88 EXPLORING THE PROGNOSTIC SIGNIFICANCE AND IMPORTANT PHENOTYPIC AND GENOTYPIC ASSOCIATIONS OF NEURAL NETWORK-DERIVED ELECTROCARDIOGRAPHIC FEATURES

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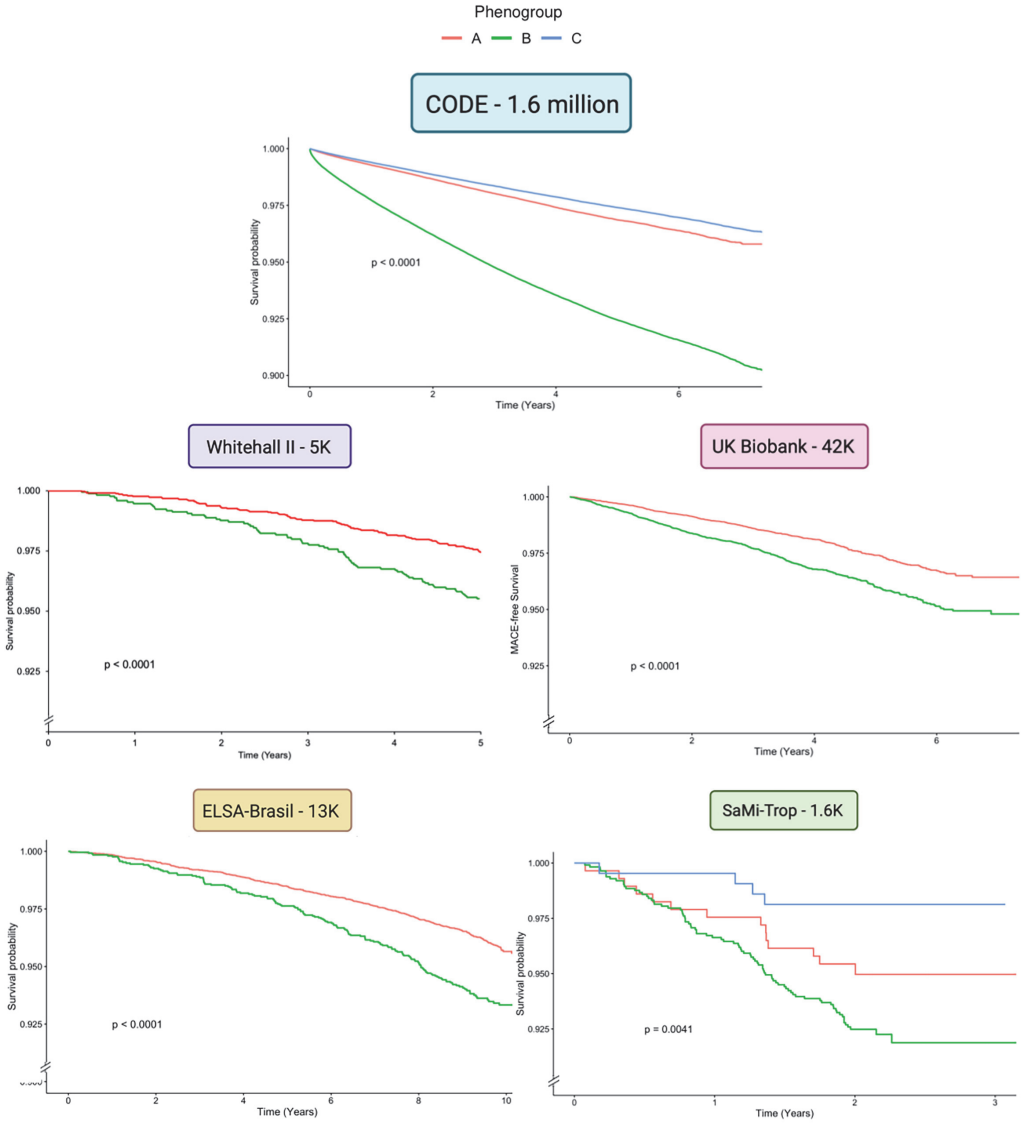
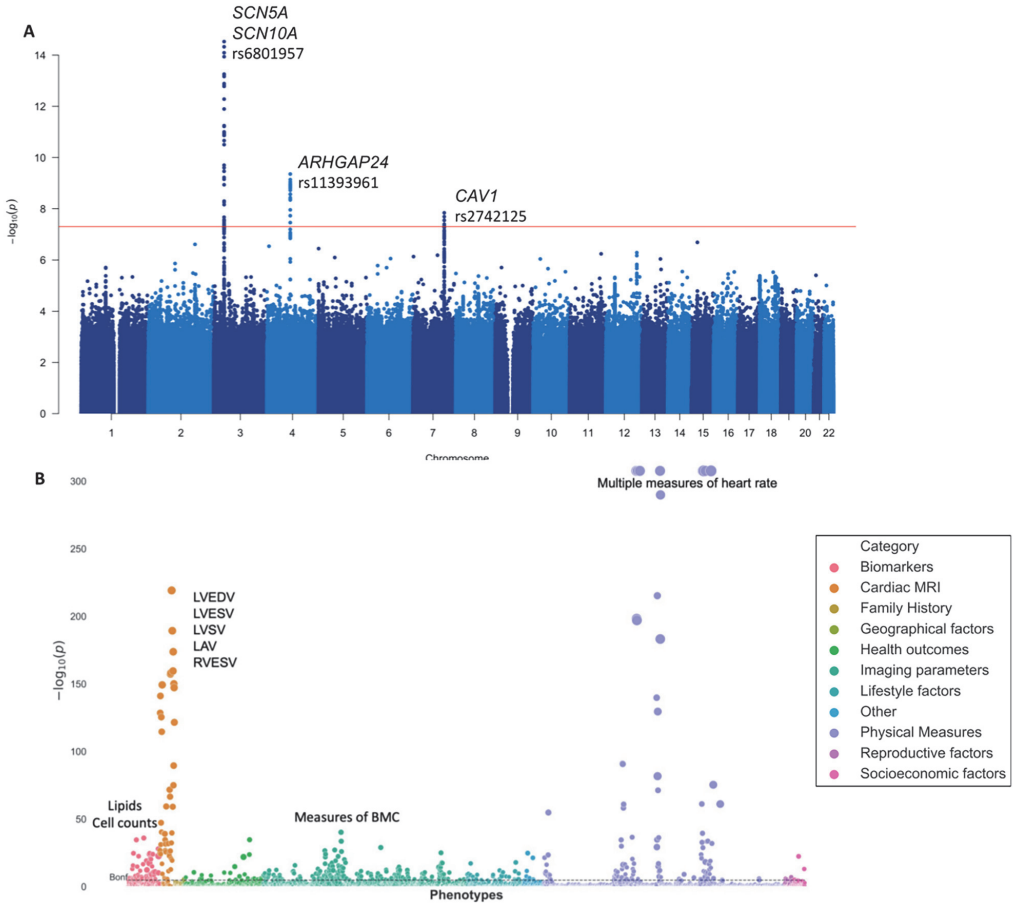
10.1136/heartjnl-2023-BCS.88

