

SEXUAL DIMORPHISM IN HEART DISEASES

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Abstract: *Sexual dimorphism exists in Homo sapiens. Many physiological and pathological differences in gender are due to different hormonal milieu in males and females. Pathology of heart is regulated by hormonal levels circulating in the blood, among those, female sex steroid hormone, estradiol is main. Drastic changes in the levels of this hormone are seen in females only. Directly or indirectly estrogens are mainly involved in showing various aspects of cardiac functioning, genesis of diseases, testing and treatment in man and woman. Now clinicians have realized that both the genders should treated differently.*

Keywords: Sexual dimorphism, Hormonal milieu

INTRODUCTION

Heart disease is the leading cause of death in men and women. The average adult male heart rate is between 70 and 72 beats per minute, while the average for adult women is between 78 and 82 beats. This difference is largely accounted for by the size of the heart, which is typically smaller in females than males [1]. Heart failure affects men and women differently. More women than men get heart failure. In fact, women tend to get a type of heart failure that often goes undetected and has no cure yet but it can develop and present in dramatically different ways across the sexes [2]. It often goes undetected because doctors have traditionally looked at the heart's pumping function rather than the way it relaxes women are more likely than men to have heart attacks that present without chest pains, and they are more

likely to die of a heart attack than men. However in general, both men and women, the most common symptom is chest pain or discomfort, described as an achy, tight or "heavy" feeling.

Women are more likely than men to experience other signs of a heart attack such as: shortness of breath, nausea, feeling faint, breaking out in a cold sweat, pain in the arms, back, neck, jaw or stomach [3].

Causes of heart disease in women: When it comes to cardiovascular disease, women have some inherent risk factors [4]. These include:

1. Age: Risk increases with age, especially after menopause. Oestrogen levels in women start to decline during menopause, raising LDL ("bad") cholesterol and risk of heart disease.

2. **Family:** The risk is higher if a direct family member develops heart disease before 55 years for male relatives, or 65 years for female relatives.
3. **Gender:** Women usually experience heart attacks a decade or so later in life than men, and are more likely to die from them.
4. **Ethnicity:** In Singapore, ethnic differences in heart disease exist, with higher heart attack rates among Indians and a higher risk of dying from a heart attack among Malays.

Other risk factors, which are the same for males and females, can be managed with lifestyle modifications and medications. They include:

1. **Smoking** – Smoking increases the risk of a heart attack by two to three times; it causes more plaque to form and become unstable.
2. **Diabetes High cholesterol** – High levels of LDL (“bad”) cholesterol or low levels of HDL (“good”) cholesterol increase the risk of coronary disease.
3. **Hypertension** (high blood pressure)
4. **Obesity** – Being overweight increases the levels of LDL cholesterol.

Heart regulatory hormones: Hormones play a key role in the health of the heart and cardiovascular system, but high levels of some hormones can contribute to cardiovascular disease. Hormones which when appearing in excess increase the heart rate are: catechol-amines, endothelins, glucocorticosteroids, thyroid hormones, leptin and PTHrP [5]. Those which decrease the heart rate include: natriuretic peptides, substance P, neurokinin A, oxytocin, angiotensin. The sympathetic nervous system (SNS) releases the hormones (catecholamines - epinephrine and norepinephrine) to accelerate the heart rate. The parasympathetic nervous system (PNS) releases the hormone acetylcholine to slow the heart rate.

Here are some facts about hormones and the heart: The heart secretes hormones like atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) that help coordinate the heart’s function

with other organs. These hormones can also inhibit the sympathetic nervous system and the renin-angiotensin-aldosterone axis.

***Epinephrine and dopamine:** These hormones are released from the adrenal gland and are involved in the “fight-or-flight” response.

***Thyroid hormone:** Too much thyroid hormone can cause the heart to beat faster and harder, which can lead to abnormal heart rhythms and high blood pressure.

