CHAPTER 5
SEX- AND GENDER-UNIQUE MANIFESTATIONS OF CVD

CWHHA ATLAS ON THE EPIDEMIOLOGY, DIAGNOSIS AND MANAGEMENT OF CARDIOVASCULAR DISEASES IN WOMEN

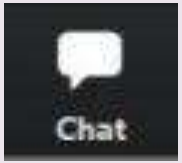
BOBBI JO GREEN
Edmonton, AB

CHRISTINE PACHECO
MD, MSc, FRCPC
Montreal, QC | @cpachecoMD

SHARON MULVAGH
MD, FRCPC, FACC, FAHA, FASE
Halifax, NS | @HeartDocSharon

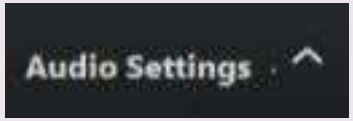
COLLEEN NORRIS
PhD, MSc, BScN, RN, FAHA,FCAHS
Edmonton, AB | @womensheart2

WELCOME & HOUSEKEEPING



To notify the presenters and moderators if you are having any technical difficulties

To ask questions through session



To check your audio settings by clicking “Test speaker and microphone”

DISCLOSURE STATEMENT

We do not have an affiliation (financial or otherwise) with a commercial organization that may have a direct or indirect connection to the content of this presentation.

Learning Objectives

At the end of this webinar, you will be able to:

- Be aware of how heart disease can be experienced by sharing in one woman's personal journey.
- Understand the symptoms of ischemic heart disease for women and diagnosis.
- Summarize sex- and some gender-associated, and unique aspects and key features of the manifestations of cardiovascular disease (CVD) in women.

Canadian Women's Heart Health Alliance (CWHHA)

LAUNCHED IN 2018

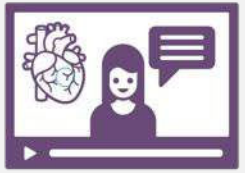
Over 120 members!

Mission: Disseminate education and best practices re: Women's cardiovascular (CV) health among **healthcare providers and women with lived experience.**

Goal: Eliminate knowledge gaps in specific CV issues and develop new practice considerations in care for women, thereby improving the health of Canadian women.

CWHHA WORKING GROUPS

Advocacy



Training and Education

Knowledge Translation and Mobilization

Health Systems and Policy

Sex and Gender Definitions

SEX

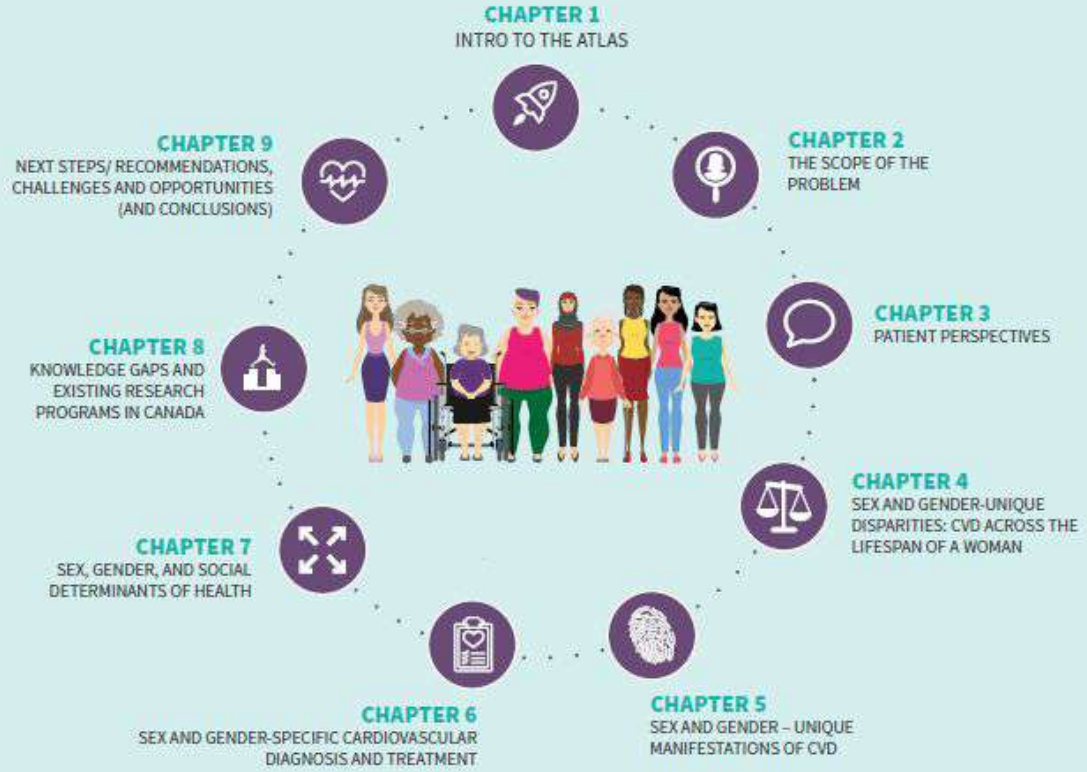
- Biology – chromosomes at birth (female/male)
- Encompasses hormones, genes, anatomy, physiology, etc.

GENDER

- Socially influenced determination (man/woman)
- Is culturally specific and temporal

CANADIAN WOMEN'S HEART HEALTH ALLIANCE ATLAS

Epidemiology, Diagnosis, and Management of Cardiovascular Diseases in Women



- 9 unique "chapters"
- CJC Open
- Editor: Dr. M. Graham
- 1st: published April 2020
- Annual chapter updates
- "Living document"

Norris CM ….. Mulvagh SL. CJC Open 2020

CJC OPEN
JCC Libre Accès

REVIEW | ARTICLES IN PRESS

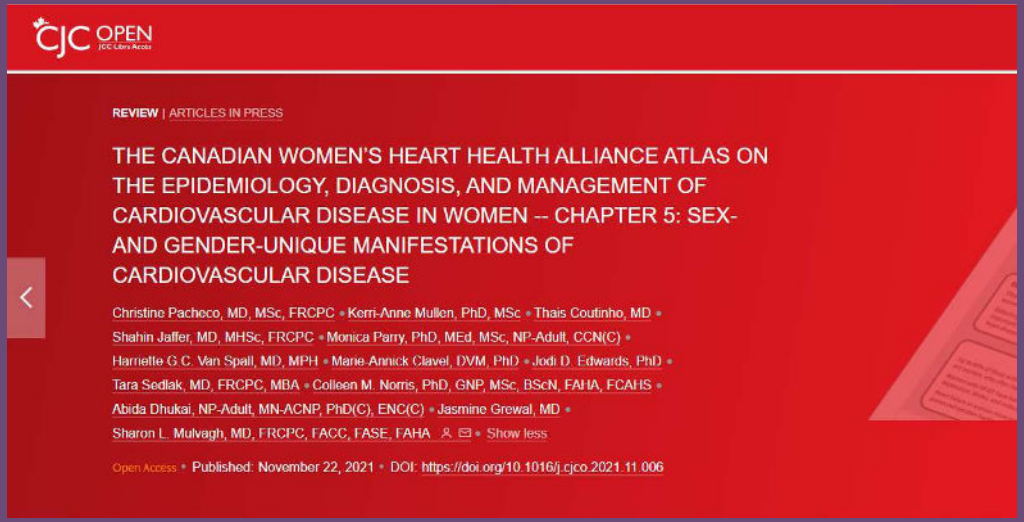
THE CANADIAN WOMEN'S HEART HEALTH ALLIANCE ATLAS ON THE EPIDEMIOLOGY, DIAGNOSIS, AND MANAGEMENT OF CARDIOVASCULAR DISEASE IN WOMEN -- CHAPTER 5: SEX- AND GENDER-UNIQUE MANIFESTATIONS OF CARDIOVASCULAR DISEASE

