CANADIAN WOMEN'S HEART HEALTH CENTRE | NATIONAL ALLIANCE

CHEST PAIN IN WOMEN IN THE ER: FOCUS ON ACUTE CORONARY SYNDROME

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] and can occur for women of all ages. 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:

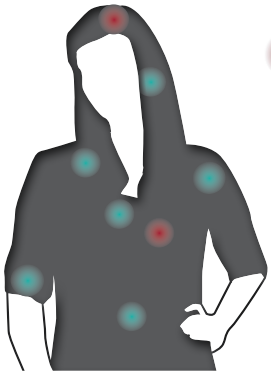
More than 50% of women who experience heart attacks have their symptoms unrecognized by healthcare providers.[4] In addition, women are 7x more likely to be sent home[5]. Chest discomfort is the most common presenting complaint in 90% of ACS, in BOTH men and women.[4] Women may, however, describe their symptoms differently than men, as discomfort or pressure rather than "pain." **Anginal equivalents**, such as dyspnea, epigastric pain, and upper back discomfort, are more often reported in women, and may lead to misdiagnosis and delays in treatment. Heart attacks are on the rise and can occur in women of all ages. Assessing for cardiac disease should be prioritized in women who experience chest pain/pressure.

Symptoms of heart attack MOST OFTEN REPORTED by women

- Chest pain or discomfort (ex. pressure, tightness, or burning)

and/or

- Pain in the jaw, neck, arm, or back
- Shortness of breath
- Diaphoresis
- Epigastric discomfort, nausea or indigestion



Other ASSOCIATED symptoms include

- Profound weakness or fatigue
- Light-headedness
- Palpitations

Women are more likely to present with 3 or more symptoms in addition to chest pain.[4] **3+**

3. RISK FACTORS:

Cardiovascular risk assessment in women requires evaluation of traditional, sex-gender specific, and under-recognized risk factors[6]:

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[7-10].

SEX & GENDER-SPECIFIC RISK FACTORS
Early menarche, polycystic ovary syndrome, gestational hypertension and diabetes, pre-eclampsia, pre-term delivery, placental abruption, inflammatory autoimmune disorders, breast cancer therapies, and early menopause (< age 40)[11,12]

UNDER-RECOGNIZED RISK FACTORS
Mast cell activation, psychosocial, economic, mental health, and cultural risk factors such as anxiety, depression, loneliness, poverty, abuse, and intimate partner violence[13,14].

CARDIOVASCULAR DISEASE

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:

Coronary Artery Disease (CAD), is a type of CVD that can be obstructive or non-obstructive. 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, **M**yocardial **I**nfarction with **N**on-**O**bstructive **C**oronary **A**rteries (MINOCA) can occur, particularly in women[15]. The coronary angiogram in MINOCA reveals < 50% stenosis in any major epicardial artery. Serial troponins, preferably high-sensitivity assays, using sex-specific thresholds, are critical, as initial results may be normal. Initial troponin should be followed by repeat sample collection 1-3 hours later for high-sensitiviy troponin and 3-6 hours later for conventional troponin assays[16]. Long term prognosis for MINOCA patients may include worse quality of life indicators, compared to obstructive MI patients.

5. POTENTIAL CAUSES OF MINOCA:

Possible causes of MINOCA include, but are not limited to, plaque rupture/erosion, coronary artery vasospasm (including ACS syndrome accompanying mast cell activation from allergic, hypersensitivity, or anaphylactic reactions: Kounis syndrome)[17], microvascular dysfunction, coronary artery embolism, and spontaneous coronary artery dissection (SCAD)[15].

6. INVESTIGATIONS AND MEDICAL THERAPY:

PATIENTS PRESENTING WITH SUSPECTED ACS/MI

Perform and interpret ECG within 10 minutes of first medical contact, draw serial troponins

Universal definition of acute MI | Acute myocardial injury with clinical evidence of acute myocardial ischemia, detection of a rise and/or fall in troponin with at least one value >99th percentile and at least one of the following[18]:

- Symptoms of myocardial ischemia
- New ischaemic ECG changes
- Development of pathological Q waves
- Imaging evidence of new loss of viable myocardium or ischemic regional wall motion abnormality
- Identification of a coronary thrombus by angiography or autopsy

Coronary angiography and appropriate treatment according to STEMI and NSTE-ACS guidelines[19-21]

Target STEMI treatment delays:
- PCI centre **<90 min**
- Transfer to PCI centre **<120 min**
- Fibrinolysis **<30 min** when PCI centre **>120 min** away

Obstructive CAD

Lifestyle modifications, continue dual antiplatelet agents, statins, ACE inhibitors/ARBs, ß-blockers, cardiac rehab and optimize cardiovascular risk factors

Non-Obstructive CAD (MINOCA)

[#]IVUS, CMRI, OCT, Provocative spasm testing, Coronary flow reserve testing for microvascular dysfunction

Plaque disruption	Coronary artery spasm*	Microvascular dysfunction	Coronary embolism	Spontaneous coronary artery dissection (SCAD)	Supply-demand mismatch
Lifestyle modifications. Aspirin, statins, ACE inhibitors/ARBs, and ß-blockers. Consider clopidogrel or ticagrelor.	Lifestyle modifications. CCB preferred. Nitrates, nicorandil, cilostazol may be used. Consider statins.	Lifestyle modifications. Antianginal therapies, e.g., CCB, nitrates, ß-blockers, ACE inhibitors, statins, consider alpha/ß-blockers, ranolazine (L-arginine, dipyridamole, aminophylline, imipramine, have been tried).	Antiplatelet or anticoagulant. Treat hypercoagulable condition if indicated. Consider ACE inhibitors, statins.	Aspirin, ß-blocker. May consider clopidogrel. Consider ACE inhibitors. Avoid triggers.	Treat underlying condition

* Coronary artery spasm (CAS) related **Kounis syndrome** is a unique and complex cause of MINOCA where it is necessary to treat both the cardiac dysfunction and allergic/sensitivity reaction. Measurement of serum tryptase should be considered in suspected cases during acute clinical presentation. In addition to CAS-focused medications, treatment should include corticosteroids, H1 antihistamines, H2 antihistamines, and mast cell stabilizers. Caution is warranted for using ACE inhibitors, epinephrine, and any patient-specific medication allergies.

[#]IVUS - Intravascular Ultrasound, OCT - Optical Coherence Tomography. Open Access (adapted from): Mukherjee, D. Journal of the American Heart Association. Myocardial Infarction With Nonobstructive Coronary Arteries: A Call for Individualized Treatment, Volume: 8, Issue: 14, pp 1-3.

7. DIFFERENTIAL DIAGNOSIS:

Beyond MINOCA, elevated troponin levels may also be found in other non-obstructive coronary artery conditions such as myocarditis, stress (Tako-tsubo) cardiomyopathy and non-ischemic critical conditions such as sepsis, pulmonary embolism, chronic kidney disease and aortic dissection.

8. ACS IN WOMEN CHECKLIST:

1. Chest discomfort and/or anginal equivalents/other accompanying symptoms
2. Perform serial troponins and ECGs
3. Initiate treatment according to current STEMI/ NSTEMI guidelines
4. Determine traditional, sex and gender specific and psychosocial risk factors
5. Consider non-obstructive causes of angina/myocardial ischemia and manage accordingly
6. Refer urgently/emergently to cardiology/internal medicine, and if possible, to specialists 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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