Boletín Médico del
Hospital Infantil de México

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REVIEW ARTICLE

Unveiling the mystery of the female heart's rhythm: a look into gender inequalities in electrophysiology

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Abstract

This review explores gender disparities in cardiac electrophysiology, highlighting differences in the electrical activity of the heart between men and women. It emphasizes the importance of understanding these variances for correct diagnosis and effective treatment of cardiac arrhythmias. Women show distinct cardiac characteristics influenced by sex hormones, affecting their susceptibility to various arrhythmias. The manuscript covers the classification, mechanisms, and management of arrhythmias in women, considering factors such as pregnancy and menopause. By addressing these gender-specific nuances, it aims to improve healthcare practices and outcomes for female patients with cardiac rhythm disorders.

Keywords: *Women. Sudden cardiac death. Channelopathy. Cardiac electrophysiology. Arrhythmias. Female hormones.*

Revelando el misterio del ritmo cardiaco femenino: una mirada a las desigualdades de género en electrofisiología

Resumen

Esta revisión explora las disparidades de género en la electrofisiología cardiaca, destacando las diferencias en la actividad eléctrica del corazón entre hombres y mujeres. Se enfatiza la importancia de comprender estas variaciones para un diagnóstico correcto y un tratamiento efectivo de las arritmias cardiacas. Las mujeres muestran características cardiacas distintas influenciadas por las hormonas sexuales, lo que afecta su susceptibilidad a diversas arritmias. La revisión abarca la clasificación, los mecanismos y el manejo de las arritmias en las mujeres, considerando factores como el embarazo y la menopausia. Al abordar estos matices específicos de género, el objetivo es mejorar las prácticas de atención médica y los resultados para las pacientes de sexo femenino con trastornos del ritmo cardiaco.

Palabras clave: *Mujeres. Muerte súbita cardiaca. Canalopatías. Electrofisiología cardiaca. Arritmias. Hormonas femeninas.*

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Date of reception: 28-02-2024
Date of acceptance: 24-06-2024
DOI: 10.24875/BMHIM.24000030

Available online: 02-10-2024
Bol Med Hosp Infant Mex. 2024;81(5):255-262
www.bmhim.com

Introduction

Women own unique cardiac characteristics, encompassing differences in signal intervals, refractory periods, wave amplitudes, and QT intervals compared to men. These disparities extend to the cellular level, influenced by sex hormones such as estrogen and progesterone, which modulate the heart's electrical activity[1-4]. Consequently, women show varying susceptibilities to different arrhythmias, with certain conditions disproportionately affecting them. Gender disparities in cardiac electrophysiology have appeared as a critical area of study, unveiling nuanced differences in the electrical activity of the heart between men and women[5,6]. Understanding these variations is paramount as they hold implications for the diagnosis, treatment, and management of cardiac rhythm disorders. While historically, research in cardiology has focused on male subjects, recent advancements have shed light on the distinct electrocardiographic and electrophysiological profiles shown by women[7-9]. This manuscript aims to comprehensively review the gender-specific differences in cardiac rhythm, unraveling the intricacies of the female heart's rhythm and its implications for clinical practice. In Fig. 1, a visual summary of the main differences is presented.

Electrocardiographic and electrophysiological differences in women

Electrocardiographic and electrophysiological variances in women display distinctive characteristics in comparison to men. Women typically present with shorter heart signal intervals (PR, AH, and HV), a diminished refractory period of the AV node, and smaller heart wave amplitudes (P, T) and QRS width. Despite adjustments for ventricular mass and body weight, women often show lower voltage in the QRS complex. In addition, the ST segment displays a slower slope, and the ascent of the T wave is less steep in women[10-12]. Notably, women's hearts show differences in the timing and strength of electrical signals, particularly at rest, where they display a longer QT interval, reflecting the heart's electrical recovery time. Although this discrepancy diminishes with increased heart rate, women present with a higher resting heart rate and show greater variability in RR intervals due to the influence of vagal tone on the sinus node. These gender-specific variations potentially contribute to women's susceptibility to certain heart rhythm disorders, such as atrioventricular nodal reentrant tachycardia (AVNRT) and long QT syndrome (LQTS), while showing reduced predisposition to arrhythmias associated with heart muscle damage[13]. At the level of individual cells, women's heart cells are smaller, contract more slowly, and have longer action periods, which increase their likelihood of experiencing irregular heartbeats. Hormonal influences, notably estrogen and progesterone, further modulate heart rate and electrical activity, with estrogen exerting protective effects against some rhythm disturbances by modulating potassium flux, while testosterone shows distinct impacts. Hormonal fluctuations throughout the menstrual cycle alter the heart's electrical dynamics, notably affecting the duration of the QT interval[14]. These insights underscore the critical importance of considering gender in the diagnosis and treatment of electrical heart conditions, emphasizing the significant impact of sex hormones on the heart's electrical system and its responsiveness to stress[15-19].

