EDITORIAL

Gender Differences in ECG Parameters and Their Clinical Implications

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It is well known that there are significant and meaningful differences in the measured ECG parameters between females and males, beginning in adolescence and persisting thereafter. During the first decade of life, the quantitative ECG parameters in females and males are remarkably similar with regard to resting heart rate, PR interval, QRS duration, QRS voltage, T-wave amplitude, T axis, ST-segment location, QRS-T angle, QT interval, and the frequency of normal U waves.¹ There are clearly racial differences in some of these parameters, but within each racial group the ECG patterns are remarkably similar in preadolescent females and males.² Beginning in adolescence, the resting heart rate is somewhat faster in females than males, the QT interval and the QTc interval become significantly longer in women than men probably as a result of female hormones,³ and the QRS amplitude and QRS duration become larger in males than females as a result of the male hormones and the associated increase in cardiac mass and left ventricular wall thickness. In addition, the ST segment is more labile with a greater degree of nonspecific ST-segment deviation in women than men. In the absence of cardiovascular disease, these differences remain significant between sexes throughout adulthood.

What are the clinical implications of these gender-related differences in healthy adults. The most obvious one relates to the longer QT and QTc intervals in women and their enhanced sensitivity to QT prolong drugs relative to men.^{4,5} Several studies have shown a greater lengthening of the QT interval with repolarization-prolonging medication and a 2–3-fold increased ventricular arrhythm-

mic risk to a host of QT-prolonging drugs in women when compared to men. In patients with the inherited Long QT Syndrome, adult women not only have longer resting QTc intervals than men, but they have a 3-fold greater risk of arrhythmic-related cardiac events in the 20–40 age range than their male brethren.^{6,7} In fact, the risk of cardiac events in adult women with Long QT Syndrome is dominated by the LQT2 genotype with some data to suggest an enhanced estrogen-prolonging QT interval effect in this genotype.⁷

Healthy adult women have smaller left ventricular mass and a narrower QRS duration that is, on average, about 10 ms shorter than men.⁸ In adult patients with ischemic and nonischemic cardiomyopathy, women also have less intraventricular conduction disturbance and less QRS duration prolongation than men. The magnitude of the QRS prolongation with cardiac disease has a direct effect on the magnitude of cardiac dyssynchrony, and for any given prolonged QRS duration value, women would be expected to have more cardiac dyssynchrony and be a greater risk for heart failure than men. Our recent Multicenter Automatic Defibrillator Implantation Trial - Cardiac Resynchronization Therapy (MADIT-CRT) study has shown that for any given QRS prolongation that women receive a significantly greater beneficial effect from biventricular left ventricular pacing than their male counterparts.⁹

The greater lability and dynamicity of ST-segment deviation in women than men adds to the difficulty in accurately diagnosing subtle ischemic-related ECG changes in women.¹⁰ For many years, the same criteria were used during treadmill

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exercise testing for diagnosing ischemic-related ST-segment shifts during peak exercise and in recovery. It became clear with improved diagnostic accuracy from stress thallium and coronary angiographic studies that these ST-segment shifts were less frequently associated with coronary disease than for the same repolarization changes in men. Subsequently, new ECG standards were developed for target heart rate and ST-segment shifts for women for identification of an abnormal ECG recording.¹¹

In the current issue of *Annals*, Mayuga et al. evaluated the circadian variation in the dispersion of repolarization as measured by the T-wave peak to T-wave end interval (TpTe) and by QT-dispersion in healthy women and men.¹² These authors found that QT dispersion was greater in men with more diurnal variation than in women. The magnitude of the QT dispersion in men was greatest in the early morning hours, the time period when the risk for arrhythmic sudden cardiac death is known to be enhanced. There were sex differences in the TpTe interval in the lateral precordial leads, with men having longer TpTe intervals than women, but no difference in the circadian pattern of TpTe between the sexes. Overall, the findings suggest a complex interaction between gender and repolarization that requires further study.

The differences that exist between healthy men and women in various ECG parameters probably reflect the interplay of anatomic, structural, hormonal, autonomic, and genetic factors. We know that the frequency and incidence of many cardiac diseases are different by gender with complex age by gender interactions. It is clear that sex and age-based ECG standards should be used when interpreting the clinical significance of heart rate, QRS duration, QRS amplitude, ST-segment deviation,

and QT interval at rest and during activity. It has been said that genders speak in different ways—*viva la difference*.

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