***Estrogen:** Estrogen can help keep blood vessels flexible, which can increase blood flow and lower blood pressure.

***Testosterone:** Low testosterone levels and high doses of testosterone supplementation can be linked with cardiovascular disease.

*Other hormones that regulate the heart include: vasopressin, renin, angiotensin, and aldosterone.

Young women can get heart failure too: “One of the big myths is that heart disease does not happen to younger women, or that it is not a big problem for women,” The cardiovascular disease – which includes heart disease and stroke – is also a women’s disease and accounts for one third of all female deaths [6].

Women any age can get it, although fewer young women than young men suffer from it. But even those who are young, lean and look fit may have high blood pressure or high cholesterol, which are the beginnings of cardiovascular disease. The incidence rises with age, and especially after menopause in women. In old age, the scales are tipped against them. “We not only catch up with men after menopause, we overtake them,”

She is concerned that women, while dutifully going for regular pap smears and mammograms, neglect to test their heart. “Take care of your heart. That’s the best thing one can do. Without an effective drug, doctors can only treat the symptoms and risk factors, and advise patients on preventive lifestyle changes in diet, stress and exercise – the latter being one of the best ways to reduce stiffening of the heart. “We

can manage their risk factors and the haemodynamics. If they have fluid overload, for instance, we give them diuretics. There are things we can do, but there is no magic pill to improve survival [7].

Differences in blood pressure: The reasons for gender differences in blood pressure are not known. Some studies demonstrated that women tend to have higher heart pump output and lower blood vessel resistance, thereby minimising blood vessel injury [8].

Younger women in their 20s to early 40s may be protected from high blood pressure and cardiovascular disease (e.g. heart attack, stroke) by oestrogen (a female sex hormone). However, this is not yet proven as it is not evident that blood pressure changes are linked to levels of endogenous sex hormones. But that is true that women's blood pressure can escalate when oestrogen levels fall after menopause (around the age of 50). By 70 years old, about 80 to 90 per cent of women are likely to have developed high blood pressure [9]. However, there may be other reasons of high blood pressure such as obesity, physical inactivity, excessive alcohol intake and a high salt diet. In addition, contraceptive pills may further compound a woman's high blood pressure risk.

Heart attacks worse in women: When it comes to heart attacks, women may fare worse than men. A study carried out by NHCS on heart attacks across Singapore showed that women who suffered these were older, had more advanced disease, and experienced more complications than men, resulting in a greater than twofold increase in long-term risk of death compared to men. Heart attacks in men usually involve big coronary arteries. This can be treated using stents to open up the arteries for blood flow to the heart to resume.

However, women's heart attacks can be due to blockages in arteries. These cannot be seen on an angiogram, and no stent is small enough to be put inside them [10]. Another cause of heart attacks in women is stress-induced cardiomyopathy (broken

heart syndrome or Takotsubo cardiomyopathy). Here, severe stress triggers a massive heart attack even when there are no blockages in the arteries. More prone to this are older, post-menopausal women receiving severe bad news [11]. The adrenalin and stress hormones can be so strong that they cause the arteries to constrict. When there's no blood supply to the heart muscle, it results in a heart attack." Symptoms of this disease may also be different in women than in men. These include central chest pain, Jaw or neck tightness, back pain or gastric pain.

Diabetes poses a risk: Diabetes and smoking have a worse impact on women than men, despite both genders having the same risk factors. "We did a study on heart attacks in Singapore, and were shocked that so many of the women were diabetic. And diabetic women with heart attacks did badly and were more likely than men to die. So, diabetes is particularly bad in women and a strong risk factor [12] said Prof Lam, who was the co-first author of the study with Dr Gao Fei, Principal Biostatistician, NHCS. She said diabetic women can prevent cardiovascular disease by taking their medicines as prescribed, controlling their diet and sugar intake, and exercising. "The saving grace is that exercise seems to protect women more than it does men." US guidelines advise women to get at least 150 minutes of moderate exercise a week, but those with heart disease should talk to their doctors before starting an exercise regimen, or be supervised when they do so. Prof Lam also advises women with a family history of heart disease and those who are at menopause – or reaching it – to go for check-ups to ensure their heart is in good order.

