ISSN: 2476-230X

Review Article

Cardiology: Open Access

Heart Disease in Women

Sudha Bansode

Professor and Head of Zoology Department, Shankararo Mohite Mahavidyalaya Akluj, India

***Corresponding author**
Sudha Bansode, Professor and Head of Zoology Department, Shankararo Mohite Mahavidyalaya Akluj, India.

Submitted: 06 Oct 2021; **Accepted:** 13 Oct 2021; **Published:** 20 Oct 2021

Citation: *Sudha Bansode (2021) Heart Disease in Women. Cardio Open, 6(3): 146-154.*

Abstract

All women face the threat of heart disease. Knowing the symptoms and risks unique to women, as well as eating a heart-healthy diet and exercising, can help protect you. Heart disease is often thought to be more of a problem for men. However, it's the most common cause of death for both women and men in the United States. Because some heart disease symptoms in women can differ f Heart attack symptoms for women. The most common heart attack symptom in women is the same as in men some type of chest pain, pressure or discomfort that lasts more than a few minutes or comes and goes. But chest pain is not always severe or even the most noticeable symptom, particularly in women. Women often describe it as pressure or tightness. And, it's possible to have a heart attack without chest pain. Women are more likely than men to have heart attack symptoms unrelated to chest pain, such as: Neck, jaw, shoulder, upper back or abdominal discomfort, Shortness of breath, Pain in one or both arms, Nausea or vomiting, Sweating, Lightheadedness or dizziness, unusual fatigue, Indigestion. These symptoms may be vague and not as noticeable as the crushing chest pain often associated with heart attacks. This might be because women tend to have blockages not only in their main arteries but also in the smaller ones that supply blood to the heart-a condition called small vessel heart disease or coronary microvascular disease. Women tend to have symptoms more often when resting, or even when asleep, than they do in men. Emotional stress can play a role in triggering heart attack symptoms in women. Because women don't always recognize their symptoms as those of a heart attack, they tend to show up in emergency rooms after heart damage has occurred. Also, because their symptoms often differ from men's, women might be diagnosed less often with heart disease than men are. If you have symptoms of a heart attack or think you're having one, call for emergency medical help immediately. Don't drive yourself to the emergency room unless you have no other options. Rom those in men, women often don't know what to look for.

What can women do to reduce their risk of heart disease?

Living a healthy lifestyle can help reduce the risk of heart disease. Try these heart-healthy strategies: Quit smoking. If you don't smoke, don't start. Try to avoid exposure to secondhand smoke, which also can damage blood vessels. Exercise regularly. In general, everybody should do moderate exercise, such as walking at a brisk pace, on most days of the week. Maintain a healthy weight. Ask your doctor what weight is best for you. If you're overweight, losing even a few pounds can lower blood pressure and reduce the risk of diabetes. Eat a healthy diet. opt for whole grains, a variety of fruits and vegetables, low-fat or fat-free dairy products, and lean meats. Avoid saturated or trans fats, added sugars, and high amounts of salt. Manage your stress. Stress can cause your arteries to tighten, which can increase your risk of heart disease, particularly coronary microvascular disease. Limit alcohol. If you have more than one drink a day, cut back. One drink is approximately 12 ounces (360 milliliters) of beer, 5 ounces (150 milliliters) of wine or 1.5 ounces (45 milliliters) of distilled spirits, such as vodka or whiskey.

Follow your treatment plan. Take your medications as prescribed, such as blood pressure medications, blood thinners and aspirin. Manage other health conditions. High blood pressure, high cholesterol and diabetes increase the risk of heart disease.

Introduction

Cardiovascular disease is the worldwide leading cause of death in women. Biological differences between the sexes, a result of genetic, epigenetic and sex hormone-mediated factors, are complex and incompletely understood. These differences are compounded by socio-cultural factors and together account for the variation in the prevalence, presentation and natural history of cardiovascular disease between men and women. Although there is growing recognition of sex-specific determinants of outcomes, women remain under-represented in clinical trials, and sex-disaggregated diagnostic and management strategies are not currently recommended in clinical guidelines. Women remain more likely to experience delays in diagnosis, to be treated less aggressively and to have worse outcomes. As a consequence, cardiovascular disease in

women remains understudied, underdiagnosed and undertreated. This review will focus on female-specific characteristics of cardiovascular disease and how these may impact on anesthetic and peri-operative risk assessment and care. We highlight significant differences between the sexes in the natural history of cardiovascular disease, including those disease entities that are more common in women, such as sudden coronary artery dissection or microvascular dysfunction. Given the rapidly rising incidence of maternal cardiovascular disease and associated complications, special consideration is given to the risk assessment and management of these conditions during pregnancy. Increased awareness of these issues has the potential to improve the effectiveness of the multidisciplinary heart team and ultimately improve the care provided to women.

Approximately one in three women in the United States has some form of cardiovascular disease, and 90 percent of women have at least one risk factor for heart disease or stroke. This contributes to a sobering fact: heart disease is the leading cause of death among American women. The good news: it is largely preventable.

One of the most important steps you can take to prevent heart disease is to learn more about both the risk factors and symptoms in women.

Risk factors in women

Risk factors are aspects of your medical history, your family's medical history, and your lifestyle that contribute to heart disease. Risk factors fall into three categories:

Those you cannot control

Those you can help manage, with your doctor's guidance

Those that can contribute to heart disease that you should discuss with your doctor.

Risk factors you cannot control

Age: As women age, their risk increases because of lower estrogen levels and the chances of developing additional health issues that can affect the heart.

Family history: You are at greater risk if an immediate family member had heart disease at an early age-55 for a male relative or younger than 65 for a female relative.

Race: African-American and Hispanic women have a higher risk than Caucasian women.

Gender: Women have a lower risk than men of developing heart disease before menopause, but after menopause, the risk is about equal.