Christine Pacheco, MD, MSc, FRCPC • Kerri-Anne Mullen, PhD, MSc • Thais Coutinho, MD • Shahin Jaffer, MD, MHSc, FRCPC • Monica Parry, PhD, MEd, MSc, NP-Adult, CCN(C) • Harriette G.C. Van Spall, MD, MPH • Marie-Annick Clavel, DVM, PhD • Jodi D. Edwards, PhD • Tara Sedlak, MD, FRCPC, MBA • Colleen M. Norris, PhD, GNP, MSc, BScN, FAHA, FCAHS • Abida Dhukai, NP-Adult, MN-ACNP, PhD(C), ENC(C) • Jasmine Grewal, MD • Sharon L. Mulvagh, MD, FRCPC, FACC, FASE, FAHA • Show less

Open Access • Published: November 22, 2021 • DOI: https://doi.org/10.1016/j.cjco.2021.11.006

Bobbi Jo's STORY

BOBBI JO GREEN
Woman With Lived Experience
Edmonton, AB



CJC OPEN
JCC Libre Accès

REVIEW | ARTICLES IN PRESS

THE CANADIAN WOMEN'S HEART HEALTH ALLIANCE ATLAS ON THE EPIDEMIOLOGY, DIAGNOSIS, AND MANAGEMENT OF CARDIOVASCULAR DISEASE IN WOMEN -- CHAPTER 5: SEX- AND GENDER-UNIQUE MANIFESTATIONS OF CARDIOVASCULAR DISEASE

Christine Pacheco, MD, MSc, FRCPC • Kerri-Anne Mullen, PhD, MSc • Thais Coutinho, MD • Shahin Jaffer, MD, MHSc, FRCPC • Monica Parry, PhD, MEd, MSc, NP-Adult, CCN(C) • Harriette G.C. Van Spall, MD, MPH • Marie-Annick Clavel, DVM, PhD • Jodi D. Edwards, PhD • Tara Sedlak, MD, FRCPC, MBA • Colleen M. Norris, PhD, GNP, MSc, BScN, FAHA, FCAHS • Abida Dhukai, NP-Adult, MN-ACNP, PhD(C), ENC(C) • Jasmine Grewal, MD • Sharon L. Mulvagh, MD, FRCPC, FACC, FASE, FAHA • Show less

Open Access • Published: November 22, 2021 • DOI: https://doi.org/10.1016/j.cjco.2021.11.006

CHRISTINE PACHECO
MD, MSC, FRCPC

Healthcare Professional Co-Chair, Knowledge Translation and Mobilization Working Group
Cardiologist, Pierre-Boucher Hospital and University of Montréal Hospital Centre (CHUM)
Faculty Member, Department of Medicine, University of Montréal
Clinical Investigator-Researcher, Centre de Recherche du Centre Hospitalier de Université de Montréal (CRCHUM)
Montreal, QC | @cpachecoMD

CHAPTER 5 | SEX- AND GENDER-UNIQUE MANIFESTATIONS OF CVD

ISCHEMIC HEART DISEASE (IHD)

Symptoms of IHD vary between sexes. There are also sex and age-related differences in symptom presentation, pathophysiology, and outcomes.

Non-obstructive atherosclerotic mechanisms, including coronary microvascular dysfunction, vasospasm, and spontaneous coronary dissection are under-recognized causes of angina and myocardial infarction in women.

OBSTRUCTIVE & NON-OBSTRUCTIVE CORONARY ARTERY DISEASE

Obstructive coronary artery disease most often affects post-menopausal women, who often have a higher cardiovascular risk burden than men.

Detecting atherosclerosis, even in the absence of obstructive lesions, is important in order to improve risk stratification and treatment of ischemic heart disease in women.

HEART FAILURE (HF)

Up to 40% of those with heart failure with reduced ejection fraction (HFrEF) are women, who often have a high burden of comorbidities.

Women with HFrEF have better survival, but higher prevalence of depression, stroke, and reduced quality of life.

Heart failure in women more commonly manifests as heart failure with preserved ejection fraction (HFpEF).

VALVULAR HEART DISEASE

Sex-specific pathophysiology in valvular heart disease is mostly unknown despite emerging evidence for distinct characteristics of valve lesions and therapies in women.

CARDIOMYOPATHIES

Women are much more likely to develop stress cardiomyopathy (Takotsubo). Women may be more susceptible to auto-immune myocarditis and restrictive cardiomyothapies. Peripartum cardiomyopathy exclusively affects women, with differences in characteristics according to ethnicity.

ARRHYTHMIA

Sex differences in clinical manifestations of arrhythmia are associated with normal cyclical hormonal changes in women.

VASCULAR ARTERIAL DISEASE

Women are at increased risk of complications when diagnosed with aortic aneurysmal and peripheral arterial disease.

STROKE AND VASCULAR COGNITIVE IMPAIRMENT

Women have unique risk factors that make them vulnerable to stroke across the lifespan, particularly during pregnancy and post-menopausal aging. Stroke can lead to vascular cognitive impairment later in life.

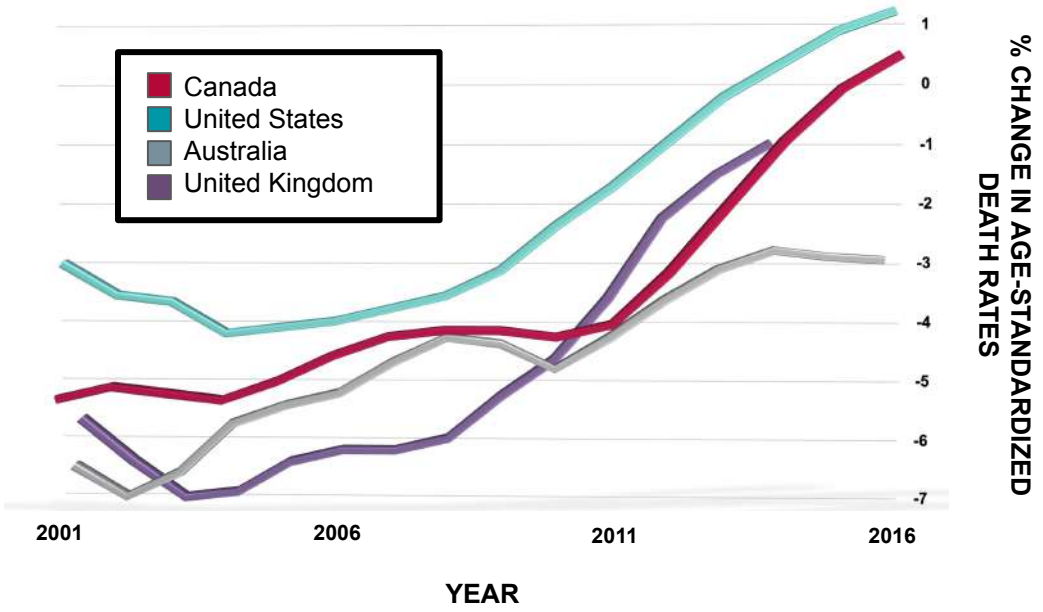
HER HEART MATTERS
WEAR RED CANADA • FEB 13

KEY MESSAGE # 1

Heart disease is on the rise and is the **leading cause of death** for women worldwide.