These problems are best picked up and managed at an early stage. If you have high blood pressure, high cholesterol or diabetes in the early stage, you can't feel it. You have to test for it," said Prof Lam.

Possible reasons for sexual dimorphism: Men and women have differences in heart and blood vessel size. Men and women display differences in their anatomy and physiology, from the lungs and brain to muscles and joints. Men and women also

have differences in their cardiovascular systems. Compared to men, women have smaller hearts and narrower blood vessels (13). “Because of these biological differences, heart disease can progress differently in women when compared to men,” And yet, until recently, women with heart disease have been diagnosed and treated like men—with the same tests, same procedures, and same medications. Men and women experience cholesterol buildup in different areas. A heart attack occurs when cholesterol plaque builds up inside the walls of arteries and causes damage in the major blood vessels. Men typically develop this plaque buildup in the largest arteries that supply blood to the heart. Women are more likely to develop this buildup in the heart’s smallest blood vessels, known as the microvasculature. Heart disease in both sexes is only partly related to the accumulation of cholesterol. “Inflammation also plays an important role and may contribute to the differences we see in women with heart disease [14].” Men and women have different symptoms of a heart attack. A heart attack does not always look or feel the same in women compared to men. Women also experience chest pressure (it’s still the leading complaint), but they are more likely than men to also report: nausea, sweating, vomiting and pain in the neck, jaw, throat, abdomen or back. Women may have diseases that mimic a heart attack. Women are more likely than men to suffer from diseases that mimic a heart attack. For instance, women are more likely to experience: A coronary spasm: A blood vessel clamps down and mimics a heart attack. A coronary dissection: The wall of a blood vessel tears. Broken heart syndrome: This is a chemical heart attack where enzymes in the blood and changes in the heart muscles resemble a heart attack, but there are no blocked arteries like you see in coronary artery disease [15].

Men and women may have different risk factors for a heart disease. Risk factors for heart disease in women include reproductive history. Certain pregnancy conditions, such as preeclampsia and gestational diabetes may be powerful predictors of future risk of heart disease. A 2016 study on endometriosis and heart disease from Brigham investigators showed that women age 40 or younger

with endometriosis were 3 times more likely to develop heart attack, chest pain, or require treatment for blocked arteries, compared to women without endometriosis in the same age group [16]. “Women with endometriosis, preeclampsia, or gestational diabetes should adopt heart-healthy lifestyle habits. Specialized care should be taken for women with cardiovascular disease before, during, and after pregnancy. At the centre, cardiologists and obstetricians collaborate to identify and modify risk factors early to prevent heart disease before it develops. Men and women require different diagnostic heart care. For instance, if a heart attack is suspected, both men and women receive a cardiac troponin (cTn) test, which measures circulating levels of troponin. This protein is released in the blood when a heart attack has damaged heart muscle. Higher levels of troponin mean more heart damage. But the clinical threshold that signals a heart attack may differ across the sexes.

Another diagnostic test, cardiac catheterization, has long been the gold standard for diagnosing a heart attack, but this test looks for blockages in large arteries. Since women are more likely than men to experience more plaque buildup in the smallest arteries, this test may not be the most appropriate to diagnose heart disease in women. “If a cardiac catheterization doesn’t give clinicians the answers they were expecting, women should ask if other testing is appropriate. This may include a cardiac MRI to look for inflammation of the heart, or intracoronary imaging to look at the inside of blood vessel walls within the heart [17]. This includes intravascular ultrasound that may better detect heart disease in women.