Risk factors you can help manage

Smoking: Smokers are two to four times more likely to have heart disease than non-smokers. When you stop smoking, your body begins to heal, and you will experience almost immediate decreases in blood pressure and heart rate.

High blood pressure: Among women of childbearing age, 20 percent have high blood pressure even though many do not realize it. The rate increases to 40 percent between ages 45 and 64, and 60 percent for those age 65 and over. High blood pressure puts added strain on the heart.

High cholesterol: About one-third of American women have cholesterol levels high enough to pose a serious heart disease risk.

Weight: Excess weight can also put added strain on your heart, raising your blood pressure, cholesterol, and glucose (sugar) levels. Another way to assess weight-related risk is to measure your waistline. For women, a waist measurement of 35" or more indicates an increased risk.

Inactivity: Inactivity can weaken the heart, and it also makes it easier to gain weight, increasing your chances of developing other health issues, such as high blood pressure and high cholesterol.

Other risk factors to consider

Diabetes: Women with diabetes are at greater risk than men with diabetes. Over time, high blood sugar (glucose) levels can damage the body's blood vessels and increase the chances that fatty deposits will build up in the arteries.

Chemotherapy and radiation treatment: Radiation therapy as well as some drugs used to treat cancer, particularly breast cancer, can increase your risk of heart disease. If you have had a cancer diagnosis, talk with your doctor about seeing a cardio-oncologist, a specialist in cancer treatments and its effects on the heart.

Pregnancy complications: Women who develop high blood pressure or diabetes during pregnancy are at higher risk for developing heart disease later in life. It is particularly important for these women to see their doctor regularly for checkups each year and to pay attention to important lifestyle issues, such as exercise and healthy eating.

Stress and depression: Both chronic stress and the sudden onset of stress seem to affect women's hearts more than men's hearts. And people with consistently high levels of stress double their risk of heart disease—equal to the risk of high cholesterol and high blood pressure. A Sudden stressful experience, such as a loved one's death or a bad accident, has been linked to stress-induced cardiomyopathy (broken-heart syndrome), particularly in women. And both stress and depression tend to affect a woman's heart more than a man.

Sleep apnea: A serious condition in which breathing suddenly stops during the night, sleep apnea may be underdiagnosed in women. During an apnea episode, the brain triggers the body to awaken to resume breathing. This frequent, rapid awakening (which you may not even be aware of) can increase blood pressure and put added strain on your heart.

Autoimmune disease: Some of these diseases, such as lupus and rheumatoid arthritis—both more common in women than men—tend to negatively affect the heart, possibly due to the inflammation they cause.

Women's symptoms of heart disease

While women can experience the crushing chest pain that men often describe, women's symptoms of a heart attack and heart disease overall are likely to be more subtle. Here are the ABCs of women's heart disease warning signs:

Angina (chest pain): Angina may feel like traditional pain, but it may also feel like a tightness or pressure in the chest or throat that radiates down the jaw or left shoulder or arm.

Breathlessness: Having shortness of breath or waking up breath-

less at night can be a warning sigh.

Chronic fatigue: Overwhelming or out-of-character fatigue may be a symptom. Severe fatigue that lasts several days can also be a heart attack symptom.

Dizziness: Feeling light-headed or dizzy can indicate heart valve disease or arrhythmia (an irregular heart rhythm).

Edema: Swelling, particularly in the lower legs and ankles, should be assessed by a doctor.

Fluttering or rapid heartbeats: These experiences may cause pain or difficulty breathing.

Gastric upset: Talk with your doctor about nausea or vomiting unrelated to diet.

Heartburn: Some women use "heartburn" or "indigestion" to describe heart-related pain.

These symptoms do not necessarily mean that you have heart disease. But you should listen to your heart and your body. Talk with your doctor about these symptoms, what triggers them, and how long they last.

Methods Section

This case-series of cardiovascular diseases presenting in pregnant females explored the medical approach to acute cardiovascular presentations in pregnant females. The cases were reviewed retrospectively through an in-depth exploration of the medical records. Individual patients were contacted by telephone and asked if their case could be published if anonymity was maintained. All living patients agreed. The deceased patient's mother agreed.

The case reviews allowed for highlighting of the clinical presentations, physical examination findings, imaging features and treatment approaches to patients with spontaneous coronary artery dissection versus paradoxical embolism to the coronary tree, stress induced cardiomyopathy, pulmonary embolism versus amniotic fluid embolism, primary pulmonary embolism, peripartum cardiomyopathy, ventricular arrhythmias, dilated cardiomyopathy, and bicuspid aortic valve associated aortopathy. Cardiovascular Urgencies and Emergencies in Pregnancy: A Case Based Review of Some Cardiovascular Diseases Affecting Pregnant Females.

Results

Cardiovascular Urgencies and Emergencies

Case 1

Cardiology was consulted on a 32-year-old female for severe shortness of breath (SOB), chest pressure, and labile hemodynamics during delivery. She had two prior normal deliveries.

Post-delivery she required intubation and had a blood pressure (BP) of 190/100 mm Hg and heart rate (HR) of 130 beats per minute (bpm). The ECG revealed sinus tachycardia, low voltage QRS and poor R wave progression with diffuse, non-specific ST changes (Figure 1).

