ECG Deep Learning Dissects Physiology of Hypertrophic Cardiomyopathy

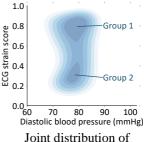
Sunil Manohar¹, Betty Raman¹, Alfonso Bueno-Orovio², Marcel Beetz³, Yuling Sang³, Zuzanna Borawska¹, Blanca Rodriguez², Raymond Y Kwong⁴, Milind Desai⁵, William S Weintraub⁶, Christopher M Kramer⁷, Stefan Neubauer¹, Hugh Watkins¹, Vicente Grau³, Sanjay G Manohar⁸, Rina Ariga¹ on behalf of HCMR investigators

¹Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, UK, ²Dept of Computer Science, University of Oxford, UK, ³Institute of Biomedical Engineering, Dept of Engineering Science, University of Oxford, UK, ⁴Cardiovascular Division, Brigham and Women's Hospital, Boston, MA, USA, ⁵Cardiovascular Institute, Cleveland Clinic, Cleveland, OH, USA, ⁶MedStar Heart and Vascular Institute, Washington, DC, USA, ⁷Cardiovascular Division, University of Virginia Health, Charlottesville, VA, USA, ⁸Nuffield Dept of Clinical Neurosciences, University of Oxford, UK

Aim: Hypertrophic cardiomyopathy (HCM) is mechanistically complex, and unravelling this would guide treatment and prognosis. One serious complication is left ventricular outflow tract (LVOT) obstruction, which increases afterload. Since afterload also increases with high blood pressure (BP), we hypothesised that obstructive HCM may share ECG features with hypertension. This study aimed to identify hypertensive-like ECG changes to discriminate physiological factors within HCM.

Methods: A deep convolutional neural network was trained to quantify ECG changes in hypertension in n=37,378 UK Biobank participants and n=2,258 HCM Registry patients, generating a novel ECG strain score (ECG-SS) from the output of the final softmax layer.

Results: ECG-SS did not track BP in HCM. Sarcomere-negative HCM patients (no diseasecausing gene) had bimodally distributed scores, suggesting two phenotypes distinguished by afterload. In this group, high ECG-SS was associated with obstruction and wall stress, but not with hypertrophy or fibrosis. A variational autoencoder allowed visualisation of clinically interpretable ECG features, demonstrating marked abnormalities in the high ECG-SS subgroup.



Joint distribution of ECG-SS and BP in sarcomere-negative HCM

Conclusions: A sensitive machine learning index trained on hypertension illuminates a disease spectrum in HCM. ECG deep learning and VAE analysis show for the first time LVOT obstruction and wall stress to be major causes of ECG abnormalities in HCM.