QUESTIONS?
Visit WearRedCanada.ca or your healthcare provider.

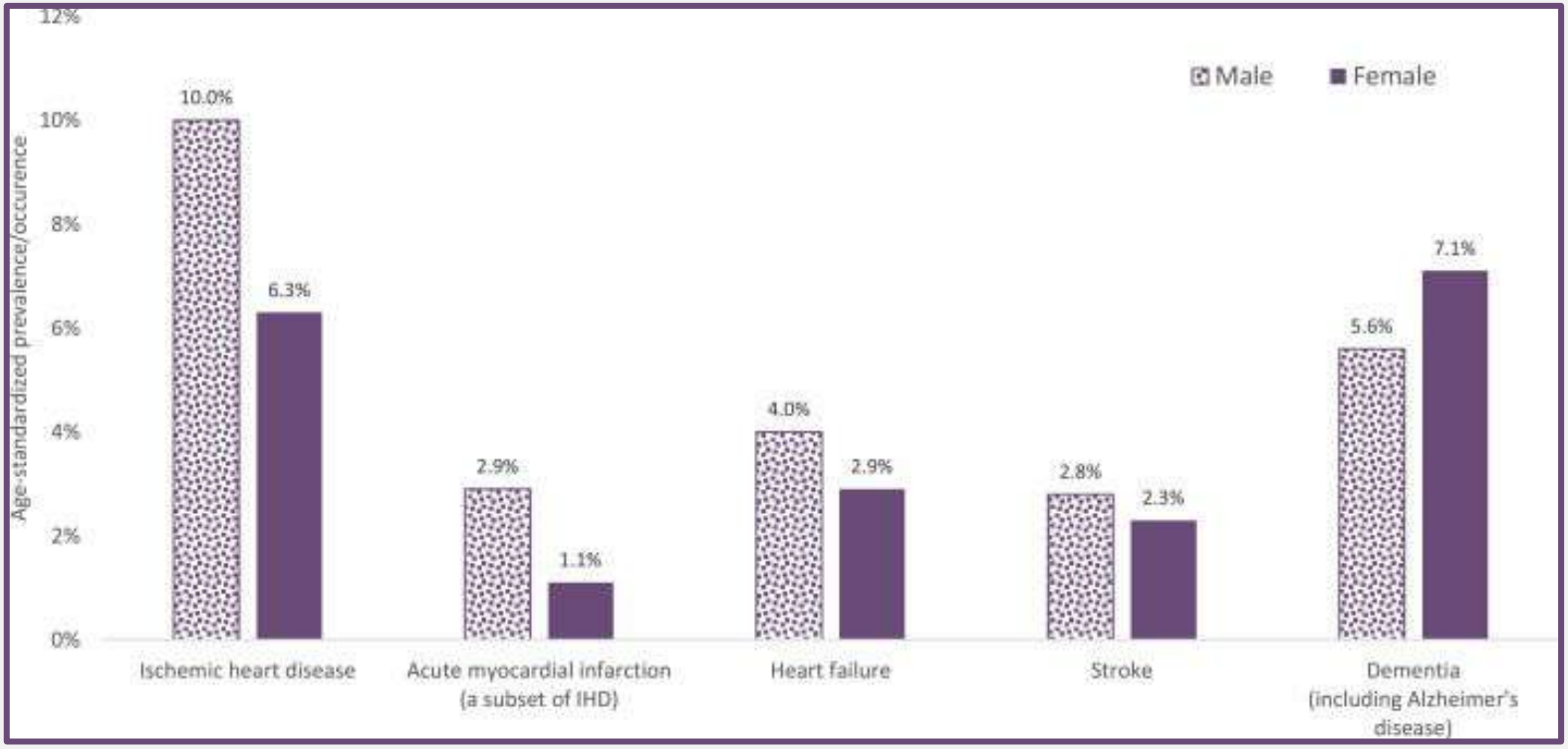
VITAL STATISTICS FROM THE
WORLD HEALTH ORGANIZATION MORTALITY DATA



Lopez et al. Int J Epidemiol, 2019, 1815-1823.

CANADIAN WOMEN'S HEART HEALTH CENTRE | NATIONAL ALLIANCE

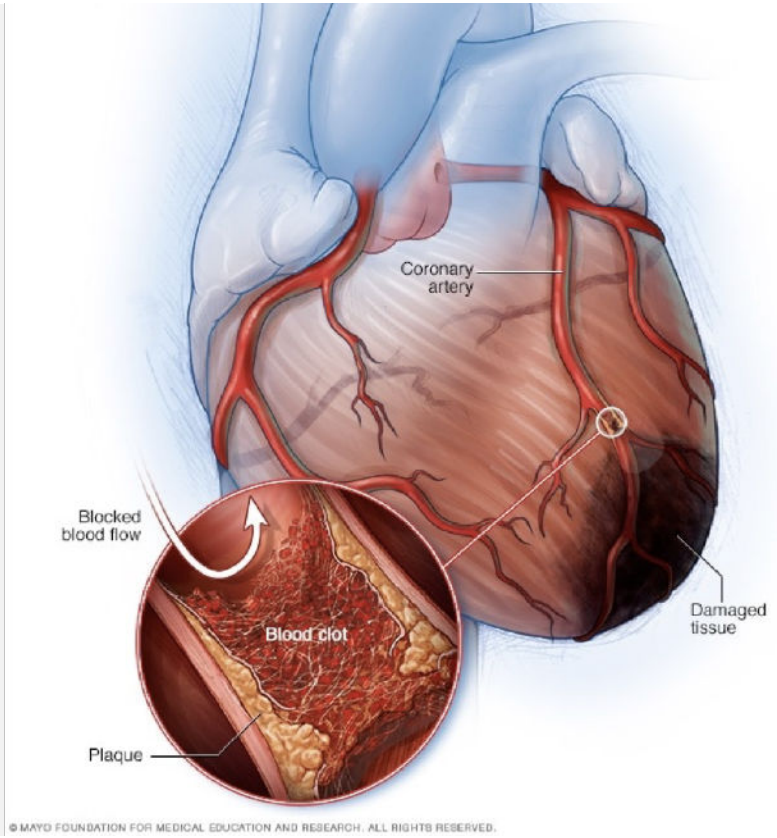
Age-Standardized Prevalence/Occurrence of Major Cardiovascular Diseases in Canada, by Sex



Ischemic Heart Disease

- Stable angina
- Acute coronary syndrome (heart attack)

- Higher mortality in younger women
- 3x higher mortality than breast cancer
- Longer diagnostic delays



HER HEART MATTERS
WEAR RED CANADA • FEB 13

KEY MESSAGE # 2

Heart attack symptoms are **not recognized** in over **50%** of women.

