Cosinor-Based Circadianity of T-Wave Alternans Activity as a Predictor of Sudden Cardiac Death in Heart Failure: a Post-Hoc Analysis of the GISSI-HF Holter Substudy

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Introduction: Many studies in the last decades associate the existence of T-wave alternans (TWA) in the ECG to the risk of suffering malignant ventricular arrhythmias and sudden cardiac death (SCD). In this work, we studied how circadian rhythms affect to TWA changes in a heart failure (HF) population and we evaluated the ability of TWA circadian rhythm characteristics to predict the risk of SCD.

Methods: 24-hour Holter ECG recordings from 388 HF patients corresponding to New York Heart Association (NYHA) classes II-IV were analyzed. Three Holter recordings were acquired for each patient, allowing to assess the evolution of TWA over 1-year period. TWA level was assessed trough the index of average alternans (IAA), which measures the average TWA activity along the whole recording, using a multilead fully automated method based on periodic component analysis (πCA) combined with the Laplacian likelihood ratio method (LLRM). The IAA was also measured for in 1- hour intervals, allowing to observe the influence of circadian rhythms on TWA. The Cosinor method was applied to adjust a sinusoidal wave to the results. Survival analysis was performed by using Kaplan-Meier method.

Results: IAA distribution follows a oscillatory pattern, being minimal during the night period ($IAA_{01\text{-}02}$=0.43 (0.261;0.743) μV) and maximal in the central hours of the day ($IAA_{11\text{-}12}$=0.931 (0.58;1.58) μV. The MESOR (medium value of the adjusted sinusoidal wave) of the IAA circadian analysis was a stronger predictor than IAA in the study population (Hazard Ratio(95%CI): 3.33 (1.38-8.06), p=0.008) as well as in the reduced LVEF subpopulation (HaR(95%CI): 3.65 (1.22-10.89), p=0.02). Considering the maximum MESOR within the three available Holters led to an improved HaR: 4.07 (1.48-11.21), (p=0.007).

Conclusion: TWA is affected by circadian pattern and MESOR parameter of the circadian variation was found to be associated with the risk of SCD in the study population.

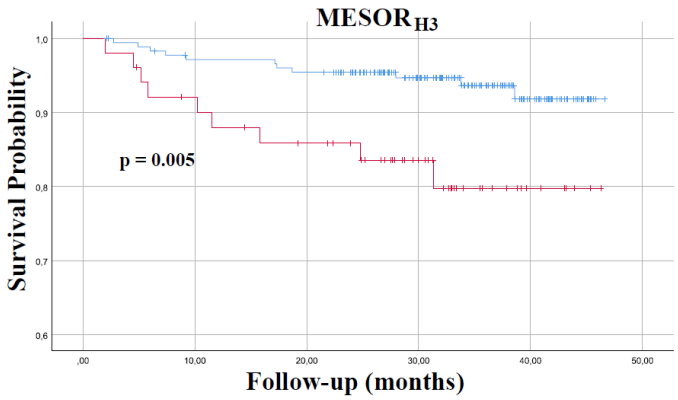

Figure 1: Kaplan-Meier curves for MESOR of IAA. In blue, survival probability curve of patients with low risk (MESOR-), in red, survival probability curve for high-risk patients (MESOR+).