Main arrhythmias in women

Arrhythmias in women encompass a wide range of conditions, from benign irregular heartbeats to severe disorders potentially leading to sudden cardiac death (SCD)[20,21].

Supraventricular arrhythmias

Supraventricular premature beats (SVPBs)

Particularly prevalent in women, SVPBs increase the risk of severe cardiac events, such as stroke and death, by up to 60%, potentially due to a heightened risk of atrial fibrillation (AF)[22,23]. Women often experience a more significant impact on their quality of life. Treatment goals include preventing other supraventricular arrhythmias, reducing cardiovascular event morbidity, preventing stroke, and avoiding death. Individual management strategies involve assessing the need for medical intervention to control underlying conditions, anticoagulation therapy, and considering catheter ablation. Diagnosis in women presenting with palpitations and a normal electrocardiogram can be challenging, often leading to misdiagnosis associated with anxiety.

AVNRT

As the most common type of paroxysmal supraventricular tachycardia, AVNRT accounts for 50% of all

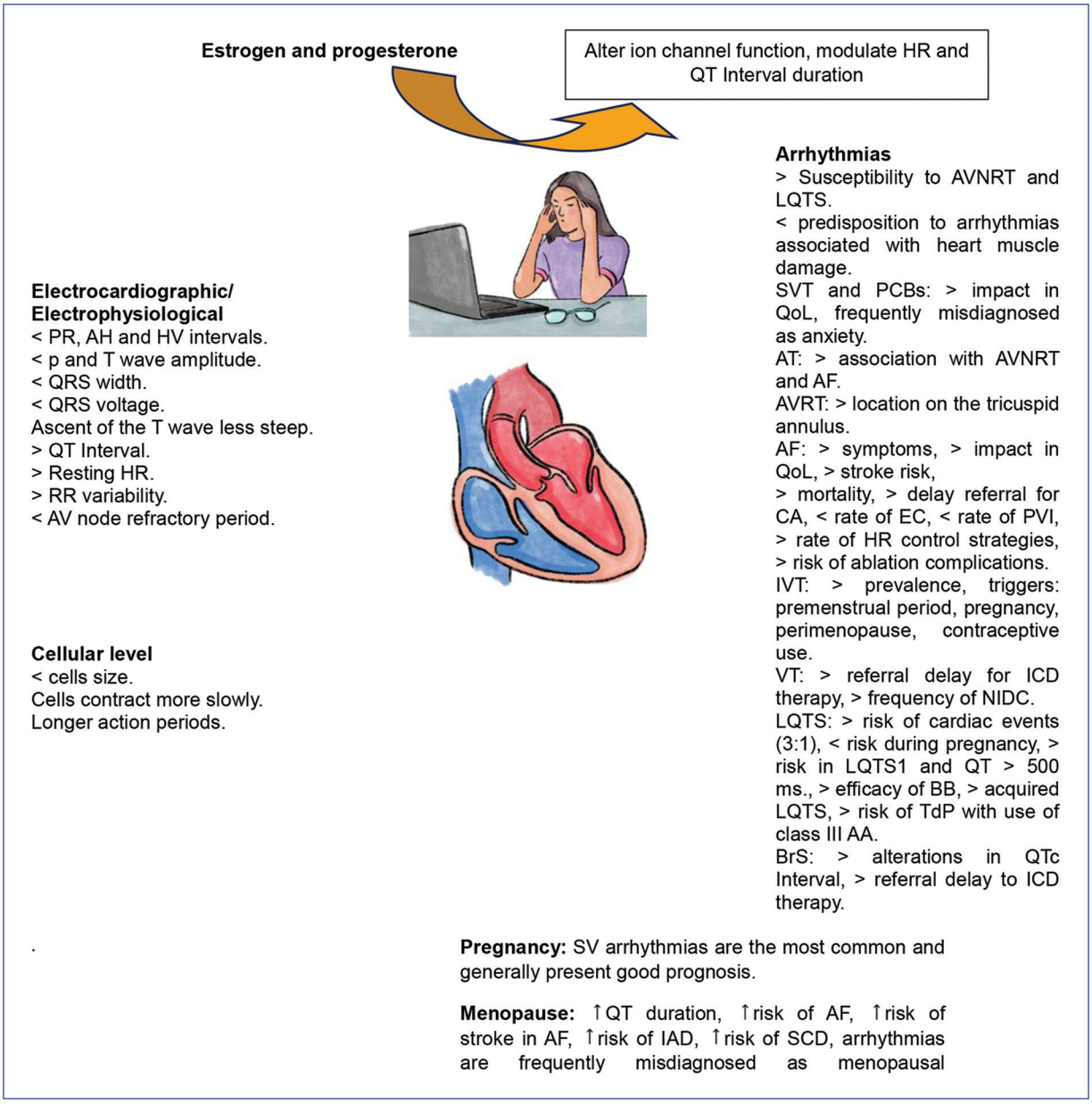

Figure 1. Most prominent electrophysiological differences in women compared to men. HR: heart rate; AVNRT: atrioventricular nodal reentrant tachycardia; LQTS: long QT síndrome; SVT: supraventricular tachycardia; PCBs: premature contraction beats; QoL: quality of life; AT: atrial tachycardia; AVRT: atrioventricular reentrant tachycardia; AF: atrial fibrillation; CA: catheter ablation; EC: electric cardioversión; PVI: pulmonary vein isolation; IVT: idiopathic ventricular tachycardia; VT: ventricular tachycardia; ICD: implantable cardioverter defibrillator; NIDC: nonischemic dilated cardiomyopathy; BB: beta-blocker; TdP: torsades de pointes; AA: antiarrhythmics; BrS: brugada síndrome; SV: supraventricular; IAD: ischemic arterial disease; SCD: sudden cardiac death.

tachycardia cases in both sexes, with a higher incidence in young women. Diagnosing AVNRT, especially in non-documented cases of short-duration paroxysmal tachycardia, can be challenging, leading to misdiagnosis associated with anxiety events. There are no observed sex differences in the acute success rate, complications, and recurrences in catheter ablation[24].

Atrial tachycardia (AT)