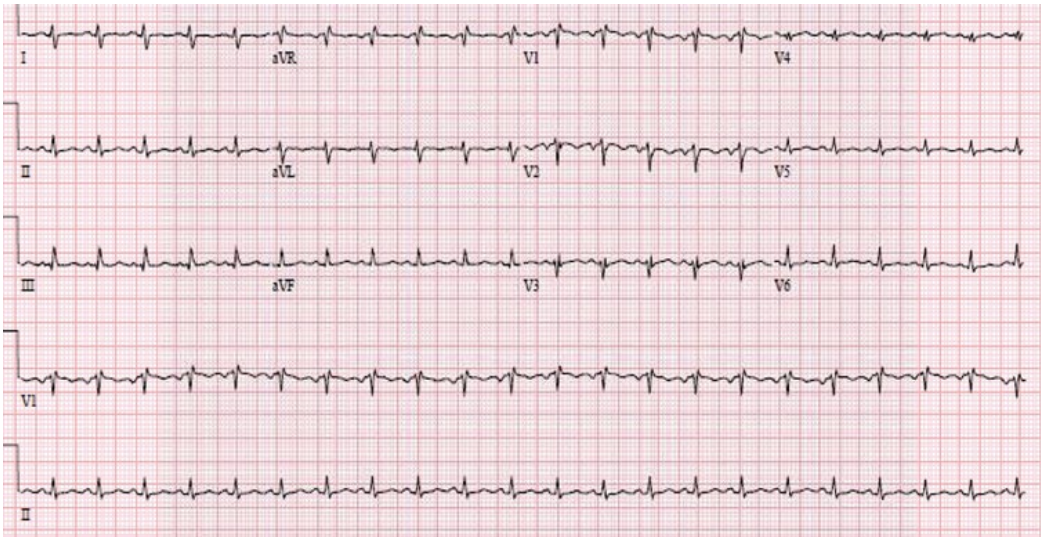

Figure 1: Sinus tachycardia with loss of R waves across the precordium and non-specific ST changes.

Treatment with a diuretic, beta-blocker, and intravenous nitroprusside resulted in a BP = 150/90 and HR = 95 bpm. Oxygenation was adequate with assisted ventilation. Urgent echocardiography revealed left ventricular (LV) systolic function was depressed with an ejection fraction of 20%, dilated right ventricle (RV) with severe reduction of RV systolic function, severe tricuspid regurgitation (TR) and elevated right heart pressure (Figure 2). Incidentally, an atrial septal defect (ASD) was identified.

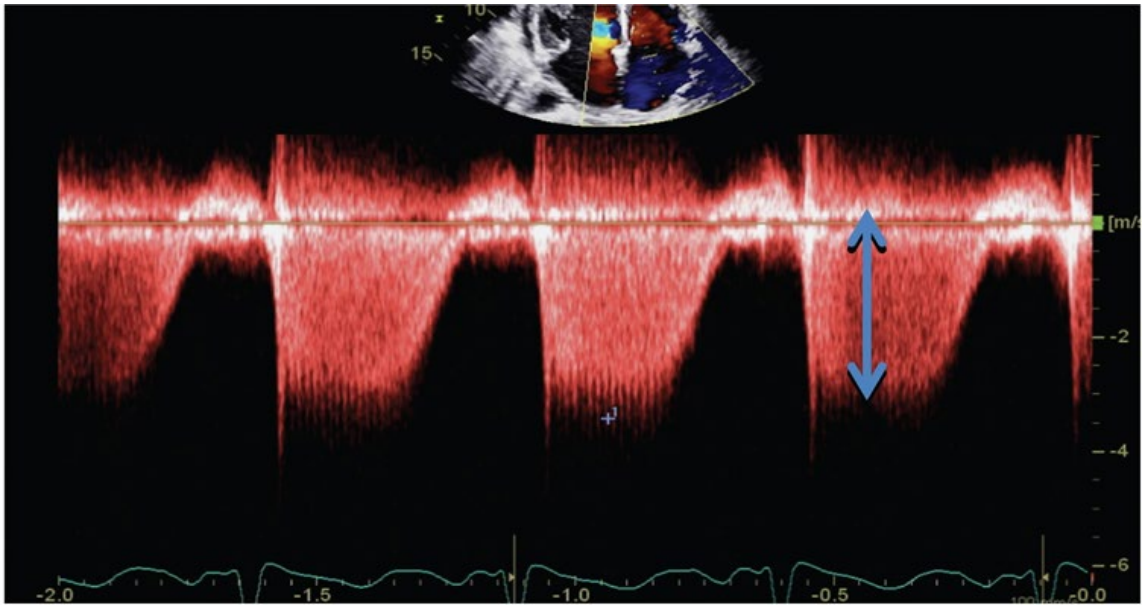

Figure 2: TR envelope: blue arrow to 3.5 m/sec. The RV-RA gradient is approximately 50 mmHg.

Urgent cardiac tomography (CT) scan was negative for pulmonary embolism (PE) and aortic dissection. Magnetic resonance (MR) imaging revealed the left ventricular ejection fraction (LVEF) was 22% and the RV was enlarged. The differential diagnosis generated was a stress-induced cardiomyopathy, paradoxical embolism to the coronary tree, and spontaneous coronary artery dissection. The patient became hemodynamically stable with medical therapy and was extubated with normal oxygen saturations. Follow up evaluation of the ASD with a trans-esophageal echocardiography (TEE) revealed a thin, dyskinetic distal anterior septum and apex, a sinus venous ASD, and normal LV and RV systolic function. Right heart pressure was normal. The patient was feeling well without symptoms and baby was doing well. Review of the case raised a question of an apical myocardial infarction due to SCAD versus embolism to the coronary tree. This led to review of the prior ECGs. The ECG analysis supported the notion of an anterior infarct, as the initial ECG was normal (Figure 3).