Background Subtle, prognostically-meaningful ECG features may not be apparent to physicians. In the course of supervised machine learning training, many thousands of ECG features are identified. These are not limited to conventional ECG parameters and morphology. These novel neural network (NN)-derived ECG features may have clinical, phenotypic, and genotypic associations and prognostic significance.

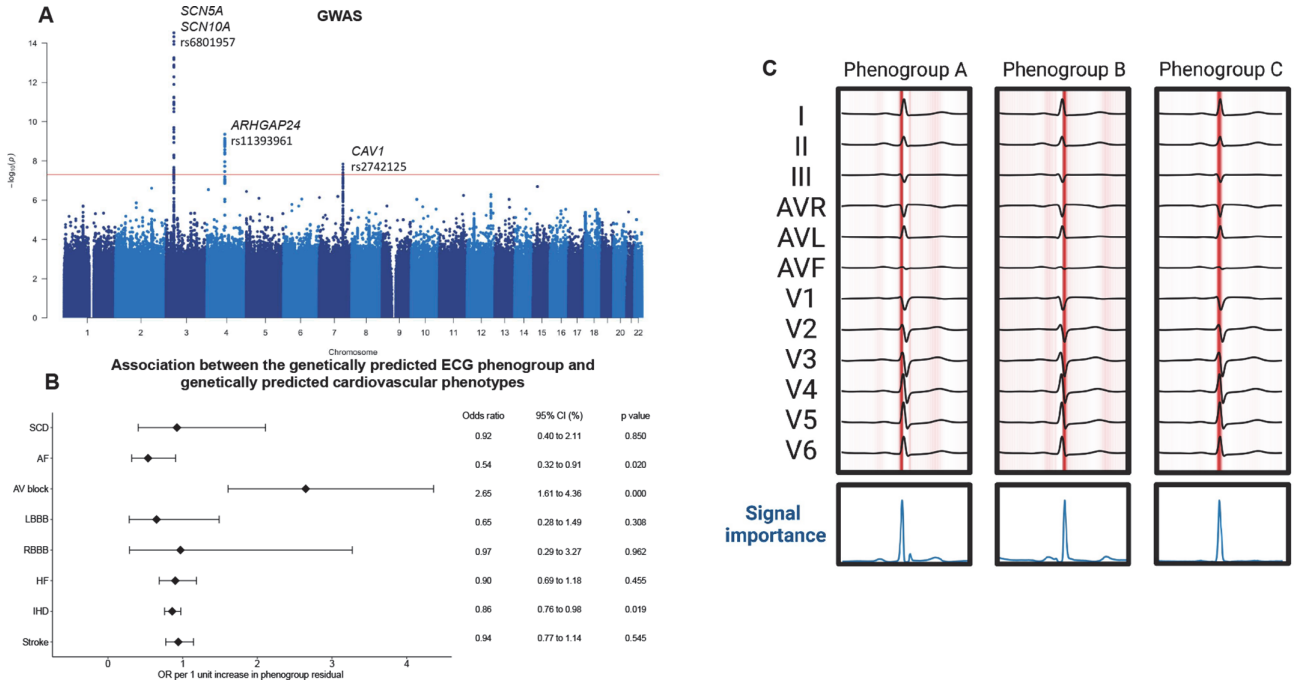
Methods and Results We extracted 5120 NN-derived ECG features from an AI-ECG model trained for six simple diagnoses and applied unsupervised machine learning to identify three phenogroups. The derivation set, the Clinical Outcomes in Digital Electrocardiography (CODE) cohort (n = 1,558,421), is a database of ECGs recorded in primary care in Brazil. The three phenogroups had significantly different mortality profiles



Abstract 88 Figure 1



Abstract 88 Figure 2



Abstract 88 Figure 5 (A) Genome-wide association study. Manhattan plots of genomic loci associated with ECG phenogroup. Nearest genes are annotated on the plot. (B) Mendelian randomisation analyses of associations between genetically predicted ECG phenogroup and cardiovascular outcomes/phenotypes (C) Grad-CAM is used to generate importance maps showing the sections of the ECG signal deemed most important for phenogroup determination. HF: heart failure, BMI: body mass index, SBP: systolic blood pressure. SCD: sudden cardiac death.

(Figure 1). After adjusting for known covariates (including age, gender, and comorbidities), phenogroup B had a 1.2-fold increase in long-term mortality compared to phenogroup A (HR 1.20, 95% CI 1.17-1.23, p < 0.0001).

We then externally validated our findings in four diverse cohorts. The Whitehall II cohort (n = 5,066) consists of British civil servants. The UK Biobank is longitudinal study of volunteers (n = 42,386). The Longitudinal Study of Adult Health (ELSA-Brasil) cohort (n = 13,739) consists of Brazilian public servants. Lastly the São Paulo-Minas Gerais Tropical Medicine Research Center (SaMi-Trop) is a cohort (n = 1,631) of patients with chronic Chagas cardiomyopathy.

We found phenogroup B had a significantly greater risk of mortality in all cohorts (Figure 1). We performed a phenome-wide association study (PheWAS) in the UK Biobank. We found ECG phenogroup significantly associated with cardiac and non-cardiac phenotypes, including cardiac chamber volumes and cardiac output (Figure 2A). A single-trait genome-wide association study (GWAS) was conducted. The GWAS yielded four significant loci (Figure 2B). SCN10A, SCN5A and CAV1 have well described roles in cardiac conduction and arrhythmia. ARHGAP24 has been previously associated with ECG parameters, however, our analysis has identified for the first time ARHGAP24 as a gene associated with a prognostically significant phenogroup. Mendelian randomisation demonstrated the higher risk ECG phenogroup was causally associated with higher odds of atrioventricular block but lower odds of atrial fibrillation and ischaemic heart disease.