Common in women, AT has a similar anatomical origin and success rates in both sexes. Women diagnosed with focal AT may have associations with other arrhythmias such as AVNRT. In elderly women and those with AF risk factors, the origin site

may be the pulmonary veins, needing a thorough assessment for AF risk at diagnosis and during follow-up[25,26].

Atrioventricular reentrant tachycardia (AVRT)

More commonly found in men, AVRT is associated with a higher occurrence of accessory pathways. In women, these accessory pathways are often found in the tricuspid annulus, while in men, they tend to be on the left side. Catheter ablation is equally effective as a definitive treatment for both women and men[27].

AF

Although more prevalent in men, AF presents differently in women, often being more symptomatic and associated with higher stroke risk, needing a gender-tailored treatment approach. Women with AF experience worse quality of life and higher mortality rates[22]. Multinational registries show delayed referral for catheter ablation[28], lower likelihood of receiving electrical cardioversion and/or pulmonary vein isolation, and a greater tendency toward rate control strategies in women. In addition, women face a heightened risk of ablation-related complications[29,30].

Ventricular arrhythmias, channelopathies, and SCD

Ventricular arrhythmias

Ventricular arrhythmias are commonly associated with structural heart disease, ranging from frequent ventricular premature beats to ventricular tachycardia (VT) and even VT-induced cardiomyopathy.

VT without structural heart disease

While being a minority (10%) of ventricular arrhythmias, idiopathic VTs (IVTs) rarely lead to sudden death and are benign. More prevalent in women, IVTs often trigger during specific periods such as the premenstrual period, pregnancy, perimenopause, and contraceptive use. Catheter ablation, the definitive treatment, shows no gender-based differences in effectiveness or safety.

VT with structural heart disease

Scar tissue from earlier infarction is the typical substrate, yet women suffer more from non-ischemic dilated cardiomyopathy (NIDCM). Women with NIDCM experience referral delays and are less likely to receive proper implantable cardioverter-defibrillator (ICD) therapy. Although post-ablation recurrence is higher in women with ischemic cardiomyopathy, success rates, and complications stay consistent across genders.