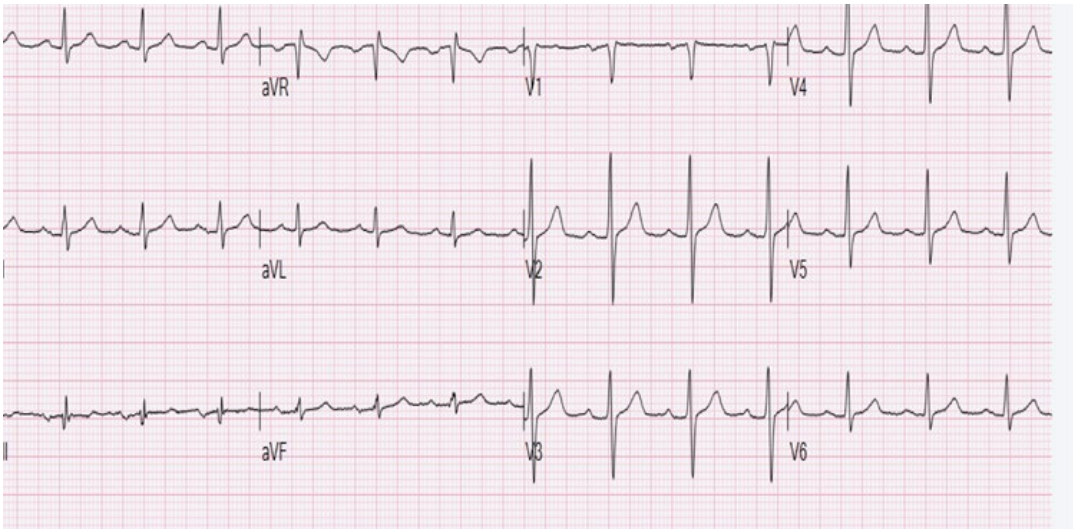

Figure 3: Normal ECG prior to delivery

The ECG post-delivery revealed loss of R waves across the precordium (Figure 1). This retrospectively raised a strong suspicion that the initial insult was an unrecognized coronary artery dissection versus a paradoxical embolism across the ASD to the coronary circulation. The interventional team felt the angiogram was supportive of a dissection. This infarct was supported on MRI and TEE imaging. Surgery was consulted for evaluation of the sinus venous ASD in the setting of enlarged right heart chambers by echocardiography and MRI. The review of the MRI revealed normal venous connections. Because of the apical infarct, surgery requested a cardiac catheterization. The catheterization revealed an occluded left anterior descending coronary artery (Figure 4).

This occluded vessel retrospectively identified the etiology of the post-delivery hemodynamic instability. The patient was feeling well and elected not to pursue surgery for the ASD or coronary disease.

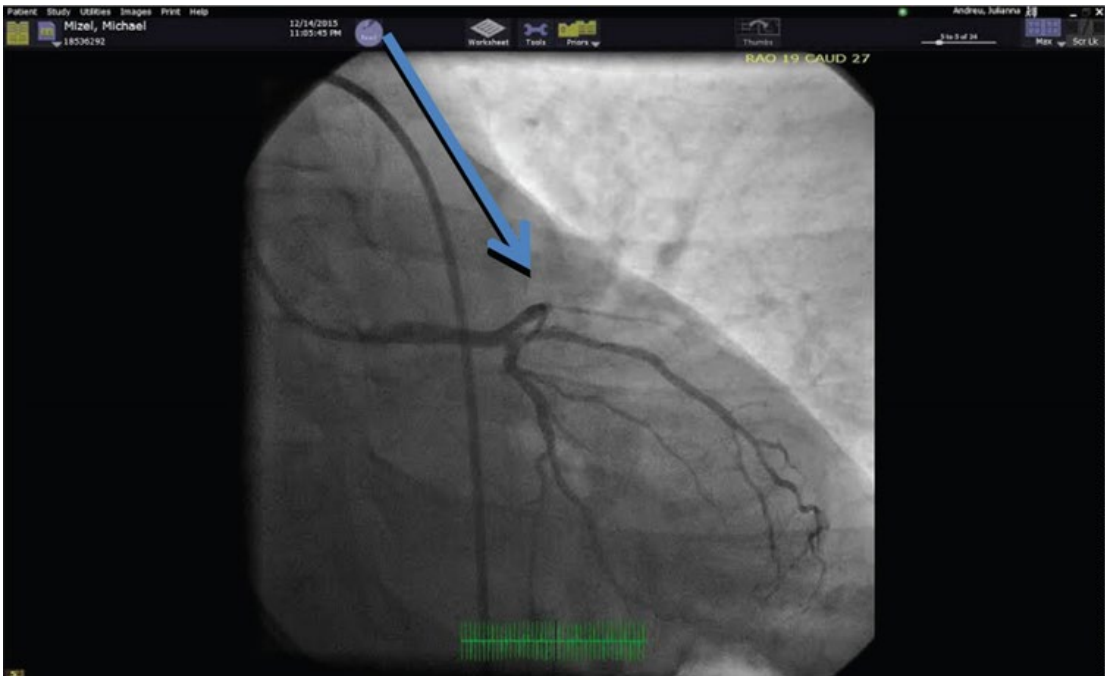

Figure 4: Coronary angiography reveals an occluded LAD (Blue arrow).

Pregnancy and Spontaneous Coronary Artery Dissection (P-Scad)

P-SCAD is a rare condition with an incidence of (0.1%) for all patients referred for coronary angiography [1]. The mean age at presentation is 35-40 years, and greater than 70% of SCAD cases are female [2]. Typically, patients with spontaneous coronary artery dissection are divided into four etiologic groups: peripartum, atherosclerotic, idiopathic, and vasculitic in patients with connective tissue disease [2]. This classification does not cover all potential etiologies of SCAD.

Approximately (33%) of P-SCAD cases occur in the peripartum period, with 1/3 late in pregnancy and 2/3 in the early puerperal period [2]. The peak incidence is two weeks after delivery. The role of the peripartum period in the pathogenesis is an enigma. Theories include hormonal changes, such as high estrogen levels, resulting in subtle changes in arterial wall architecture with ensuing susceptibility to spontaneous dissections. These changes include hypertrophy of the smooth muscle cells, loosening of the intracellular matrix due to increase in acid mucopolysaccharides, and decreased collagen production in the media [3,4]. Additionally, increased total blood volume, high cardiac output, and straining and shearing forces during labor may result in increased wall stress. Thus, hemodynamic and hormonal changes are thought to increase the risk of intimal tears. Patients in the pregnancy subset with underlying connective tissue disorders, such as Marfan syndrome, Ehler-Danlos type 4 and systemic lupus erythematous with vasculitis, may be at even higher risk for P-SCAD [5,6].