Conclusion NN-derived ECG features have important applications beyond the original model from which they are derived and may be transferable and applicable for risk prediction in a wide range of settings, in addition to mortality prediction. We have shown the significant potential of NN-derived ECG features, as a highly transferable and potentially universal risk marker, that may be applied to a wide range of clinical contexts.

Conflict of Interest None

89 LEADLESS PACEMAKER IMPLANTATION, DATA FROM A TERTIARY CARDIOLOGY CENTRE IN LONDON, UK

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10.1136/heartjnl-2023-BCS.89

Background Leadless pacemakers have a lower incidence of pacemaker-related infection than transvenous devices and have been shown to be safe and effective in patients on chronic haemodialysis. UK guidelines recommend the use of leadless pacemakers in patients in whom conventional devices are contraindicated, otherwise they should only be used in the context of research.

Methods This was an observational study of patients who underwent implantation of Micra Transcatheter Pacing System (TPS) (Medtronic, Minneapolis, MN) in a tertiary cardiology centre in London, UK. All patients who underwent a first implantation of Micra TPS at STH from 1st January 2017 to 30th October 2022 were included in this study.

Results A total of 136 patients had first Micra implanted at St Thomas' Hospital, London. Mean age (± standard deviation, SD) of patients was 68.9 ± 17.1y (ranged from 13-100y) and 64.7% were men. Seventy percent of the patients underwent Multi-Disciplinary Team discussions prior to insertion of the leadless pacemaker. With regards to contraindications for conventional pacemakers, 52 (38.2%) patients had infection of a conventional pacemaker device requiring system extraction. Forty-eight (35.3%) patients had a high risk of infection (haemo/peritoneal dialysis, previous history of device infection, presence of indwelling vascular access, or immunocompromised), 14 (10.3%) patients had prohibitive venous access or anatomy, and 12 (8.8%) patients had a high pre-existing trans-venous burden. A Micra was implanted in 7 (5.1%) patients due to young age rather than an absolute contraindication to a conventional device, with mean age (±SD) of 25.3 ± 7.7y. There was no intra-procedural major complication due to Micra implantation. Specifically, there was no pericardial effusion, pulmonary embolism, device dislodgement, major vascular complication, or death. Three patients (2%) underwent implantation of a second Micra device within 14 months due to increased pacing thresholds. One of these patients had their original device snared and removed at the time of reimplant. Mortality was 26.4% by the time of data collection, and median survival post implantation was 13 months (interquartile range 4.25 – 26 m). Mortality data was not available for 22 (16.2%) of the patients who were treated and transferred back to their hospitals.

Conclusion The Micra Leadless pacemaker is a safe alternative to conventional transvenous pacemakers, in particular where the risk of infection is high. Given the safety profiles seen, revising current guidelines to increase the use of leadless devices in selected patient populations should be considered.

Conflict of Interest None

90 THROMBOEMBOLIC EVENTS AND VASCULAR DEMENTIA IN CONTEMPORARY PATIENTS WITH ATRIAL FIBRILLATION AND LOW APPARENT STROKE RISK

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10.1136/heartjnl-2023-BCS.90

Background Thromboembolism in patients with atrial fibrillation (AF) can be prevented, however oral anticoagulation is typically reserved for older patients or those with specific historical comorbidities. Risk scores are in widespread use, but with limited predictive accuracy for stroke and no consideration of current major challenges such as dementia. This study provides contemporary data on the risk of thromboembolism, including both cardiac and cerebral damage.

Methods Population-based matched cohort study of primary care patients across the UK from 2005 to 2020 using structured, electronic healthcare record data. Inclusion criteria were patients with a pre-defined coded entry for AF (exposed group; including past or resolved AF), aged between 40-75, no previous history of stroke, CHA_2DS_2-VASc risk score zero or one, and not receiving an oral anticoagulant. Patients were matched by age, sex and region with up to 4 patients without an AF exposure diagnosis. Outcomes were all-cause mortality, stroke, arterial thromboembolism, ischaemic heart disease and dementia (categorised into all-cause, Alzheimer's and vascular dementia), analysed by Cox proportional hazard ratios (HR) adjusted for age, sex, socioeconomic deprivation, ethnicity and clinical factors.