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

If you think someone is having a heart attack, **seek immediate medical attention.**

SYMPTOMS OF HEART ATTACK MOST OFTEN REPORTED BY WOMEN

- Chest pain or discomfort (ex. pressure, tightness, or burning)
- Pain in the jaw, neck, arm, or back
- Abnormal excessive sweating
- Shortness of breath
- Stomach pain or discomfort, or feelings of nausea or indigestion

OTHER ACCOMPANYING OR ASSOCIATED SYMPTOMS

- Unusual weakness or fatigue
- Back, shoulder or right arm pain
- Sleep disturbance
- Dizziness or light-headedness
- Fast or irregular heartbeat

Lichtman JH, et al. Circulation. 2018;137:781–790

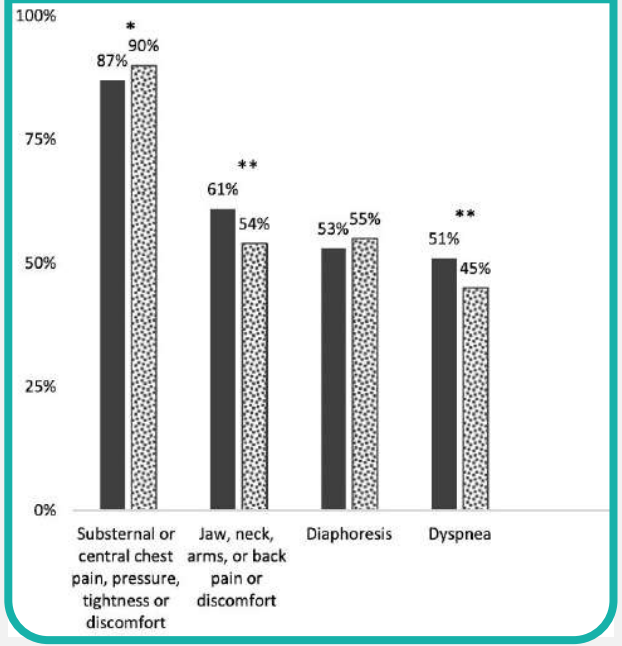
CANADIAN WOMEN'S HEART HEALTH CENTRE | NATIONAL ALLIANCE

Symptoms

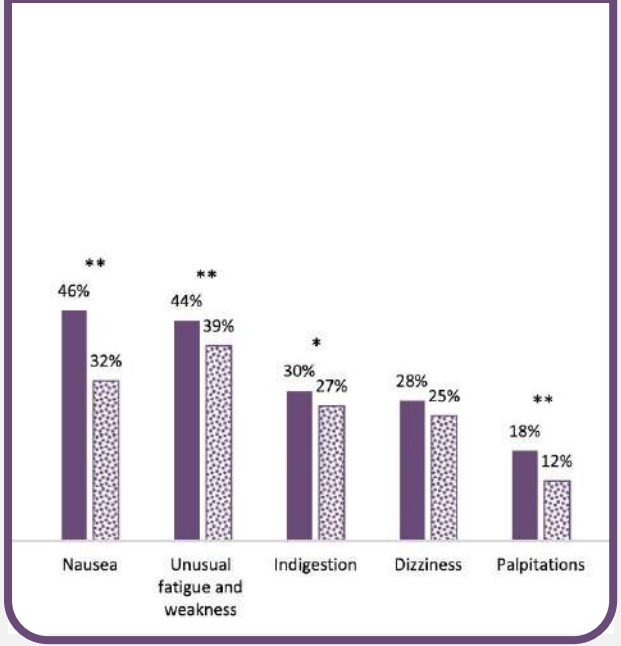
Women Men

Proportion of the time symptom is reported

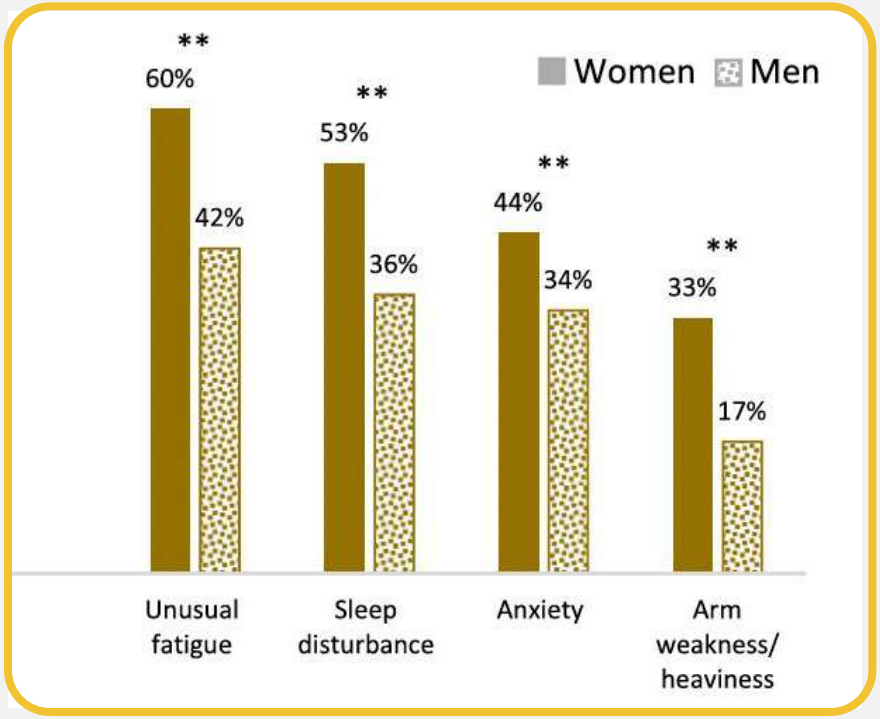
Most frequently reported symptoms



Additional symptoms women are more likely to describe



Frequently Reported Prodromal Symptoms

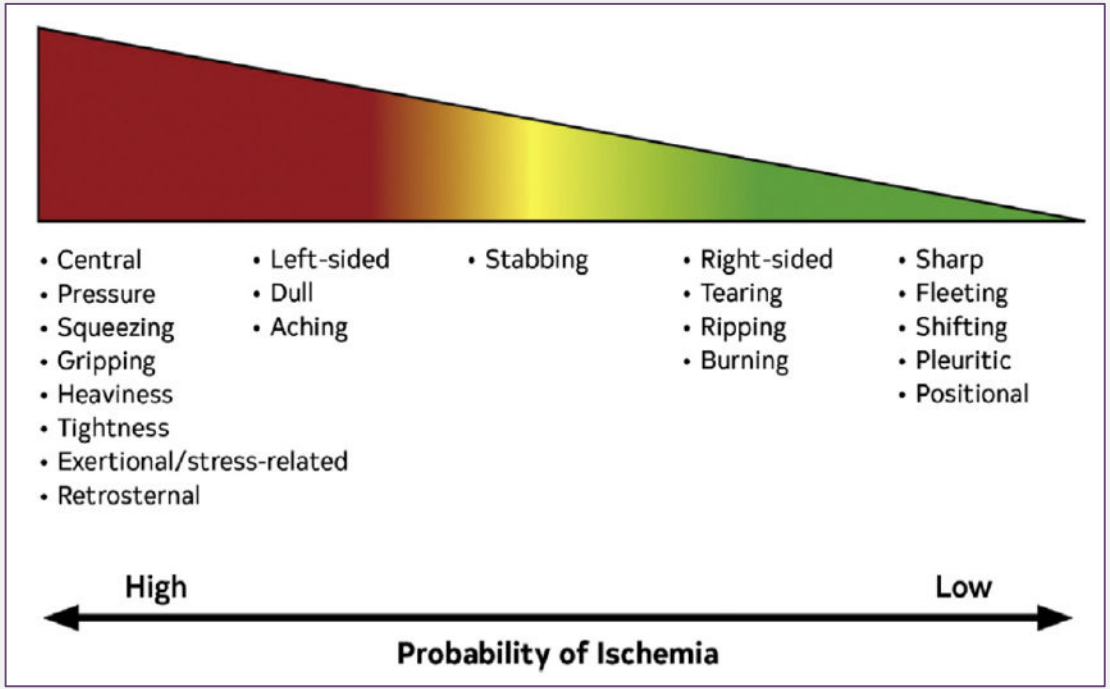


Terminology

~~Atypical vs. Typical chest pain~~

Cardiac vs. Possibly cardiac vs. Non-cardiac

Index of Suspicion That Chest "Pain" is Ischemic in Origin on the Basis of Commonly Used Descriptors



Aggarwal et al. Circulation: Cardiovascular Quality and Outcomes. 2018;11:e004437

HER HEART MATTERS
WEAR RED CANADA • FEB 13

KEY MESSAGE # 4

Women can be at **greater risk** for heart disease than men.