P-SCAD is thought to be the consequence of an intramural hematoma of the coronary artery, resulting in a false lumen compressing the true lumen, resulting in myocardial ischemia [7]. The clinical presentation ranges from unstable angina to sudden cardiac death. Young woman with angina and ECG changes should lead to a high suspicion for SCAD and urgent evaluation and angiography should be considered. In young women the left anterior descending coronary artery is the most common location [2]. When angiography is performed the approach ranges from mostly conservative to rarely revascularization with stenting depending on the angiographic and clinical circumstances.

Take home messages for P-SCAD

- Awareness and recognition of P-SCAD is critical to the diagnosis. Acute myocardial infarction (AMI) in pregnancy should be treated similarly to AMI in the general population [8].
- A multidisciplinary approach between cardiology and obstetrics is mandatory as data is lacking regarding the safety of guideline directed medical therapy (GDMT) in pregnancy. Expert opinion is that low dose aspirin (ASA), beta-blocker (BB) therapy and short-term heparin during percutaneous intervention (PCI) are reasonable therapies [8].
- The most experienced operators, due to the risk associated with PCI, should undertake revascularization. Generally, coronary intervention should be limited to cases that are unstable. The approach to P-SCAD must be determined on a case-by-case basis by the multidisciplinary team [8].

Case 2

29-year-old female was in her sixth month of pregnancy. She had no prior personal or family history of cardiovascular disease. She had experienced a prior miscarriage. The miscarriage was emotionally draining and resulted in depression. Psychology consultation resulted in treatment for anxiety and depression.

Resting at home, she developed chest pain, nausea, and loss of consciousness. Emergency medical services were summoned and the paramedics performed an ECG revealing ST elevation inferolaterally (Figure 5). Upon arrival to the emergency room, she developed ventricular fibrillation requiring cardiac defibrillation to restore sinus rhythm.

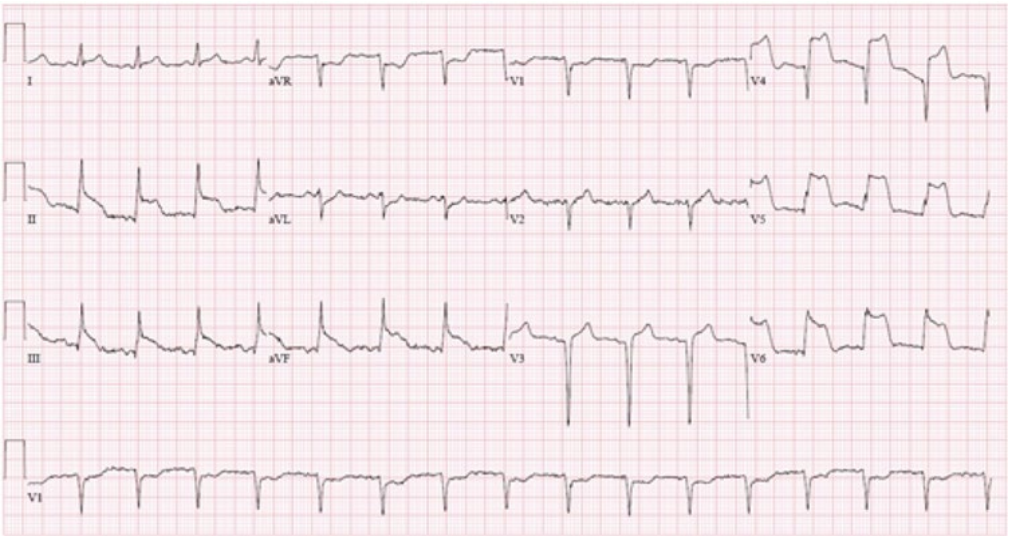

Figure 5: ECG revealing ST elevation inferiorly and laterally.

In the intensive care unit, the patient was hemodynamically stable with an infusion of intravenous dobutamine. She was alert and cognitively intact. Urgent echocardiography revealed an akinetic apex with hypercontractile basal segments. LVEF was estimated to be 35%. There was no associated outflow tract obstruction. There was mild mitral regurgitation. Urgent angiography revealed normal coronary arteries. Laboratory results revealed a mildly elevated troponin and normal electrolytes. The patient was treated with a beta-blockers and diuretic. She clinically recovered without chest pain, shortness of breath, or further rhythm disturbance. Troponin levels normalized and the ECG evolved from ST elevation to inverted t waves inferolaterally. Repeat echocardiography on day 7 revealed normalization of the apical hypokinesis. LVEF = 60%. The patient was discharged home and at nine months gave birth via caesarian section to a healthy baby without newborn cardiovascular deformity.

Takotsubo cardiomyopathy in pregnancy (P-TC)

This case represents a rare form of P-TC with a malignant, life-threatening rhythm disturbance. There is no available evidence that pregnancy predisposes to a stress-induced cardiomyopathy. The majority of stress induced cardiomyopathies recover to normal LV function. In patients where LV dysfunction persists, GDMT is the standard of care and the criteria for implantation of an implantable cardio-defibrillator are determined on a case-by-case basis [9,10].

Takotsubo cardiomyopathy (TC) is a unique form of transient non-ischemic cardiomyopathy that typically occurs in a setting provoked by a stressor - physical, emotional, or both - and hence, is also given the nickname of stress-induced cardiomyopathy. The syndrome occurs most commonly in post-menopausal females. The characteristic clinical syndrome of TC involves acute LV dysfunction with distinctive echocardiographic feature of apical to mid ventricular hypo- to akinesis and sparing of the basal myocardium in the absence of significant obstructive coronary artery disease (CAD).

Alternatively, patients may exhibit reverse TC with basal hypokinesis and hyperkinesia of the apical and mid segments of the left ventricle [11]. Even though the apical ballooning phenotype is the most common and typical presentation, much confusion has resulted from various nomenclatures being used for different presentations of this syndrome. A well-recognized syndrome now, it is also being reported in populations other than postmenopausal women. The occurrence in premenopausal women is rare, and a literature search reveals there are few cases reported in pregnancy [11].

