# Assessing a Warping Methodology for the Identification of Increased Cardiovascular Risk Based on the HR Profile Morphology

Julia Ramírez, Stefan van Duijvenboden, Pablo Laguna, Esther Pueyo, Andrew Tinker, Pier D. Lambiase, Patricia B. Munroe, Michele Orini

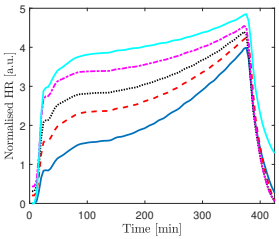
William Harvey Research Institute, Queen Mary University of London
London, United Kingdom

**Background:** Heart rate (HR) response to exercise and recovery are strong predictors of cardiovascular mortality. We hypothesize that the analysis of the HR profile morphology (HRPM) during an exercise stress test would improve risk prediction accuracy.

**Methods:** 1-lead ECG recordings of 17,691 participants from the general population in an exercise stress test from the UK Biobank study were analyzed. The test used a bicycle ergometer, and included 6 minutes cycling and 1 minute recovery. Non-linear time warping was used to: (1) Compute the average HRPM representative of the physiological response to exercise and recovery and (2) Quantify the difference between each individual HRPM and the average HRPM, $d_a$. The primary endpoint included deaths or admissions to hospital due to cardiovascular disorders. Probability of reaching the primary endpoint at 5 years was assessed with Cox regression survival analysis.

**Results:** In a multivariate Cox model, $d_a$ was a significant predictor of the primary endpoint (p<0.0001), independently of age, gender, body mass index, resting HR, maximum HR increase during exercise or HR recovery at 1 minute. Individuals in the first quintile of $d_a$ (low-risk group, blue HR profile in Figure 1) had a hazard ratio of 1.48 (95% CI 1.52-210, p = 0.012) compared to those in the fifth quintile (high-risk group, cyan HR profile in Figure 1), suggesting that cardiovascular risk is associated with a slower and attenuated response to exercise manifesting in an abnormal HRPM.

**Conclusions:** Our methodology for assessing HRPM abnormalities captures relevant prognostic information independent of resting, peak and recovery HR and may potentially be used to improve risk-prediction accuracy of ECG exercise stress test for screening of the general population.




*Five most representative HR profile morphologies corresponding to the first (blue), second (dashed red), third (dotted black, and representing the average HRPM), fourth (dashed-dotted magenta) and fifth (cyan) quintiles of $d_a$.*