab.<sup>27</sup> Depression is another important comorbidity that affects quality of life and is associated with worse outcomes in individuals with CHD. Depression is more prevalent in women and more likely to be underdiagnosed in men. Therefore it is also important to diagnose and treat comorbid depression in this population.

### Conclusion

There is growing evidence that it is possible to improve outcomes in older patients with CHD while closing gender gaps in performance. An increased emphasis on risk factor modification among older adults, a high index of suspicion for CHD and recognition of "atypical" presentations in this population, and awareness that older adults in general and older women in particular are at risk for underuse of indicated diagnostic procedures and therapeutic interventions are needed. Clinical management should also focus on reducing morbidity by optimizing symptom management. Tools and guidelines are available to foster adherence to evidence-based practice for patients, providers, and health care organizations in order to achieve this goal.



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