Channelopathies

Cardiac channelopathies are heritable disorders caused by pathogenic variants in genes encoding cardiac ion channel subunits and ancillary proteins essential for human cardiomyocyte electromechanical function. This group includes congenital LQTS, Brugada syndrome (BrS), catecholaminergic polymorphic VT, and short-QT syndrome, each characterized by unique genetic and clinical features, electrocardiogram signatures, and typical presentation modes[14].

LQTS

Presents gender-specific considerations in risk assessment for ventricular arrhythmias, with a heightened risk seen in pre-pubertal children and women post-puberty. Following puberty, women with LQTS face a threefold increased risk of cardiac events, although their risk during pregnancy is lower, escalating postpartum[31,32]. High-risk women typically show the LQTS2 phenotype and a QTc > 500 ms, calling for primary prevention strategies such as ICD therapy to mitigate SCD risk.

LQTS1 arises from mutations in the *KCNQ1* gene, predisposing boys to a greater risk of ventricular arrhythmias and fatal events compared to girls. Risk patterns during puberty show a decline in boys but an escalation in girls.

LQTS2, associated with mutations in the *KCNH2* gene, poses a persistent risk of lethal arrhythmic events in women, even post-menopause. Beta-blockers show greater efficacy in women and remain a cornerstone of treatment.

LQTS3, linked to mutations in the *SCN5A* sodium channel gene, shows a lower risk in childhood but escalates significantly in adulthood, with reports suggesting a higher risk in men for severe events.

Acquired LQTS, more prevalent in women, often stems from factors, such as electrolyte imbalances and QT-prolonging medications[33]. These factors, combined with female sex and underlying conditions, such as renal dysfunction, heighten the risk of *torsades de pointes* (TdP) with class IIA and III antiarrhythmics.

BrS

Prevalent in adult males, particularly post-pubertal individuals, tends to manifest with more severe events in males, due to androgen modulation of Ito channel dysfunction. Female patients may show pronounced QTc interval alterations in response to certain medications, needing careful monitoring. The *SCN5A* gene mutation underlies BrS, with post-pubertal males showing a higher incidence of severe or lethal events compared to women[34,35].

SCD

Accounting for approximately 20% of all fatalities, with a higher incidence seen in men, SCD can be up to 35% of total cardiac deaths in women. Risk factors include smoking, hypertension, and diabetes. Women show specific electrophysiological traits associated with SCD, including a longer QT interval post-puberty, lower QRS voltage compared to men, and potential hormonal effects altering ion channel function. Increased vagal tone, manifested as bradycardia, and heightened heart rate variability are also prevalent[36].

The presentation and mechanism of SCD in women show distinct features, with only one-third of cases attributed to ischemic heart disease. Symptoms preceding sudden death are often absent, with shortness of breath being the primary reported symptom. Mechanistically, arrhythmias play a pivotal role, with VT/ventricular fibrillation being predominant in men, while pulseless electrical activity appears as the primary rhythm in women, influencing survival outcomes.

Women diagnosed with heart failure (HF) show a more favorable prognosis compared to men, attributed to factors such as sex hormones, differences in intracellular calcium handling, and myocardial remodeling.

In women, SCD is often associated with non-ischemic causes, as found in post-mortem analysis. Left ventricular ejection fraction serves as an independent predictor of mortality in men but lacks similar prognostic significance in women.

Regarding sports related to SCD, channelopathies may have a lesser impact on women compared to men. Diagnostic measures such as resting and exercise electrocardiograms, along with molecular genetic screening, play a pivotal role in showing underlying mutations and assessing disease severity[37].

Implantable cardioverter defibrillator

ICDs have proven efficacy in preventing SCD from arrhythmias, yet their use still is suboptimal, particularly among women. Despite both genders receiving proper therapies at similar rates, women are less often offered ICD therapy, underscoring disparities in access and treatment.

Cardiac resynchronization therapy (CRT)

CRT, a pivotal innovation in HF management, proves significant benefits, particularly for patients with severe systolic dysfunction and electrical dyssynchrony. Despite evidence suggesting a favorable response to CRT in women, there exists a notable underutilization of this therapy among female patients. Factors contributing to this disparity include delayed recognition of symptoms, diagnostic delays, and concerns on implantation-related complications in women.

Gender-specific ventricular remodeling

Gender-specific differences in ventricular remodeling are clear, as women show a slower reduction in ventricular mass over time due to lower rates of apoptosis. Women also show greater left ventricular hypertrophy, smaller ventricular diameters, and preserved ventricular function, albeit with more pronounced relaxation disorders.