The following conditions lead to a greater risk of heart disease:

Certain pregnancy complications
(ex. Premature birth, diabetes or hypertension during pregnancy, preeclampsia)

Earlier menopause
(Average age of menopause 50-52)

Polycystic ovary syndrome

Systemic inflammatory and autoimmune disorders
(ex. Rheumatoid arthritis, lupus)

Cigarette smoking
(Women have 3x higher risk of heart attack due to cigarette smoking compared to men)

Diabetes mellitus
(Women living with diabetes are 3x more likely to die from heart disease compared to men)

Questions? Visit WearRedCanada.ca or your healthcare provider.

Garcia, M. et al. (2016). Circ Res, 118(8), 1273-1293.
Yusuf, S. et al. (2004). Lancet, 364(9438): 937-52.

CANADIAN WOMEN'S HEART HEALTH CENTRE | NATIONAL ALLIANCE

HER HEART MATTERS
WEAR RED CANADA • FEB 13

KEY MESSAGE # 3

Causes of heart disease **can be different** for women than men.

Common causes of heart disease:

- Coronary artery disease
- Valvular heart disease
- Arrhythmia (irregular heart beat)

Women are more likely than men to have:

- Spontaneous coronary artery dissection (SCAD)
- Coronary vasospasm
- Microvascular dysfunction (small-vessel disease)
- Takotsubo (stress-induced) cardiomyopathy (disease of the heart muscle)
- Peripartum cardiomyopathy (weakened heart during or after pregnancy)

Some health providers may be less aware of the differences between women and men.

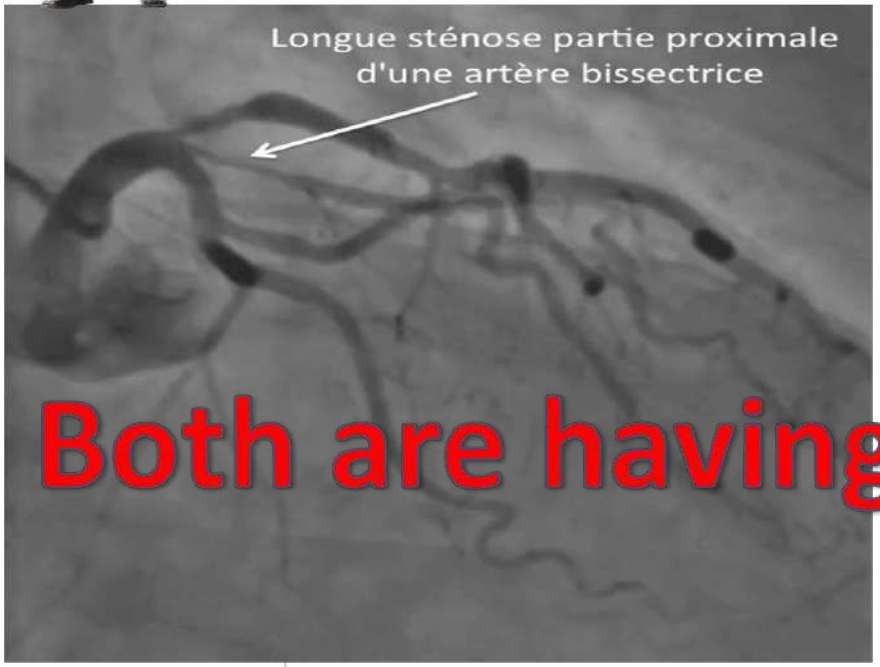
Questions? Visit WearRedCanada.ca.

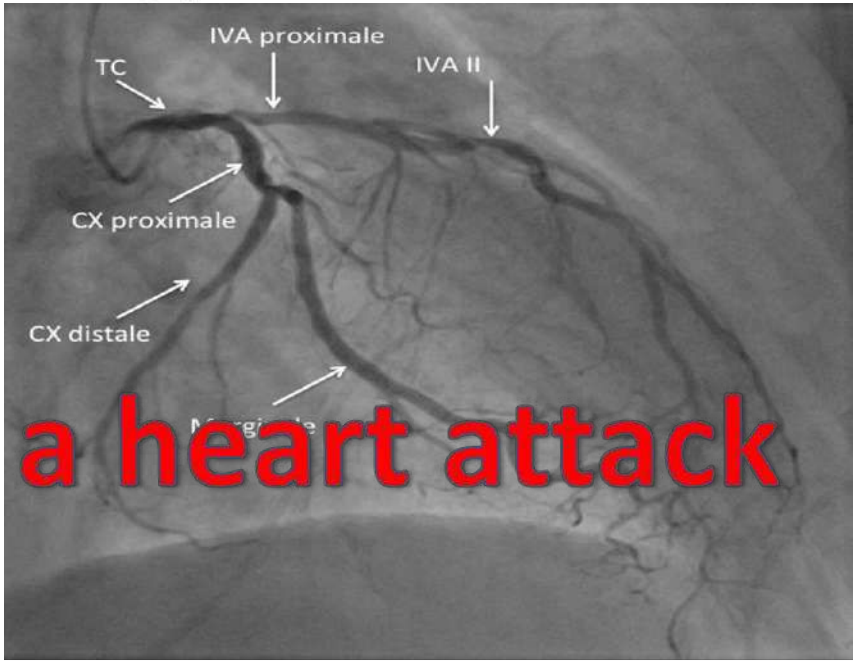
Norris CM, et al. J Am Heart Assoc 2020 Feb 16; 9(4): e015634.

