Heart rate variability as a biomarker in chronic chagas cardiomyopathy patients with or without concomitant digestive involvement, for prediction of rassi score risk classes

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Introduction: The pathogenesis of Chronic Chagas Cardiomyopathy (CCC) is not yet fully elucidated. However, dysautonomia is one of the factors involved, in addition to being the essential mechanism in the pathogenesis of the Digestive Form of Chagas Disease (DFCD). The prognostic value of dysautonomia remains speculative, and there are no correlative studies of dysautonomia in CCC and DFCD.

Purpose: This study has three aims: a) to investigate in patients with CCC the relationship between cardiac dysautonomia, indirectly studied by heart rate variability (HRV), and the prognostic stratification assessed by the Rassi score; b) to compare the HRV in groups with isolated CCC and with the mixed form, i.e. CCC associated with DFCD; c) to evaluate the power of combining HRV indices to predict the risk class of each patient, using machine learning.

Methods: Thirty-one patients with CCC were classified into three risk groups (low, intermediate and high) according to their Rassi score and had two electrocardiograms (ECG) recorded, i.e. the conventional 12-lead and a single lead, the latter for a period of 10 to 20 minutes. From the single lead ECG, two equally sized RR series were generated and 31 HRV indices were calculated from each. The HRV was then compared between the three risk groups and also regarding the presence or not of concomitant digestive impairment. Taking HRV indices as inputs, four machine learning models were compared in its ability to predict the risk class of each patient. A previous step of attribute selection (sequential feature selection) was applied to identify the most relevant HRV indices for each algorithm.

Results: Comparing the HRV indices in the three risk groups obtained with the Rassi score, the phase entropy is decreased [0.91 (0.90, 0.91) vs 0.87 (0.86, 0.89); p=0.039] and the percentage of inflection points is increased [66.4 (63.5, 71.2) vs 58.2 (53.4, 63.3); p=0.032] in patients in the high-risk group, compared to the low-risk group. Of the 31 patients with CCC, 14 had the mixed form of the disease, i.e. with associated digestive impairment. In the latter, the triangular interpolation of the RR interval histogram decreased significantly [78.1 (62.5, 101.6) vs 121.1 (80.1, 146.5), p=0.046], while the absolute power in the low-frequency band decreased with strong trend to statistical significance [28.5 (17.1, 97.5) vs 86.9 (44.1, 171.7), p=0.06]. The best predictive model for each risk group was obtained with the Support Vector Machine, reaching an overall F1-score of 0.61.

Conclusions: The worst prognosis, indicated by the Rassi score, is associated with increased heart rate fragmentation. The combination of HRV indices enhanced the accuracy of the risk stratification. Compared to CCC the mixed form of Chagas' disease displays a decrease in the components of slow heart rate oscillation, suggesting a higher degree of sympathetic autonomic denervation associated with parasympathetic impairment.