Patients usually present with typical chest pain (70-90%) and dyspnea (20%); other less common presentations include syncope, pulmonary edema and cardiac arrest [10]. Dynamic electrocardiographic changes and elevated cardiac biomarkers (reflecting acute myocardial injury) are usually present [11]. Coronary angiography, however, typically does not reveal any evidence of epicardial coronary obstruction. However, patients with CAD can experience stress-induced cardiomyopathy. Symptoms can be severe and lead to death in 2% of patients [12]. Song and colleagues reported 32% (n = 16) of their patients with TC (n = 50) presented with cardiogenic shock as the initial presentation [1].

The most common electrocardiographic changes reported in TC are ST-segment elevations in precordial leads on admission (range, 46-100% of patients). Subsequent deep symmetrical T-wave inversion in multiple leads and Q-wave formation (range, 6-31% of patients) are frequently found [9,10]. Also, QT interval prolongation (range, 450-501 ms) can be present [8,13]. The combination of clinical symptoms and electrocardiographic changes at patient's initial presentation makes differentiation of TC from ACS very challenging. Most TTC patients present with elevated cardiac biomarkers and have a modest peak in levels within 24 hours, but

levels are markedly lower than would be anticipated on the basis of the extent of wall motion abnormalities and electrocardiogram findings [14-17].

Management focuses on supportive care in the acute phase, while avoiding vasopressor medications because hyperdynamic basal LV can result in outflow tract obstruction. Mortality is low if patients survive the initial critical period and, by definition, they go on to have a full recovery. Recurrence has been reported but recurrences are rare. TC follow-up revealed the rate of major adverse cardiac and cerebrovascular events were 9.9% per patient year, and the rate of death was 5.6% per patient year [17].

Take Home Messages For P-Tc

- P-TC is very rare
- P-TC ventricular arrhythmias are rare
- Patients with P-TC presenting with an acute coronary syndrome (ACS) should be managed according to guidelines for the general population including revascularization techniques [8].
- P-TC patients presenting with heart failure (HF) should be treated according to HF guidelines. Management goals are similar to non-pregnant HF therapy, while avoiding medications toxic to the fetus including angiotensin converting enzyme (ACE) inhibitors, angiotensin 11 receptor blockers (ARBs), angiotensin - nephrilysin inhibitors (ARNI), aldosterone receptor antagonists (MRA) and atenolol. HF with congestion should be treated with loop diuretics, but avoided if feasible due to potential reduction in placental blood flow. Hydralazine and nitrates are safe in pregnancy, although less effective than ACE inhibitors, and should only be used in the presence of hypertension and LV dysfunction with or without congestion. Beta-blockers should be up- titrated starting at low dose to desired effect [8].
- Management of electrical disturbances in P-TC can include: cardioversion, as it is presumed safe in all stages of pregnancy as it does not compromise fetal blood flow. The risk of fetal arrhythmias or initiation of pre-term labor is low [8].

Case 3

25-year-old female presented to the emergency room with severe shortness of breath and hypoxia. She had delivered a full-term baby girl via caesarian section and was discharged five days previously. She was short of breath post-delivery and upon discharge. She became progressively shorter of breath. Her chest X-ray revealed diffuse alveolar infiltrates suggesting pulmonary edema.

Cardiology was consulted. She was hemodynamically stable with a blood pressure of 160/90 and heart rate of 95 bpm. Respiratory rate was elevated at 20 per minute. Her jugular venous pressure (JVP) was elevated and she had a 2/4-holosystolic-murmur at right 4th intercostal space. There was no leg edema.

An urgent echocardiogram revealed an enlarged RV with decreased systolic function with severe tricuspid regurgitation (TR) and estimated pulmonary artery systolic pressure (PASP) was 55 mm Hg (Figure 6). LV systolic function was normal. Treatment included a beta-blocker, diuretic, and low dose angiotensinogen converting enzyme inhibitor. An urgent CT pulmonary angiogram was negative for pulmonary embolism. The working exclusionary diagnosis became amniotic fluid embolism (AFE).

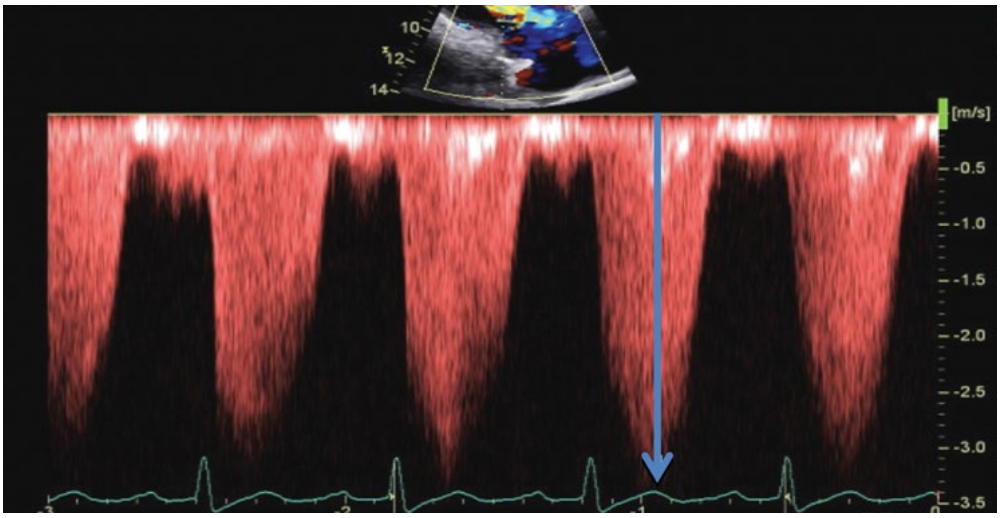

Figure 6: TR envelope is 3.35 m/sec. The RV - RA gradient + RAP (10 mmHg) ~ 55 mmHg

She stabilized clinically with improved hemodynamics and respiratory status. She was discharged on medical therapy. In 6 weeks, she had a repeat echocardiogram revealing normal LV systolic function, decreased RV size, and mild TR with an estimated PASP = 25 mm Hg. The patient and the baby were both doing well. Pulmonary embolism versus Amniotic Fluid Embolism in Pregnancy (P- PE/AFE) Pregnancy and the puerperium are well-established risk factors for venous thromboembolism and anaphylactic syndrome of pregnancy related amniotic fluid embolism. Both pulmonary embolism (PE) and amniotic fluid embolism (AFE) should be considered in a pregnant or post-partum patient with hypotension, hypoxia, hypertension, and right heart failure [18].

