

seX & whY Episode 4: Sex Differences in Heart Disease
 Show Notes

Sex & Gender Differences in Heart Disease

By Jeannette Wolfe, Basmah Safdar and Rachel Dryer

	Men	Women
Average age of MI	65	72
Weighted traditional risk scores <ul style="list-style-type: none"> • Smoking • DM • HTN • Hyperlidemia • Obesity 	↑ (increased weighted risk factor in younger men)	↑ About 25% higher risk of CAD ↑ DM increases risk 4-5 fold in women ↑ High triglycerides and low high density lipo proteins increased risk
Most common complaints	Chest discomfort	Chest discomfort <ul style="list-style-type: none"> • More likely to have cluster of symptoms • Compared to men more likely to present with their ACS without chest pain

		<ul style="list-style-type: none"> Increased risk of presenting in new heart failure <i>Tip ask if any new chest discomfort or fatigue</i>
Conventional Troponin		<p>Less sensitive:</p> <ul style="list-style-type: none"> smaller heart size microvascular disease <p>Newer high sensitivity troponin may be more helpful</p>
Type of MI	STEMI	NSTEMI
Type of Vessel injury	<ul style="list-style-type: none"> plaque rupture 	<ul style="list-style-type: none"> Plaque rupture Plaque erosion*
Type of ischemia	<ul style="list-style-type: none"> Obstructive (big pipes) 	<ul style="list-style-type: none"> Obstructive Non-obstructive Microvascular dysfunction Combo of all of above
Death (after age adjustment) <ul style="list-style-type: none"> 1st year 5 years 	<ul style="list-style-type: none"> 19% 36% 	<ul style="list-style-type: none"> 26% 47% <p>younger women with MI are at particularly high risk</p>
STEMI Treatment <ul style="list-style-type: none"> Percutaneous Coronary Intervention better than thrombolytics if available in timely fashion for both 		<ul style="list-style-type: none"> Compared to men slightly delayed door to balloon time Increased risk of bleeding: <ul style="list-style-type: none"> Groin pseudo-aneurysm Retroperitoneal bleed Smaller vessels

		<ul style="list-style-type: none"> Increased risk of radial artery spasm
NSTEMI	<ul style="list-style-type: none"> advantage in early invasive strategy Glycoprot IIb/IIIa inhibitors may be more beneficial 	<ul style="list-style-type: none"> Immediate revascularization likely helpful only in high risk pts (elevated trop, significant ekg changes and high TIMI score) <p>Early invasive strategy may actually be harmful for low risk patients**</p>
STEMI mimickers		<ul style="list-style-type: none"> Takotsubo Spontaneous Coronary Artery Dissection (SCAD) Spasm <p>↑ 90% women</p> <p>risks include:</p> <ul style="list-style-type: none"> ↑ fibromuscular dysplasia ↑ hormonal change
Post MI	More likely to be referred and to go to rehab	Report lower quality of life after MI

Of note symptoms associated with delay of presentation for ACS include: female sex, age, Hispanic or African American race, living alone, fear, attributing symptoms to non-urgent cause, *embarrassment*, lower education/socio economic status

* The ability to distinguish between plaque rupture versus erosion on routine angiography is currently limited as it requires specialized tests like intravascular ultrasound or optical coherence tomography.

**may be due to increased risk of MINOCA myocardial infarction with no obstructive coronary artery and treatment for MINOCA should be tailored to underlying cause: dissection, spasm, takotsuba, microvascular/endothelial dysfunction

Additional Risk Factors to Consider in Women

Depression Polycystic Ovarian Disease Pre-eclampsia/Eclampsia Connective Tissue Disease Elevated CRP Decreased HR beat to beat variability (reflection of lack of vagal tone)
--

Cardiac Imaging Modality

Test	Type	Male Sensitivity	Female Sensitivity	Comments
Traditional Stress test (meta-analysis)*	Functional	72%	61%	False positive 4.5x more likely in females False negative more likely in men (32% vs 17%) May be less sensitive in diabetic women
Stress Echo**	Functional	48-88%	55-96%	Good test overall about 85% no significant sex differences No radiation involved Can do with exercise or pharmacological agents
Myocardial Perfusion Scans**	Functional	81-100%	61-100%	New techniques have decreased false positive from excessive breast tissue Involves radiation Also can do with exercise or pharm. agents

Coronary CTA***	Anatomical	85-95%	85-95%	<p>No significant gender difference in identifying large vessel disease but not good for microvascular dz</p> <p>- Good test to rule “out” but hard to tell if “positive” test is cause of chest pain</p> <p>can be used as a secondary test in intermediate risk pts with indeterminate other testing who are not going directly to cath</p> <p>involves radiation</p>
-----------------	------------	--------	--------	---

* Meta-analysis of exercise testing to detect coronary artery disease in women.
 Kwok Y, Kim C, Grady D, Segal M, Redberg R *Am J Cardiol.* 1999 Mar 1; 83(5):660-6