Arrhythmias in pregnancy

Arrhythmias during pregnancy can arise de novo or worsen preexisting conditions, with risk factors including structural heart disease, channelopathies, and advanced maternal age. While the majority of cases follow a benign course and respond well to treatment, factors, such as labor and delivery can elevate risk levels[38]. Physiological changes in pregnancy, such as increased heart rate and cardiac axis deviation due to uterine expansion, contribute to the development of rhythm disturbances, along with hormonal fluctuations, autonomic tone variations, and hemodynamic shifts. Supraventricular arrhythmias, such as AF/flutter and supraventricular tachycardia are common, while ventricular arrhythmias occur less often. Women with underlying heart conditions require careful management due to heightened risk[39].

Cardiac arrhythmias during labor have been associated with negative outcomes, such as higher rates of

cesarean section, preterm delivery, neonatal care admission, and extended hospital stays. Among these arrhythmias, ventricular ones pose the greatest risk to both the mother and the fetus[40]. Management typically involves standard protocols to ensure maternal and fetal well-being, including telemetry during labor and maintenance of normal electrolyte levels and euvolemia. Device placement, like pacemakers or defibrillators, is safest during the second trimester, and breastfeeding is safe due to compatible medications. Supraventricular tachycardias are common and often benign, but ventricular arrhythmias and channelopathies like LQTS require specialized treatment to prevent complications, including SCD.

A collaborative approach that integrates maternal-fetal medicine, obstetrics, and arrhythmia specialists is crucial. Tailored strategies, such as using antiarrhythmic drugs, performing catheter ablation, and considering device placement, should be carefully weighed to balance risks and benefits. In high-risk cases, the recommendation is to consider ICD during pregnancy. However, it requires careful consideration of potential complications, as well as optimization of device programming and medication regimens. Alternative options like subcutaneous and wearable defibrillators require further investigation about their utility in pregnancy. Close monitoring and collaboration among specialists are crucial for ensuring the best outcomes for both mother and baby.

Arrhythmias in menopause

During menopause, disruptions in the delicate balance of estrogen and progesterone receptors in the myocardium contribute to increased susceptibility to AF[41]. Postmenopausal women also experience heightened periatrial adipose tissue, impairing ionic and voltage transport function[42]. Fluctuations in sex hormone levels correlate with tachycardia paroxysms, with estrogen deficiency linked to more frequent events and a higher likelihood of requiring catheter ablation. Despite a lower prevalence of AF in women compared to men, the risk becomes comparable or higher after age 75, particularly among postmenopausal women with comorbidities, such as hypertension and obesity. While studies like the Framingham Heart Study have not linked menopause onset with AF incidence[43], female sex combined with advanced age and comorbidities elevates the risk of cerebral embolism. Postmenopausal women face increased risks of ischemic heart disease and SCD due to the loss of estrogen's cardioprotective effects. Hormone replacement therapy's effects on arrhythmia induction remain controversial since it has been suggested an increase in QT interval post-replacement. Palpitations, accompanied by vasomotor symptoms, are common manifestations of arrhythmias in perimenopausal and postmenopausal women, often overlooked as menopausal symptoms. Sex hormones significantly contribute to arrhythmogenesis during menopause, underscoring the importance of prompt evaluation and referral for specialized treatments like ablation procedures or cardiac stimulation device implantation.

Antiarrhythmics in women

Antiarrhythmic therapy presents distinctive challenges in women due to their heightened risk of TdP and susceptibility to adverse drug effects. It is imperative for patients to be vigilant in recognizing symptoms indicative of TdP, such as dizziness or palpitations differing from their usual ones. Extensive research has uncovered gender-specific differences, with up to 70% of women facing an elevated TdP risk when prescribed class IA and III antiarrhythmics[15,44]. Higher doses of sotalol, exceeding 320 mg/day, have been associated with a 4.1% risk in women, compared to 1.9% in men. Similarly, dofetilide administration in women, particularly those with risk factors, such as HF and prolonged QTc, carries a heightened proarrhythmic risk, reaching 47% versus 28% in men, especially in patients with functional class III/IV or recent infarction and ventricular dysfunction. Ibutilide usage in women entails a proarrhythmic risk of 5.6% versus 3% in men, while quinidine, known for its proarrhythmic potential, poses a 4.8% risk in women, contrasting with no clear risk in men. Given women's longer QT duration due to reduced repolarization reserve, they are particularly vulnerable to developing malignant arrhythmias when exposed to medications prolonging the QT interval, with 65-75% of drug-induced TdP cases occurring in women.