CANADIAN WOMEN'S HEART HEALTH CENTRE | NATIONAL ALLIANCE

Classic findings

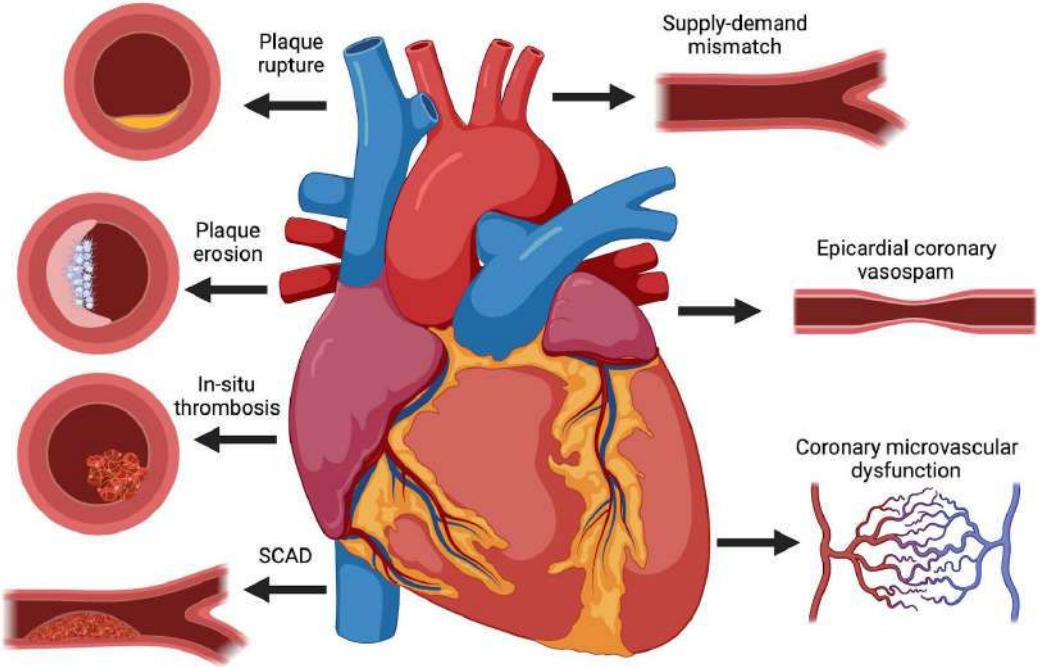
No visible lesion





Both are having a heart attack

Myocardial Infarction (MI) with Non-obstructive Coronary Artery Disease (MINOCA)



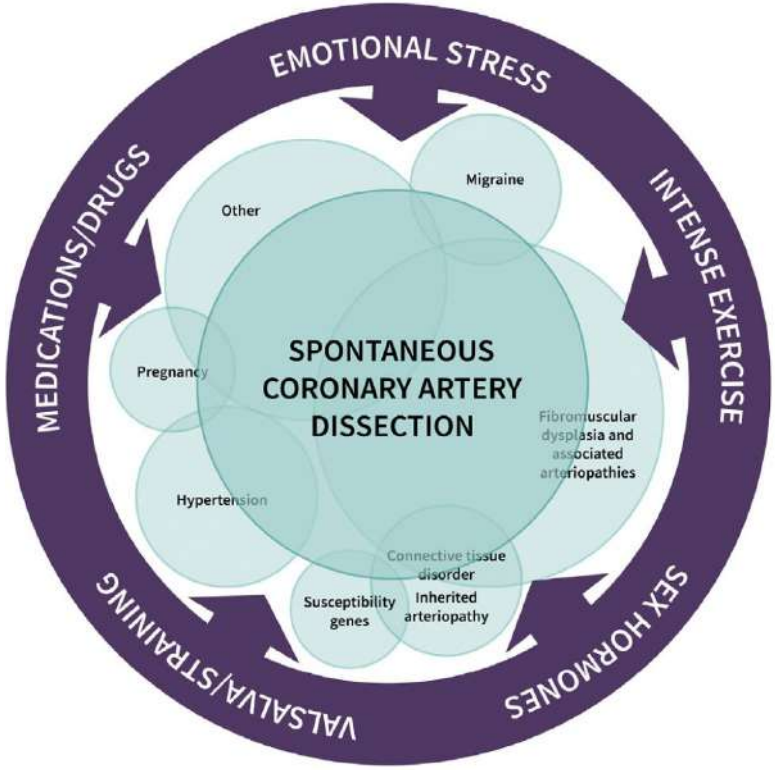
Tamis-Holland et al, 2019, Circulation, 139(18): e891-e908

Myocardial Infarction (MI) with Non-obstructive Coronary Artery Disease (MINOCA)

Potential underlying mechanisms of MINOCA	Diagnostic testing
• Coronary plaque disruption (eg, plaque rupture, or ulceration, erosion, calcific nodules) • Epicardial coronary vasospasm • Coronary microvascular dysfunction • Spontaneous coronary artery dissection • Hypercoagulable disorders • Coronary emboli • Paradoxical emboli • Takotsubo or other cardiomyopathy • Myocarditis	• Coronary angiogram • IVUS • OCT • Coronary Vasoreactivity testing (acetylcholine, ergonovine) • Coronary function testing (CFR, IMR) • Myocardial PET • Coronary angiogram • IVUS • OCT • Hypercoaguable work-up • TTE, TEE, bubble contrast echocardiography • Cardiac MRI

Testing and treatment differs based on the underlying diagnosis and cause. Therefore, it's important that work up be thorough.

Associated Conditions and Risk Factors for SCAD

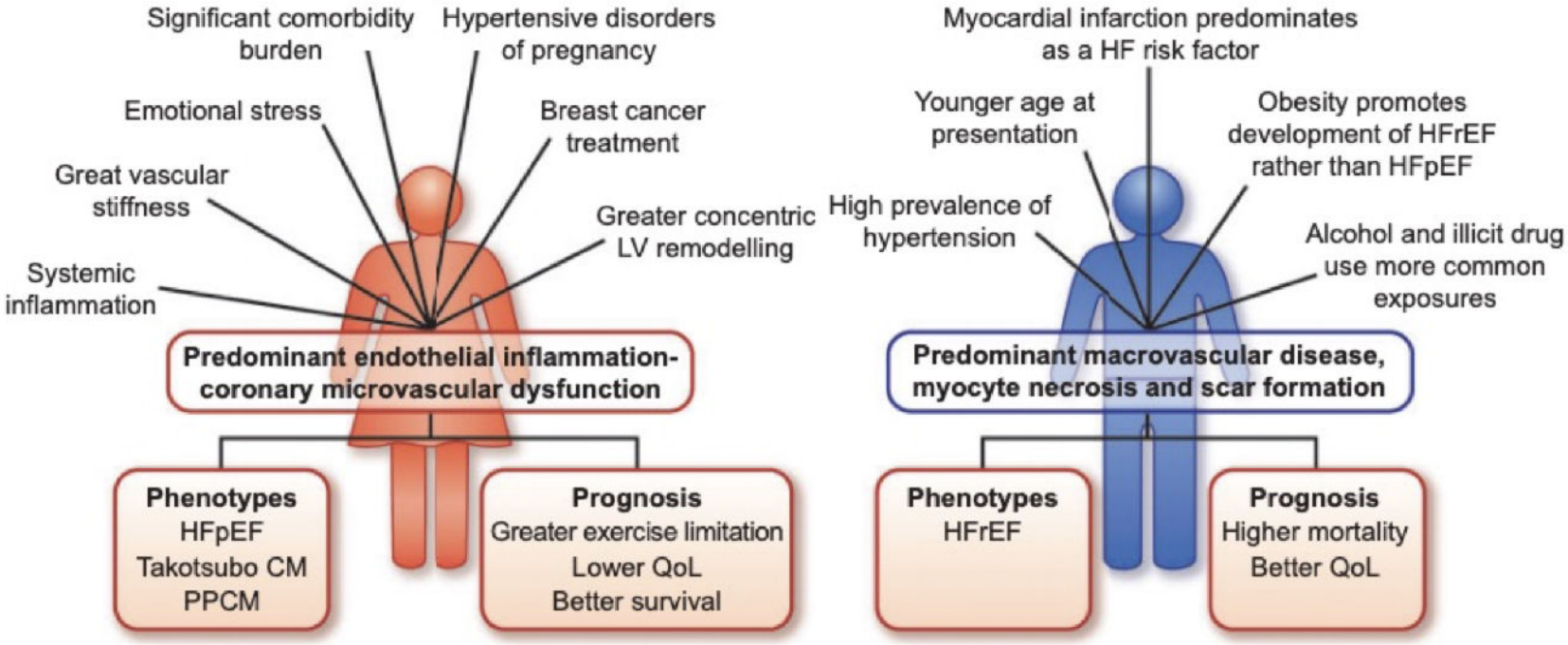


Modified from Hayes et al. with permission from Elsevier.