There are no clinical symptoms or signs that are specific for pulmonary embolism (PE). There is an overlap between symptoms of PE and normal physiologic changes of pregnancy [18]. Thus, iden-

tifying a clinically important PE during pregnancy, or post-partum, is challenging. It is essential that clinicians understand the potential for over diagnosing and under diagnosing PE during pregnancy. PE is a common cause of death in the hospital and should always be considered when pregnant patients have tachycardia and shortness of breath.

Diagnostic considerations include D-dimer levels, leg ultrasound imaging, and CT pulmonary angiography (CTPA). CTPA has high sensitivity and specify (100%, 89%) for detecting pulmonary emboli [19,20]. Rapid diagnosis leads to appropriate anticoagulation therapy and improved survival of the infant and mother. Undiagnosed PE has a mortality rate approaching 30%, which is reduced to approximately 2-8% when diagnosed and treated appropriately [21,22].

When the CTPA is negative for a pulmonary embolism there should be thoughtful consideration for AFE. AFE is a rare and potential fatal obstetric emergency. AFE may occur during pregnancy, but is more commonly identified during labor and early post-partum. Risk factors for AFE include fetal distress, maternal age, placental abnormalities, eclampsia, polyhydramnios, cervical lacerations, and cesarean section, and rapid delivery. AFE is an allergic like reaction to amniotic fluid entering the mother's circulation. Management is monitoring and treating the respiratory, cardiovascular, and hematological perturbations that arise. AFE is not preventable, but it is essential to recognize it and treat it expectantly [23].

Take Home Message For P- Pe/Afe

- Pulmonary emboli (PE) and deep venous thrombosis (DVT) are known etiologies of pregnancy related morbidity and mortality. The risk of venous thromboembolism (VTE) is paramount in the immediate post-partum period and does not return to normal risks until 6 weeks post-delivery. A high index of suspicion and low threshold for investigation is imperative in pregnant patients [8].
- The optimum diagnostic approach for pregnant females is undefined. A Wells score in combination with D-dimer (low specificity in pregnant patients) testing is a strategy attempting to determine when imaging is needed. A negative D-dimer is helpful, but low D-dimer concentrations have been observed in normal pregnancies [8].
- If VTE suspicion is high, then compression ultrasonography should be performed and if negative, but suspicion remains high, then further testing with low-dose CT scanning should be performed [8].
- When the suspicion is high and testing is underway, the patient should be treated with low molecular weight heparin (LMWH). LMWH is the drug of choice for treatment of VTE in pregnancy and the puerperium [8].
- When CTPE is negative, AFE is the diagnosis of exclusion and careful monitoring is necessary with treatment of organ system complications [23].

Case 4

21-year-old primigravida female presented to the emergency room at 32 weeks of gestation. She had a 7-week history of progressive shortness of breath associated with central chest pressure and tachycardia. She had not sought prior medical care. She was unaware of any health issues. On physical examination she had tachycardia at 110 bpm and tachypnea with a respiratory rate of 22 per minute. Blood pressure was 100/60. Jugular venous pressure was elevated to the angle of the jaw while sitting up. She had a right parasternal heave and lower extremity-pitting edema. Her second heart sound was accentuated. She had a pan-systolic murmur at the right sternal border. The electrocardiogram revealed P pulmonale, RAD, and RV strain pattern. The chest X-ray revealed prominent RV silhouette and dilated pulmonary arteries. The echocardiogram revealed severe RV dilation and hypertrophy (RVH), moderate RV systolic dysfunction, a large right atrium (RA), severe PR, severe TR, plethoric IVC with a calculated right ventricular systolic pressure (RVSP) of 80 mm Hg (Figure 7) and the plethoric inferior vena cava (IVC) revealed systolic flow reversal in the hepatic vein (HV). The mitral inflow Doppler and tissue Doppler were normal.

Discussion

Heart disease is the leading cause of death for women. Women often experience heart disease differently than men. For example, men have more heart attacks than women, but women have a higher heart attack death rate. Women experience higher bleeding rates during percutaneous coronary interventions (PCI) performed through femoral arterial access. Women are also more susceptible to drug-induced cardiac arrhythmias.

FDA's Office of Women's Health (OWH) supports research to provide valuable insight into sex differences in the diagnosis and treatment of cardiovascular disease. OWH has worked across several FDA Centers to support studies on issues ranging from sex differences in cardiac interventions to the cardiotoxicity of breast cancer drugs. Since 1994, OWH has funded 69 studies (14 ongoing and 55 completed). The results of the completed studies have led to a better understanding of cardiovascular disease in women and contributed to the development of guidance documents for drug and device development for men and women.

Current OWH-funded Research on Heart Disease. Completed OWH-funded Research on Heart Disease. Research on the Effects of Drugs on Women's Heart Health. QT Prolongation: Research on the Effects of Drugs on Women's Hearth Health. The FDA Office of Women's Health has been a leader in supporting research to better understand and predict drug-induced heart arrhythmias in women. Heart rate is controlled by electrical signals that pass through the heart each time it contracts and relaxes. These signals make up the heart's electrical cycle – which is commonly measured by the waves on an electrocardiogram (ECG).