Gender disparities in pediatric arrhythmias

Some differences in arrhythmias based on gender have been observed in pediatric populations. In a study involving 3556 patients aged 12-21 years, significant disparities were noted in the gender distribution of AVRT and AVNRT, with females exhibiting a higher likelihood of AVNRT than AVRT ($p < 0.0001$). Conversely, no significant gender discrepancies were identified in

younger age groups[45]. In another study comprising 233 cases of SVT in individuals aged 0-18 years, male predominance was observed across all SVT subtypes, except for AVNRT[46]. Regarding hereditary arrhythmogenic diseases, differences in gender have also been noted. In prepubescent children, boys with LQT1 exhibit an elevated risk of arrhythmias compared to girls, while the risk is similar between genders in LQT2 or LQT3[47]. However, after puberty, the risk pattern reverses, with post-pubertal females with LQT1 facing a higher risk of arrhythmias[47], and those with LQT2 show a greater risk for ventricular arrhythmias compared to males. In addition, a study of 967 consecutive cases of sudden arrhythmic death syndrome (SADS) demonstrated a male predominance, particularly in younger age groups[48]. Notably, in BrS, an exception to the male-predominant arrhythmic risk exists in the pediatric age group, where spontaneous BrS ECG was associated with earlier onset of arrhythmic events, particularly related to fever, in girls compared to boys[49].

Conclusion

This study emphasizes the significance of recognizing and addressing gender disparities in cardiac electrophysiology and arrhythmias. Variations in electrocardiographic and electrophysiological profiles between men and women have significant implications in clinical practice, affecting correct diagnosis and tailored treatment approaches. Unique hormonal and physiological factors contribute to differences in women's heart electrical activity, influencing the prevalence and manifestation of certain arrhythmias. Considering these gender-specific factors is essential for managing arrhythmias during pregnancy and menopause and selecting proper antiarrhythmic therapies. We need a combined approach that mixes basic and clinical research to better understand the underlying causes of health issues and create better treatment plans tailored specifically to each gender. By acknowledging and addressing these disparities, we can strive for more inclusive and effective cardiological care for individuals of all genders.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

References

1. Shufelt CL, Pacheco C, Tweet MS, Miller VM. Sex-specific physiology and cardiovascular disease. Adv Exp Med Biol. 2018;1065:433-54.
2. Burke JH, Goldberger JJ, Ehlert FA, Kruse JT, Parker MA, Kadish AH. Gender differences in heart rate before and after autonomic blockade: evidence against an intrinsic gender effect. Am J Med. 1996;100: 537-43.
3. Stramba-Badiale M, Spagnolo D, Bosi G, Schwartz PJ. Are gender differences in QTc present at birth? MISNES investigators. Multicenter Italian study on neonatal electrocardiography and sudden infant death syndrome. Am J Cardiol. 1995;75:1277-8.
4. Insulander P, Vallin H. Gender differences in electrophysiologic effects of mental stress and autonomic tone inhibition: a study in health individuals. J Cardiovasc Electrophysiol. 2005;16:59-63.
5. Taneja T, Mahnert BW, Passman R, Goldberger J, Kadish A. Effects of sex and age on electrocardiographic and cardiac electrophysiological properties in adults. Pacing Clin Electrophysiol. 2001;24:16-21.
6. Okin PM, Roman MJ, Devereux RB, Kligfield P. Gender differences and the electrocardiogram in left ventricular hypertrophy. Hypertension. 1995;25:242-9.
7. Zeitler EP, Poole JE, Albert CM, Al-Khatib SM, Ali-Ahmed F, Birgersdotter-Green U, et al. Arrhythmias in female patients: incidence, presentation and management. Circ Res. 2022;130:474-95.
8. Yang PC, Clancy CE. Effects of sex hormones on cardiac repolarization. J Cardiovasc Pharmacol. 2010;56:123-9.
9. Abi-Gerges N, Philp K, Pollard C, Wakefield I, Hammond TG, Valentin JP. Sex differences in ventricular repolarization: from cardiac electrophysiology to Torsades de Pointes. Fundam Clin Pharmacol. 2004;18:139-51.
10. Tran H, White CM, Chow MS, Kluger J. An evaluation of the impact of gender and age on QT dispersion in healthy subjects. Ann Noninvasive Electrocardiol. 2001;6:129-33.
11. Bidoggia H, Maciel JP, Capalozza N, Mosca S, Blaksley EJ, Valverde E, et al. Sex-dependent electrocardiographic pattern of cardiac repolarization. Am Heart J. 2000;140:430-6.
12. Surawicz B, Parikh SR. Prevalence of male and female patterns of early ventricular repolarization in the normal ECG of males and females from childhood to old age. J Am Coll Cardiol. 2002;40:1870-6.
13. Magnano AR, Holleran S, Ramakrishnan R, Reiffel JA, Bloomfield DM. Autonomic nervous system influences on QT interval in normal subjects. J Am Coll Cardiol. 2002;39:1820-6.
14. Asatryan B, Yee L, Ben-Haim Y, Dobner S, Servatius H, Roten L, et al. Sex-related differences in cardiac channelopathies: implications for clinical practice. Circulation. 2021;143:739-52. Erratum in: Circulation. 2021;143:e1028.
15. Martínez-Solano J, Martínez-Sellés M. Sudden death in men versus women with heart failure. Curr Heart Fail Rep. 2023;20:129-37.
16. Saba S, Link MS, Homoud MK, Wang PJ, Estes NA 3rd. Effect of low estrogen states in healthy women on dispersion of ventricular repolarization. Am J Cardiol. 2001;87:354-6.

