1. SCOPE OF THE PROBLEM:
Cardiovascular disease (CVD) is the leading cause of premature death in women in Canada\(^1\). Mortality rates in men have stabilized in the last decade but have continued to increase in women in Canada\(^2\). Sex and gender-specific differences exist in awareness, symptom presentation, diagnosis, prognosis and treatment\(^3\). The diagnosis of acute coronary syndrome (ACS) in women presenting to the ER can be complex and challenging. Rapid diagnosis and treatment are vital.

2. SYMPTOMS:
Chest discomfort is the most common presenting complaint in ACS in BOTH men and women. However, symptoms in women can differ from those in men and anginal equivalents, such as dyspnea, epigastric and upper back discomfort, more often reported in women, may lead to misdiagnosis and delays in treatment. Heart attack symptoms are not recognized in over 50% of women.

Symptoms of heart attack MOST OFTEN REPORTED by women
- Chest pain or discomfort (ex. pressure, tightness, or burning) \(\text{and/or}\)
- Pain in the jaw, neck, arm, or back
- Shortness of breath
- Diaphoresis
- Epigastric discomfort, nausea or indigestion

Other ASSOCIATED Symptoms
- Profound weakness or fatigue
- Light-headedness
- Palpitations

Symptoms of heart attack MOST OFTEN REPORTED by women

Women are more likely to present with 3 or more symptoms in addition to chest pain. 3+


3. RISK FACTORS:
Cardiovascular risk assessment in women requires evaluation of traditional, sex-gender specific and under-recognized risk factors:

ASSESSING RISK FACTORS FOR CV DISEASE IN WOMEN

TRADITIONAL RISK FACTORS
Hypertension, diabetes, obesity, smoking, and dyslipidemia, pose a disproportionately higher mortality and morbidity burden in women\(^4,5,6,7\).

SEX & GENDER-SPECIFIC RISK FACTORS
Early menarche, polycystic ovarian disease, gestational hypertension and diabetes, pre-eclampsia, pre-term delivery, placental abruption, autoimmune disorders, breast cancer therapies and menopause\(^8,9\).

UNDER-RECOGNIZED RISK FACTORS
Psychosocial, economic, mental health and cultural risk factors such as anxiety, depression, loneliness, poverty, abuse and intimate partner violence\(^10,11\).

PREGNANCY IS REGARDED AS A WOMAN’S FIRST STRESS TEST.
Following the reproductive system, the CV system has the most sex-based differences.

4. PATHOPHYSIOLOGY:
Obstructive coronary artery disease (ST and non-ST elevation myocardial infarction) is common in both men and women. However, in 5-15% of ACS cases, MI/Angina with No Obstructive Coronary Arteries (MINOCA/ANOCA) can occur, particularly in women. The coronary angiogram in MINOCA reveals < 50% stenosis in any major epicardial artery. Serial troponins and electrocardiograms are critical in the work up as initial results may be normal.

5. DIFFERENTIAL DIAGNOSIS OF MINOCA/ANOCA:
Plaque rupture/erosion, coronary artery vasospasm (including ACS syndrome accompanying mast cell activation from allergic, hypersensitivity, or anaphylactic reactions, Kounis syndrome), microvascular dysfunction, coronary artery embolism and spontaneous coronary artery dissection.

6. INVESTIGATIONS AND MEDICAL THERAPY:

**PATIENTS PRESENTING WITH MI**

**Coronary Angiography**

- **Obstructive CAD**
  - (Dual antiplatelet agents, statins, ACE inhibitors/ARBs, and β-blockers)

- **MI-CAD**

**Non-Obstructive CAD (MINOCA)**

- IVUS, OCT
- Provocative spasm testing
- Coronary flow reserve testing for microvascular dysfunction

**Plaque disruption**
Aspirin, statins, ACE inhibitors/ARBs, and β-blockers
Consider clopidogrel or ticagrelor

**Coronary artery spasm**
CCB preferred. nitrates, nicorandil, cilostazol may be used
Consider statin, ACE inhibitors

**Microvascular dysfunction**
Antiarrhythmic therapies, e.g., CCB, β-blocker
Consider ACE inhibitors. statins (L-arginine, ranolazine, dipyridamole, aminophylline, imipramine, α-blockers have been tried)

**Coronary embolism**
Antiplatelet or anticoagulant
Treat hypercoagulable condition if indicated
Consider ACE inhibitors, statins

**Spontaneous coronary artery dissection**
Aspirin, β-blocker
May consider clopidogrel
Consider ACE inhibitors, statins

**Supply-demand mismatch**
Treat underlying condition

7. OTHER:
Beyond MINOCA, elevated troponin levels may also be found in other non-obstructive coronary artery conditions such as stress (Tako-tsubo) cardiomyopathy and non-ischemic critical conditions such as sepsis, pulmonary embolism and chronic kidney disease.
8. ACS IN WOMEN CHECKLIST:

1. Chest discomfort and/or anginal equivalents/other accompanying symptoms
2. Determine traditional, sex and gender specific and psychosocial risk factors
3. Perform serial troponins and ECGs
4. Consider non-obstructive causes of angina/myocardial ischemia and manage accordingly
5. Refer urgently/emergently to cardiologist/internist with expertise in women’s CVD

9. ADDITIONAL RESOURCES:

1. Canadian Women’s Heart Health Alliance ATLAS of the Epidemiology, Diagnosis and Management of CVD in Women
2. A free and accredited Canadian Women’s Heart Health Education Course and Toolkit

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