Characterization of the TU-wave complex of Andersen-Tawil syndrome with KCNJ2 mutations using high-frequency ECG data

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Introduction: Andersen-Tawil syndrome (ATS) is characterized by ventricular arrhythmias, periodic paralysis, and dysmorphic facial and skeletal features. Electrocardiograms (ECGs) of ATS are characterized by large U waves, a prolonged repolarization process, frequent premature ventricular contractions (PVCs), and polymorphic/bidirectional ventricular tachycardia. However, the exact differences between the U-waves of ATS and those of healthy individuals remain to be investigated. We tried to characterize the TU-wave complex of ATS using high-frequency ECG data.

Methods: ECGs were recorded as time series data with a 2kHz frequency ECG amplifier in 10 patients with ATS type 1 (positive for KCNJ2 mutation, ATS1 group) and age-matched healthy individuals (control group). Conventional temporal parameters (corrected by √RR) were measured, and independent component analysis (ICA) were applied to TU-wave complex on raw tracings. Data obtained were compared between the 2 groups.

Result: Although QUc and QUp (Q to U peak) were longer in the ATS1 group than the control group, QTc and QTp (Q to T peak) were comparable between the groups. Time from T end to U end (TeUe), time from T peak to U peak (TpUp), time from bottom to U peak (BUp), and time from bottom to U end (BUE), where bottom is the lowest point between T and U waves, were all significantly longer in the ATS1 group than the control group (p<0.0001). ROC curve analysis revealed that AUC values of U wave-related parameters (QUc, TeUe, TpUp, BUp, and BUe) were >0.9 (indicating high accuracy). Particularly, the AUC of BUe was 1.0. Multivariate logistic regression analysis revealed that BUe could completely differentiate the 2 groups with no overlaps. More importantly, ICA extracted one or two U wave-specific independent components (ICs) that exclusively comprise the U wave in ATS1, whereas U waves in the control group were composed of some ICs that also comprised T waves. Figure is an example of the results of ICA in a patient with ATS1, showing that one U-wave specific IC (IC6) is extracted.

Conclusion: This study indicates that U waves in patients with ATS1 can be differentiated from those in healthy individuals by several U wave-related temporal parameters, particularly BUe. Furthermore, the existence of U wave-specific ICs, extracted in the ICA, is useful for differentiation of U waves in ATS1
from those in healthy individuals, although the mechanisms of independency of the ICs from T wave remain to be clarified.