17. Larsen JA, Tung RH, Sadananda R, Goldberger JJ, Horvath G, Parker MA, et al. Effects of hormone replacement therapy on QT interval. Am J Cardiol. 1998;82:993-5.
18. Altunkeser BB, Ozdemir K, Içli A, Celik C, Akyürek C, Gök H. Effects of long-term hormone replacement therapy on QT and corrected QT dispersion during resting and peak exercise electrocardiography in post-menopausal women. Jpn Heart J. 2002;43:1-7.
19. Yang PC, Kurokawa J, Furukawa T, Clancy CE. Acute effects of sex steroid hormones on susceptibility to cardiac arrhythmias: a simulation study. PLoS Comput Biol. 2010;6:e1000658.
20. Prajapati C, Koivumäki J, Pekkanen-Mattila M, Aalto-Setälä K. Sex differences in heart: from basics to clinics. Eur J Med Res. 2022;27:241.
21. Odening KE, Choi BR, Liu GX, Hartmann K, Ziv O, Chaves L, et al. Estradiol promotes sudden cardiac death in transgenic long QT type 2 rabbits while progesterone is protective. Heart Rhythm. 2012;9:823-32.
22. Rodríguez-Reyes H, Laguna-Muñoz CI, Gallegos-de Luna CF, de-Los-Ríos-Ibarra MO, Salas-Pacheco JL, Leyva-Pons JL, et al. Fibrilación auricular en población mexicana: Diferencias en presentación, comorbilidades y factores de riesgo entre hombres y mujeres [Atrial fibrillation in Mexican population: differences in presentation, comorbidities and risk factors between men and women]. Arch Cardiol Mex. 2022;92:349-57.
23. Anselmino M, Battaglia A, Gallo C, Gili S, Matta M, Castagno D, et al. Atrial fibrillation and female sex. J Cardiovasc Med (Hagerstown). 2015;16:795-801.
24. Irie T, Kaneko Y, Nakajima T, Ota M, Iijima T, Tamura M, et al. Electroanatomically estimated length of slow pathway in atrioventricular nodal reentrant tachycardia. Heart Vessels. 2014;29:817-24.
25. Turkmen Y, Insulander P, Bastani H, Drca N, Saluveer O, Tapanainen J, et al. Focal atrial tachycardia-the localization differences between men and women: a study of 487 consecutive patients. Anatol J Cardiol. 2020;24:405-9.
26. Doi S, Furukawa T, Kameshima H, Tanaka O, Harada T, Akashi YJ. Speech-induced atrial tachycardia with presyncope. Intern Med. 2023;62:2517-20.
27. Maury P, Zimmermann M, Metzger J. Distinction between atrioventricular reciprocating tachycardia and atrioventricular node re-entrant tachycardia in the adult population based on P wave location; should we reconsider the value of some ECG criteria according to gender and age? Europace. 2003;5:57-64.
28. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al. Sex differences in cardiac arrhythmia: a consensus document of the Europe and Heart Rhythm Association, endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. Europace. 2018;20:1565.
29. Mendonca-Rivera MA, Berni-Betancourt A, Cárdenas I, Escobar J, Hardy C. From the pathophysiology to the treatment of atrial fibrillation in women. Cardiovasc Metab Sci. 2022;33:S477-9.
30. Ehdaie A, Cingolani E, Shehata M, Wang X, Curtis A, Chugh S. Sex differences in cardiac arrhythmias. Clinical and research implications. Circ Arrhythm Electrophysiol. 2018;11:e005680.
31. Seth R, Moss AJ, McNitt S, Zareba W, Andrews ML, Qi M, et al. Long QT syndrome and pregnancy. J Am Coll Cardiol. 2007;49:1092-8.
