Introduction

Strictly speaking, there are no arrhythmias that are specific to women. However, as with most diseases, the diagnosis of arrhythmias presents unique challenges when applied to women. Women have distinct symptoms, different etiologies and incidences of arrhythmias, and even differing outcomes compared with men.

This article will discuss both the benign and more malignant arrhythmias and their effect on women. It will begin by discussing palpitations and conclude by describing sudden death outcomes in females.

Palpitations

Palpitations are a very common complaint of patients seeing their internists. Large studies have examined what the etiology of palpitations is, and it comes down to either an actual arrhythmia (supraventricular tachycardia (SVT), atrial fibrillation (AF), premature ventricular complexes (PVCs), etc.) or psychiatric issues such as somatization disorders. However, an arrhythmic cause of palpitations is quite common.

Most palpitations that are due to arrhythmias are not life-threatening. The types include SVTs such as atrioventricular nodal re-entry tachycardia (AVNRT), Wolff-Parkinson-White Syndrome (WPW), or an accessory-pathway mediated tachycardia, and atrial tachycardia. Isolated extra beats coming from the top of the heart (the atrium or premature atrial complexes (PACs)) or the bottom of the heart (PVCs) can also produce the sensation of palpitations. Finally, AF, a very common, irregular heart rhythm, can also cause palpitations.

There is no real gender predilection for the incidence of palpitations. However, a common, outdated diagnosis is that of mitral valve prolapse syndrome (MVP). This was given to women who had MVP on echocardiogram of physical exam, palpitations, and anxiety disorder. The implication was that many of these women have SVTs, causing their palpitations and hearts to race – certainly having a heart rate of 200 beats per minute (bpm) can make one feel anxious. This isn’t a real syndrome, and the diagnosis of MVP has no physiologic meaning. Indeed, patients with MVP who do not have mitral regurgitation (leakiness of their mitral valve) do not even need antibiotic prophylaxis.

SVTs

Men and women can both develop SVTs. However, for unclear reasons, there is a 2:1 female predominance for AVNRT, the most common type of SVT. In contrast, there is a 2:1 male predominance for WPW, or SVTs that occur due to a congenital accessory pathway.

Several studies have found that women have an increased incidence of SVT episodes during the luteal phase of the menstrual cycle. The reasons for this are unclear, but it may be due to hormonal control of the electrical conduction system in the heart.

One large study looked at the safety and efficacy of cardiac ablation in patients with SVT. Ablation is a new technology that provides a curative procedure for most patients with SVTs. One might think that women could suffer increased complications with ablation since women tend to have smaller hearts. In this study of 894 patients (47% male) referred for SVT ablation, the authors found that women were referred for ablation later were more symptomatic, and had tried more medications to treat their arrhythmias than their male counterparts. Fifty-eight per cent of the arrhythmias were due to WPW, and 42% were due to AVNRT. The study found that women had a similar success rate and low complication rate for the ablation procedure compared with their male counterparts. However, as is seen with other cardiac procedures, women were referred for this curative procedure much later than men.

AF

AF is probably the most common arrhythmia. It leads to substantial morbidity and mortality in that it carries...
In another interesting paper, the authors gave 12 healthy males and 12 healthy females the antiarrhythmic drug quinidine versus placebo in a blinded fashion. Quinidine is a drug used for AF which is a common cause of torsades and QT$_C$ prolongation. The authors found that the women had a 44% greater QT$_C$ prolongation than the males did when given quinidine. This paper highlights the gender differences in the response to drugs.

Another very interesting paper looked at the effect of ibutilide, a QT$_C$-prolonging antiarrhythmic drug, on the QT$_C$ interval in women during their menstrual cycle. Thirty-eight men and 20 healthy women received the drug, and the women received it on three separate occasions across their menstrual cycle. The authors found that the QT interval prolonged the most during the menstrual and ovulation phases in the women, and all phases were associated with longer QT intervals than the men. This article highlights the strong hormonal connection for this arrhythmia.

### Sudden Death in Women

The Nurses Healthy Study began in 1976 with 121,701 female nurses aged 30–55 years. Study participants filled out questionnaires regarding their health, etc., at regular intervals. From 1976 to 1998, there were 1,110 cardiovascular deaths and 244 sudden cardiac deaths in the cohort. Of those who died suddenly, a surprising 69% had no previous history of cardiac disease. Only 14% of the cardiac deaths had evidence for an MI at the time of death by autopsy, and only 10% had symptoms consistent with an acute coronary syndrome in the previous three weeks. For women who smoked one pack of cigarettes per day or more, this increased the risk of sudden death by four-fold. This study emphasizes that sudden cardiac death in women is often preceded by no prodrome or symptoms.

One study from 1996 looked at 355 survivors of cardiac arrest between 1978 and 1992. Of these patients, 84 were female and 271 were male. One major gender difference that was found in this study was the underlying etiology of the cardiac arrest. Eighty per cent of the men had underlying coronary artery disease (CAD), whereas 55% of the women had non-ischemic cardiac disease. Ten per-cent of the women had structurally normal hearts versus just 3% of the men, which was statistically different (p < 0.0001). Women tended to have a better ejection fraction (better cardiac function) and be less inducible for ventricular arrhythmias compared with men at electrophysiology study.

---

**The QT interval**

The QT interval or the QT$_C$ interval (QT interval corrected for the heart rate) is one of the biggest gender-specific differences that can be identified for arrhythmias. Roughly speaking, the QT$_C$ is a measurement of ventricular repolarization, or the time it takes for the heart to repolarize or ‘reset’. This time is critical, and many life-threatening arrhythmias originate from abnormalities in repolarization. Different ion channels, particularly potassium channels, govern ventricular repolarization, and research has shown that hormones regulate the function of these ion channels.

At birth through puberty, males and females have equally long QT intervals. However, with the advent of puberty, males shorten their QT intervals, whereas females fail to shorten, leaving them with baseline longer QT and QT$_C$ intervals. These findings imply that testosterone in particular allows the males to shorten their QT intervals. Other studies have found that testosterone seems to be protective against some of these QT-prolonging drugs.

### Torsades de Pointes

*Torsades de pointes*, or ‘twisting of the points’, is a potentially life-threatening arrhythmia seen most commonly after administration of certain drugs. Most of these drugs are antiarrhythmic medications like ibutilide, sotalol, procainamide, quinidine, etc. However, certain drug classes can also cause torsades including tricyclic antidepressants, antihistamines, and antipsychotics.

It is well-known that most episodes of drug-induced torsades occur in women. The precise reason for this is not known, but it may be due to women having longer baseline QT$_C$ intervals. One meta-analysis of 93 articles on drug-induced torsades published between 1980 and 1992 found that 70% of the cases occurred in women.
Bibliography