Interaction between ECG and Genetic Markers of All-Cause Mortality Risk

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Background: Genetic risk scores (GRS) have shown to be useful for examining the cumulative predictive ability of genetic variation on cardiovascular disease, and they have been reported to be independent to conventional demographic risk factors. However, whether they can independently contribute to refine risk prediction in combination with traditional ECG markers is unknown. Our aim was to study the predictive value of a model combining ECG and a GRS for all-cause mortality (ACM).

Methods: ECG and genetic data was analysed in 53,079 individuals without known cardiovascular disease from the UK Biobank. We included several established ECG markers: heart rate, PR interval, QRS duration, corrected QT interval (QTc), and resting T-peak-to-T-end interval (Tpe). A GRS for coronary artery disease was derived based on 192 genome-wide significant variants previously downloaded from the Polygenic Score Catalog. The primary end point was ACM.

Results: A total of 986 ACM events were recorded during a median follow-up period of 7 years. Variables significantly associated with ACM in a univariate Cox regression analysis were sex (hazard ratio, HR = 1.86, $P = 2.38$ x 10^{-21}), age (HR = 2.08 per standard deviation [SD], $P = 1.88$ x 10^{-73}), heart rate (HR = 1.12 per SD, $P = 4.34$ x 10^{-7}), QTc (HR = 1.12 per SD, $P = 1.31$ x 10^{-6}) and the GRS (HR = 1.07 per SD, $P = 3.46$ x 10^{-2}). When combining them together in a multivariate Cox regression analysis model, sex (HR = 1.80, $P = 3.58$ x 10^{-19}), age (HR = 2.05 per SD, $P = 2.72$ x 10^{-71}), heart rate (HR = 1.14 per SD, $P = 1.24$ x 10^{-9}) and the GRS (HR = 1.08 per SD, $P = 1.54$ x 10^{-2}) remained significantly associated with ACM.

Conclusions: Our findings suggest that ECG parameters and GRSs independently contribute to ACM risk prediction, indicating they can be combined together into standard predictive scores.