32. Díez-Escuté N, Arbelo E, Martínez-Barrios E, Cerralbo P, Cesar S, Cruzalegui J, et al. Sex differences in long QT syndrome. Front Cardiovasc Med. 2023;10:1164028.
33. James AF, Choisy SC, Hancox JC. Recent advances in understanding sex differences in cardiac repolarization. Prog Biophys Mol Biol. 2007;94:265-319.
34. Martínez-Barrios E, Arbelo E, Cesar S, Cruzalegui J, Fiol V, Díez-Escuté N, et al. Brugada syndrome in women: what do we know after 30 years? Front Cardiovasc Med. 2022;9:874992.
35. van der Crabben SN, Kowsoleea AI, Clur SB, Wilde AA. Pregnancy in women with Brugada syndrome: is there an increased arrhythmia risk? A case-series report. J Cardiovasc Electrophysiol. 2022;33:123-7.
36. Teodorescu C, Reinier K, Uy-Evanado A, Ayala J, Mariani R, Wittwer L, et al. Survival advantage from ventricular fibrillation and pulseless electrical activity in women compared to men: the Oregon Sudden Unexpected Death Study. J Interv Card Electrophysiol. 2012;34:219-25.
37. Rajan D, Garcia R, Svane J, Tfelt-Hansen J. Risk of sports-related sudden cardiac death in women. Eur Heart J. 2022;43:1198-206.
38. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, et al. ESC Scientific Document Group. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39:3165-241.
39. Vaidya VR, Arora S, Patel N, Badheka AO, Patel N, Agnihotri K, et al. Burden of arrhythmia in pregnancy. Circulation. 2017;135:619-21.
40. Sharma N, Coleman K, Ma R, Gurciullo D, Bimal T, Ansari U, et al. Prevalence and clinical significance of arrhythmias during labour in women with structurally normal hearts. Open Heart. 2022;9:e002117.
41. Ko D, Rahman F, Schnabel RB, Yin X, Benjamin EJ, Christophersen IE. Atrial fibrillation in women: epidemiology, pathophysiology, presentation, and prognosis. Nat Rev Cardiol. 2016;13:321-32.
42. Gerdts E, Regitz-Zagrosek V. Sex differences in cardiometabolic disorders. Nat Med. 2019;25:1657-66.
43. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22:983-8.
44. Chaudhry GM, Haffajee CI. Antiarrhythmic agents and proarrhythmia. Crit Care Med. 2000;28:N158-64.
45. Anand RG, Rosenthal GL, Van Hare GF, Snyder CS. Is the mechanism of supraventricular tachycardia in pediatrics influenced by age, gender or ethnicity? Congenit Heart Dis. 2009;4:464-8.
46. Quattrocelli A, Lang J, Davis A, Pflaumer A. Age makes a difference: symptoms in pediatric supraventricular tachycardia. J Arrhythmia. 2018;34:565-71.
47. Zareba W, Moss AJ, Locati EH, Lehmann MH, Peterson DR, Hall WJ, et al. Modulating effects of age and gender on the clinical course of long QT syndrome by genotype. J Am Coll Cardiol. 2003;42:103-9.
48. Mellor G, Raju H, de Noronha SV, Papadakis M, Sharma S, Behr ER, et al. Clinical characteristics and circumstances of death in the sudden arrhythmic death syndrome. Circ Arrhythm Electrophysiol. 2014;7:1078-83.
49. Milman A, Gourraud JB, Andorin A, Postema PG, Sacher F, Mabo P, et al. Gender differences in patients with Brugada syndrome and arrhythmic events: data from a survey on arrhythmic events in 678 patients. Heart Rhythm. 2018;15:1457-65.