Heart Failure

- Second cause of hospitalization, third cause of death in women
- Symptoms
  - Shortness of breath, fatigue, swelling
- Underlying mechanisms
  - Heart is too stiff (HFpEF) - more frequent in women (55%)
  - Heart is too weak (HFrEF) (29% women)
- Causes
  - Previous heart attacks (ischemic)
  - Toxic: alcohol, illicit drugs, chemotherapy
  - Valvular heart disease
  - Genetic
  - Cardiomyopathies

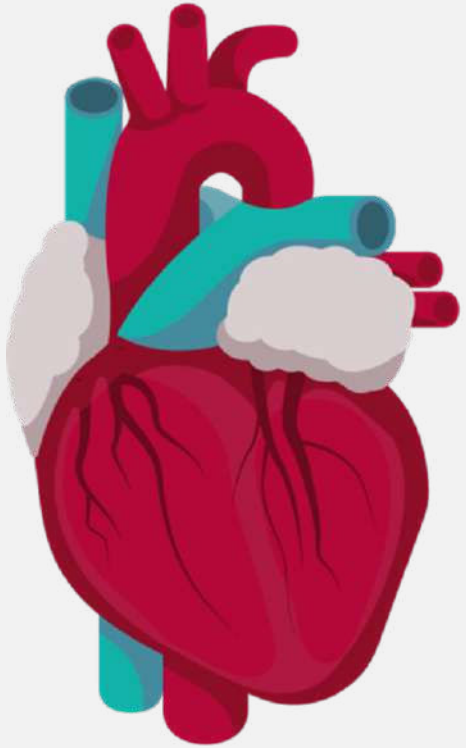
Heart Failure



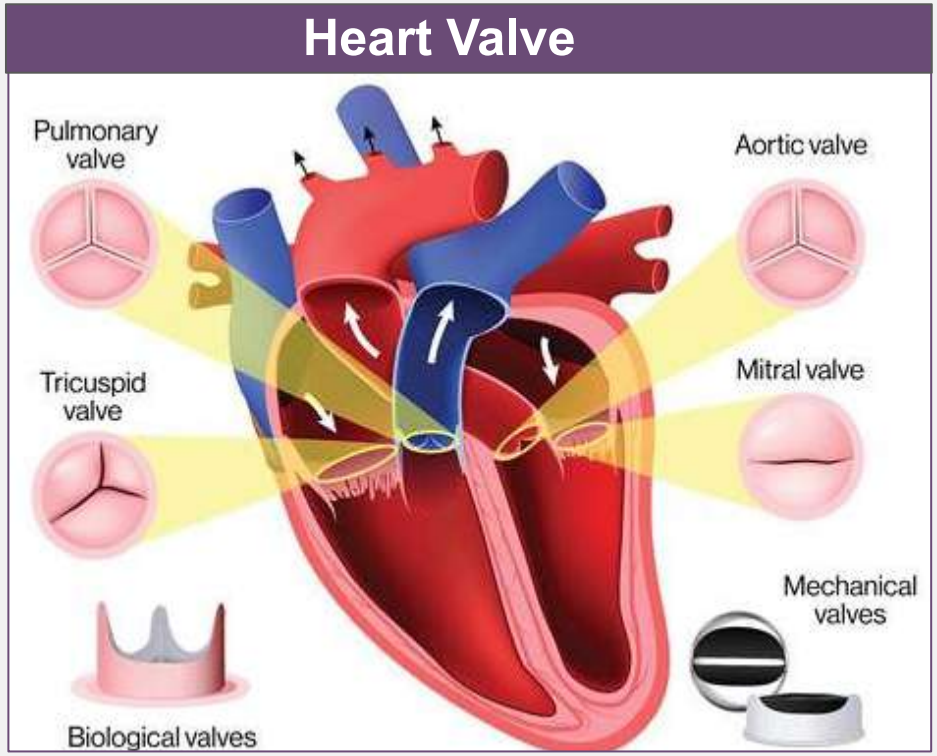
Lam CSP. Eur Heart J. 2019;40(47):3859-68c. 10.1093/eurheartj/ehz835
Accesible en ligne: https://academic.oup.com/eurheartj/article/40/47/3859/5652224

Cardiomyopathies

- Takotsubo cardiomyopathy (“Broken Heart syndrome”)
  - 90% of cases in post-menopausal women
  - Psychological or physical stressor
  - Poorly understood
  - Complete recovery common, but risk of complications and recurrence
- Peripartum cardiomyopathy
  - Late in pregnancy or in the 6 months following delivery
  - Weakened heart muscle
  - Recovery uncertain
- Sarcoidosis, Hypertrophic cardiomyopathy, Infiltrative, Myocarditis



Valvular Heart Disease

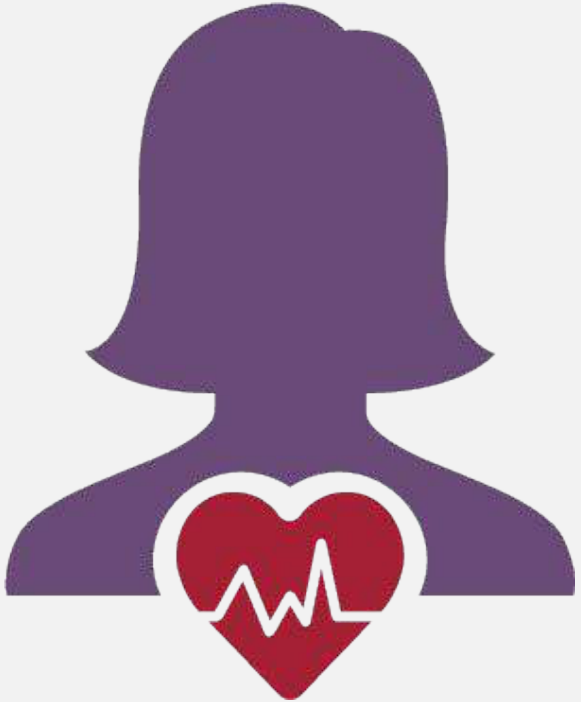


- 5-10% of adults over 65, 47.5% women
- Women are underrepresented in clinical trials
- Smaller heart cavities
- Hormonal differences
- Diagnostic delays
- Worse outcomes following surgery

https://www.heartandstroke.ca/heart-disease/conditions/valvular-heart-disease

Arrhythmias

- Irregular heart beat
- Risk increases in pregnancy
- Higher likelihood in women
  - Atrial fibrillation - 60% of those over 75 are women
  - Supraventricular tachycardia - menstrual cycle
  - Longer QT interval - Estrogen-related
  - Sick sinus syndrome, postural orthostatic tachycardia syndrome
- Outcomes
  - More symptoms, higher rate of recurrence
  - Less likely to undergo cardioversion, ablation