When the heart's electrical cycle is abnormal, this can cause irregular heart rhythms (arrhythmias). A type of arrhythmia more common in women than in men is Torsade de Pointes (TdP). TdP events are rare but dangerous and can lead to sudden death. Several drugs have the potential to cause TdP and up to 70% of the drug-induced cases of TdP occur in women. Almost all drugs that cause TdP prolong the QT-interval on the ECG (which corresponds to the heart's relaxation phase). Since TdP events are rare, the drug-induced prolongation of the QT-interval on the ECG is used as an indicator for increased risk of TdP. Since its inception in 1994, the Office of Women's health has worked with FDA's other research programs to support studies on drug-induced QT prolongation.

Phase 1: Understanding the Sex Differences

The exact reason for the higher rate of drug-induced TdP in women is unknown. However, a number of factors may play a role in this sex difference including higher drug levels in women due to smaller body size, influence of sex hormones, differences in how drugs are broken down and transported to the heart or greater sensitivity to drugs that cause abnormal heart rhythms. OWH funded studies to understand the mechanism of the sex differences in drug-induced QT prolongation. OWH also funded research within the Center for Drug Evaluation and Research (CDER) enabling post-market drug analysis to better recognize drug safety effects in women.

Learn more about current OWH-funded research on QT and other CVD topics. Learn about other FDA CVD research at the National Center for Toxicological Research

Phase 2: Supporting the Development of FDA Guidance

Building on the previous studies, OWH partially funded additional research on metabolic drug-drug interactions that contribute to QT prolongation. This research contributed to FDA guidance on the assessment of the QT prolongation potential of drugs for both men and women. As part of this guidance, FDA recommended that drug sponsors conduct a comprehensive study, called the Thorough-QT (TQT) study when seeking FDA approval of a new drug. The TQT study, implemented in 2005, has been an effective screening tool. Although certain commonly used drugs, such as antihistamines and antibiotics, had to be withdrawn from the US market because of drug-in.

Reference

1. Alexandrowicz JS (1932) Innervation of the heart of crustacean (Decapoda) QJ Miros Sci 75: 182-249.
2. Anderson M, Cooke IM (1971) Neural activation of the heart of the lobster Homarus americanus. J Exp Biol 55: 449-468.
3. Barning E (2003) The physiological dock circadian rhythmicity and bio chronometry. J Exp Biol 86: 91-98.
4. Brown FA (1970) The physiological dock Academic Press, New York.
5. Beck S d, Holt Rinehart, Winston (1980) Animal photoperiodism, significance and relation to circadian 14: 167-172.
6. Brady J (1979) Biological clocks: Daily tidal lunar and annual rhythms examples for circadian rhythm & Time sense sun campus orientation, photoperiodism, mechanism of biological clocks. Stud in Bisogy 104.
7. Berlind A, Cooks IM, Goldstone MW (1970) Do the monoamines in crab pericardial organs play a role in peptide neurosecretion? J Exp Biol 53: 669-677.
8. Benson JA (1980) Octopamine shers rhythmic activity in the isolated Cardiac ganglion of the crah, Pertumu song Neuroed Lett 441:59-64.
9. Carlson AJ (1906) Comparative physiology of the invertebrate heart the heart rhythm under normal and experimental condition. Arech J Physiol. 16: 47-66.
10. Cooke IM (1988) Studies on the crustaceans Cantiac ganglion. Comp Biochem Physiol C Comp Pharmacol Toxicol 91: 205-218.
11. Comongis G (1960) Visual responses in crayfish recording responses to light with remote electrodes. J Cell Comp Physiol 55: 189-194.
12. DeCouresy PJ, Walker JK, Smith SA (2000) A circadian pacemaker in free-living chipmunks: essential for survival. J Comp Physiol A 186: 169-180.
13. Durand JP, Goudard F, Barbot C, Pieri J, Fowler SW, et al (2021) Ferritin and hemocyanin: 210Po molecular traps in marine fish, outer and lobster. Mar Ecol Prog Ser 233: 199-205.
14. DeCoursy PJ, Jill R Krulas (1998) Behavior of SCN-Lesioned Chipmunks in Natural Habitat: A Pilot Study. J Biol Rhythms 13: 229-244.
15. Fanjul-Moles ML, Prieto-Sagredo Julio (2003). The circadian system of crayfish: a developmental approach. Microsc Res Tech 60: 291-301.
16. Florey E, Rathmayer M (1978) The effects of octopamine and other amines on the heart and on the neuromuscular transmission in decapod crustaceans: Further evidence for a role as neurohormone. Comp Biochem Physiol C Comp Pharmacol 61C: 229-237.
17. Foster R (1997): A stroboscopic method to investigate the effect of Caffeine on Daphnia heart rate. J Biol Edu 31: 253-255.
18. Gribble NA, Broom DM (1996) Time series analysis and model of heart beat rate, oxygen consumption and locomotor activity from the sand crab, Portumus, pelagicus. Biol Rhythm Res 27: 113-129.
19. Hokkaness A (2000) Chaotic or periodic viridian looking at crustacean beards. J Biol 2014: 451-454.
20. Krijgsman BJ (1952) Contractile and pacemaker mechanism of the heart of arthropods. Biol Rev 27: 320-346.
21. Kuramoto T, Ebara A (1984) Effects of perfusion pressure on the isolated heart of the lobster Panulirus japonicus. J Exp Biol 109: 121-140.
22. Kuramoto T, Ebara A (1985) Effects of perfusion pressure on the isolated heart of the lobster Panulirus japonicus. J Neurosci Res 13: 569-580.
23. Kuramoto T, Yamagishi H (1990) Physiological anatomy Burst formation and Burst frequency of the Cardiac Ganglion of Crustaceans. Physiol Zool 63: 102-116.

Copyright: ©2021 Sudha Bansode. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.