Men and women may require different treatments for heart disease. Medical providers have decades of experience treating the typical cholesterol plaque buildup in largest blood vessels of the heart. But there’s a weaker understanding of how to treat plaque in the microvasculature, or inflammation of the heart. A growing number of clinicians are beginning to approach treatment decisions with the knowledge that women may benefit from treatments that are different from those used in men, from subtle

calibrations in pacemakers to variations on angioplasty. Ultimately, clinical trials will better inform clinicians about treatment differences between men and women.

Lower the risk of heart disease holistically:

Heart disease is avoidable, even if you have a family history [18,19]. Lifestyle changes, like eating healthy foods, staying active, and managing stress can have a large impact in preventing cardiovascular disease, or in keeping it from worsening heart disease is preventable, and women should take action to reduce their risk of heart disease by exercising regularly, not smoking, eating healthily and maintaining a healthy weight, getting their blood pressure and cholesterol levels checked regularly. These protective lifestyle factors have been shown to markedly decrease the risk of cardiovascular disease for women in Singapore. Women who already suffer from cardiovascular disease can lower their risk of having a heart attack by up to 80 per cent by leading a healthy lifestyle

REFERENCES

- [1] St Pierre SR, et al. 2022. Sex Matters: A Comprehensive Comparison of Female and Male Hearts. *Front Physiol.* 22;(13):831179.
- [2] Regitz-Zagrosek V. 2020 Sex and Gender Differences in Heart Failure. *Int J Heart Fail.* 13;2(3):157-181.
- [3] Charatan F 2003 ;. Women with heart attacks have characteristic symptoms, says new study. *BMJ.* 327(7424):1128).
- [4] Bozkurt B, Khalaf S. 2017 Heart Failure in Women. *Methodist DeBakey Cardiovasc J* 13(4):216-223
- [5] Babiker FA, et al. 2002. Estrogenic hormone action in the heart: regulatory network and function. *Cardiovasc Res.* ;53(3):709-19..
- [6] <https://womenshealth.gov/heart-disease-and-stroke/heart-disease>
- [7] Duschek, S., et al. 2009. Hemodynamic determinants of chronic hypotension and their modification through vasopressor application. *J Physiol Sci* 59, 105–112 .
- [8] Jane F. Reckelhoff 2001. Gender Differences in the Regulation of Blood Pressure. *Hypertension.*;37:1199-1208.)
- [9] Everett B, Zajacova A. 2015. Gender differences in hypertension and hypertension awareness among young adults. *Biodemography Soc Biol.*;61(1):1-17.
- [10] Patel H, et al. 2020. Microvascular Disease and Small-Vessel Disease: The Nexus of Multiple Diseases of Women. *J Womens Health (Larchmt).* 29(6):770-779..
- [11] Ramaraj R. 2007. Stress cardiomyopathy: aetiology and management. *Postgrad Med* 83(982):543-6.
- [12] Martín-Timón I, et ai. 2014. Type 2 diabetes and cardiovascular disease : Have all risk factors the same strength? *World J Diabetes.* 5(4):444-70.,”
- [13] Kleisner, K., et al. 2021 How and why patterns of sexual dimorphism in human faces vary across the world. *Sci Rep* 11, 5978.
- [14] Kottlilil S, Mathur P. 2022 The influence of inflammation on cardiovascular disease in women. *Front Glob Womens Health.* 3:979708.
- [15] Akashi, Y.J. et al.: 2015 Epidemiology and pathophysiology of Takotsubo syndrome. *Nature Reviews Cardiology.* 12 (7): 387–397
- [16] Krina T. 2020, Endometriosis . *N. Engl. J. Med.* 382: 382 (13) 1244-1256 .
- [17] Tseng WY, et al. 2016. Introduction to Cardiovascular Magnetic Resonance: Technical Principles and Clinical Applications. *Acta Cardiol Sin.* 32(2):129-44.,”
- [18] Levine, G.N.: The mind-heart-body connection. *Circulation* 2019; 140: 13635.
- [19] [https://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease-prevention/art-20046502.](https://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease-prevention/art-20046502)