** Nguyen P, Nag D, Wu J. Sex Differences in the Diagnostic Evaluation of Coronary Artery Disease. *Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology.* 2011;18(1):144-152. doi:10.1007/s12350-010-9315-2.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3657505/#!po=44.6970>

***positive cta is considered > 50% diameter stenosis, problematic as significant flow impairments do not occur until >70% limiting specificity, coronary CTA can also can give a calcium score
 Cardiac stress MRI and PET scans may become more available in future and have better sensitivity in identifying microvascular disease
 Canpolat U¹, Özer N, *Anadolu Kardiyol Derg.* 2014 Dec;14(8):741-6. doi: 10.5152/akd.2014.5406. Epub 2014 Jun 23.
https://www.journalagent.com/anatoljcardiol/pdfs/AnatolJCardiol_14_8_741_746.pdf

Shah’s BMJ High Sensitivity Troponin Study

Change of “rule” in rate by conventional trop versus high sensitivity troponin

	Conventional	High Sensitivity
Men	19%	21%
Women	11%	22%

Gender based differences in MI treatment diagnosed by + conventional troponins

	Seen by Cardiologist	Cardiac Cath	Rx with Statin
Men	95%	74%	85%
Women	80%	47%	60%

Of note, outcome (death or recurrent heart attack) for women with “missed” heart attacks (meaning positive high-sensitivity troponin but “negative” traditional troponin) was the same as those who ruled in by conventional troponin (25% versus 24%).

Shah, A. S. V, Griffiths, M., Lee, K. K., Mcallister, D. A., Hunter, A. L., Ferry, A. V, ... Mills, N. L. (n.d.). High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women : prospective cohort study, 1–8. <http://doi.org/10.1136/bmj.g7873>

Pelletier’s Genesis Praxy Study

Genesis Praxy 12 month outcome in patients <55 with ACS

Biological Male	Biological Female	Score < 66	Score >66
3%	3%	2%	5%

Outcome was recurrent ACS or MACE

Gender index scores

Score: 0-33 associated with more masculine traditional traits

33-66 mixed feminine and masculine traits

66-100 associated with more feminine traditional traits

Genesis Praxy Study: Pelletier, R., Khan, N. A., Cox, J., Daskalopoulou, S. S., Eisenberg, M. J., Bacon, S. L., Pilote, L. (2016). Sex Versus Gender-Related Characteristics. *Journal of the American College of Cardiology*, 67(2), 127–135. <http://www.onlinejacc.org/content/67/2/127>

Miscellaneous tidbits:

- If BP controlled in women would likely decrease rate of MI by > 1/3
- Smoking increases women <55 risk factor for MI 7X
- Diabetes in particular combo with obesity and metabolic syndrome significantly increases risk of MI especially in women less than 50
- US population baseline women twice as likely as men to be depressed, aggregate composite of depression/life stressors/low locus of control increased AMI odds ratio to 3.5
- In INTERHEART study and individuals with known increased life stressors had poorer 30 day outcomes.

- Approximately 63% of women with ACS symptoms and non obstructive coronaries have evidence of microvascular dysfunction. Up to 42% of ED patients also tested positive for microvascular dysfunction after being ruled out for infarction in the ED and were tested by PET.
- African American women compared to white women, have their first MI at earlier age and have 1/3 chance of surviving out of hospital arrest
- American Indian women have risk of CAD at almost twice the rate of US population
- Hispanic women, even though they have increased risk burden seem to be somewhat protected from mortality, theory "Hispanic Paradox" more optimistic and better social support system due to extended family ties.

Other Resources:

Safdar, B. (2017). Ranolazine and Microvascular Angina by PET in the Emergency Department: Results From a Pilot Randomized Controlled Trial. *Clinical Therapeutics* Nice review on NSTEMI +/- early revascularization for men and women

MICROVASCULAR ANGINA IN THE ABSENCE OF CORONARY ARTERY DISEASE IS COMMON IN UNDIFFERENTIATED CHEST PAIN PATIENTS IN THE EMERGENCY DEPARTMENT

Article · April 2016

DOI: 10.1016/S0735-1097(16)31825-3

<http://www.openaccessjournals.com/articles/percutaneous-coronary-intervention-in-women-should-management-be-different.html>

Mehta (2016). Acute Myocardial Infarction in Women A Scientific Statement From the American Heart Association. *Circulation*, 1–33. <http://doi.org/10.1161/CIR.0000000000000351>

Boersma (2002). Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *The Lancet*, 2002 www.ncbi.nlm.nih.gov/pubmed/11812552

<http://jaha.ahajournals.org/content/4/7/e001995.full>

<http://www.health.harvard.edu/heart-health/takotsubo-cardiomyopathy-broken-heart-syndrome>

https://openi.nlm.nih.gov/detailedresult.php?img=PMC3823253_jcmm0011-0739-f3&req=4

<http://imaging.onlinejacc.org/article.aspx?articleid=1660179>