Sex Differences in the Morphology of RR-Matched T-waves Are Highly Heterogeneous Across Leads

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Background: The quantification of T-wave morphology changes using time-warping is a strong cardiovascular risk factor, and the electrophysiology underlying the T-wave, and its associated risk, are different in males and females. We aimed at quantifying the T-wave morphological differences between males and females in different leads in an unselected population.

Methods: We analysed 12-lead ECG recordings from 23,962 participants in the UK Biobank, split them into males and females, and subsequently clustered them into bins of RR interval (width of 50 ms). In each cluster, we derived an RR-matched mean warped T-wave (TWM). Then, we quantified, for each lead, the T-wave morphological variability between each TWM in males and females using two markers of temporal, d_w, and amplitude, d_a, morphological variability. Finally, we quantified, for each lead and sex, the T-wave morphological variability between two TWMs located at extreme RR interval values.

Results: The T-wave morphological differences between males and females were lowest in V4 (d_w = 1.57 [0.58] ms, median [IQR]), and largest in V1 (d_w = 25.10 [19.95] ms), while the values of d_w when comparing the TWMs at extreme RR values were 6.50 (4.33) ms in males and 5.82 (3.24) ms in females. Regarding morphological variations in the amplitude domain between males and females, aVR showed the lowest difference (d_a = 3.96 [3.45] a.u.), whereas V1 showed, again, the largest differences (d_a = 166.24 [137.85]). The values of d_a measuring TWMs variations at extreme RR values were 64.01 (38.02) a.u. in males, and 29.69 (14.79) a.u. in females.

Conclusions: Sex differences in the T-wave morphology are comparable to or higher than differences due to RR changes, and are markedly heterogeneous across leads. While this indicates that sex should be considered when using T-wave morphologies for cardiovascular risk prediction, further studies are needed to elucidate the underlying mechanisms.