Vascular Arterial Disease

Thoracic Aortic Aneurysm

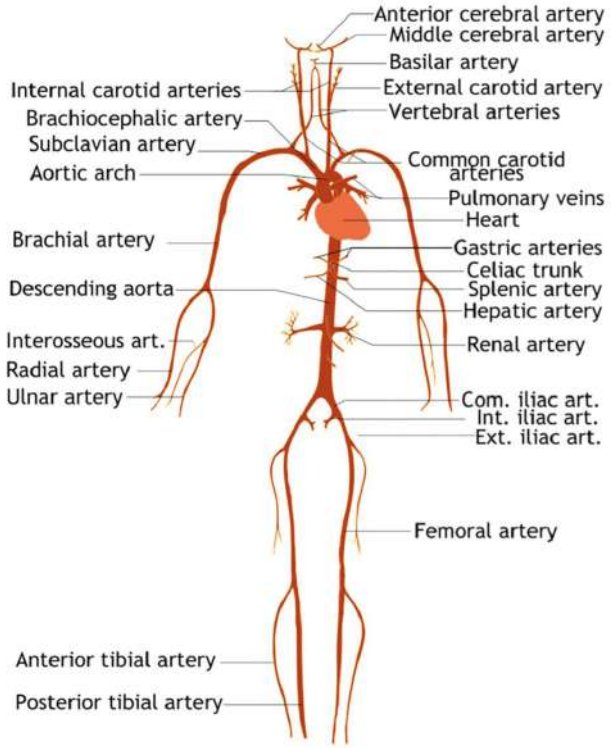
- Lower prevalence
- Faster growth
- Higher mortality and stroke following surgery

Abdominal Aortic Aneurysm

- Faster growth and higher risk of rupture
- Hormonal, molecular, hemodynamic differences
- Higher elasticity, stiffness, lower strength
- Sex specific cut-offs for surgery

Peripheral Vascular Disease

- 3x higher risk following HTN disorders in pregnancy
- Greater functional impairment, depression
- Higher morbidity and mortality following surgery



doi: https://doi.org/10.1371/journal.pcbi.1007259.g001

Stroke

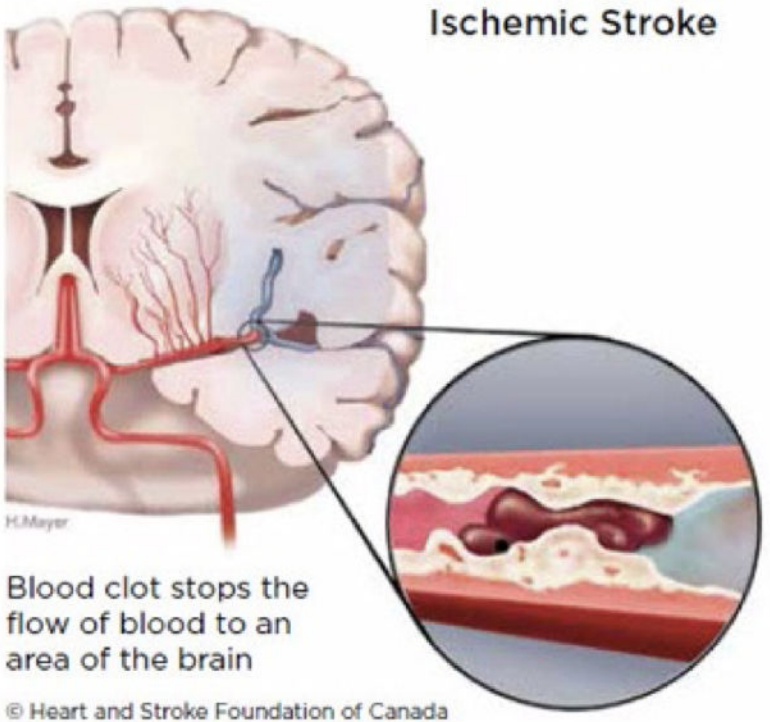
Face is it drooping?

Arms can you raise both?

Speech is it slurred or jumbled?

Time to call 9-1-1 right away.

Act **F** **A** **S** **T** because the quicker you act, the more of the person you save.

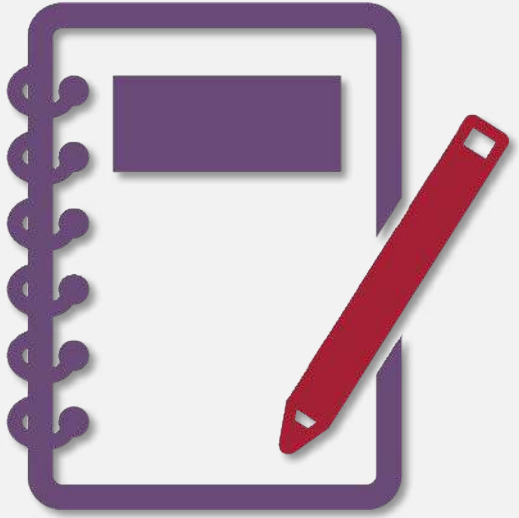


Stroke

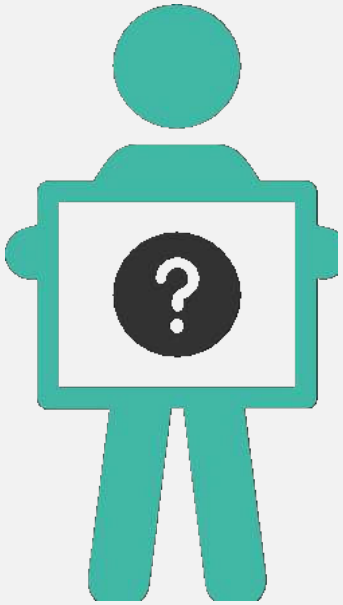
- Women over 75 are disproportionately affected
- Higher risk of stroke related disability, reduced quality of life, increased levels of post-stroke depression, institutionalization
- Possible higher risk of stroke with atrial fibrillation
- Unique female-specific risk factors across the lifespan
- Higher risk of dementia

In Summary

- CVD is the primary cause of premature death in women in Canada.
- Sex- and gender-unique differences exist in symptoms and pathophysiology of CVD in women.
- These differences must be considered when evaluating CVD manifestations, because they affect management and prognosis of cardiovascular conditions in women.



Q&A



WE WANT TO HEAR FROM YOU.

Questions, Comments...

THANK YOU!

EVALUATION
Please complete the evaluation form after the webinar.

For more information visit
CWHHA.CA

Table 1. Mechanisms and diagnosis of MINOCA

Potential underlying mechanisms of MINOCA*	Diagnostic testing
Coronary plaque disruption (eg, plaque rupture, or ulceration, erosion, calcific nodules)	Coronary angiogram IVUS OCT
Epicardial coronary vasospasm	Coronary vasoreactivity testing (acetylcholine, ergonovine)
Coronary microvascular dysfunction	Coronary function testing (CFR, IMR) Myocardial PET
Spontaneous coronary artery dissection	Coronary angiogram IVUS OCT
Hypercoagulable disorders	Hypercoaguable work-up
Coronary emboli	TTE, TEE, bubble contrast echocardiography
Paradoxical emboli	Cardiac MRI
Takotsubo or other cardiomyopathy†	TTE
Myocarditis†	Cardiac MRI TTE