Assessment of aortic valve function in over 47,000 people using deep learning

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Background: Aortic valve (AV) stenosis (AS) is associated with a high global burden of mortality and morbidity. Previous studies suggest that even mild AS is associated with worse outcomes, prompting interest in AV function in a healthy population. The UK Biobank is a prospective cohort study with ~500,000 participants of whom ~10% have undergone cardiovascular MRI (cMRI).

Purpose: We aimed to develop a deep learning model to study AV function in cMRI at population level in the UK Biobank.

Methods and Results: We developed a U-Net based segmentation model with a ResNet34 encoder to study the velocity-encoded image series, computing peak velocity (cm/sec), mean peak gradient (“mean gradient”; mmHg), and aortic valve area (cm²) (AVA) in 47,223 participants.

Next, we calculated reference values stratified by age and sex in participants without CVD. In healthy individuals (n=31,909), AVA was lower in older age groups, whereas peak velocity and mean gradient remained similar across age groups. Compared to women, men had greater AVA but similar peak velocity and mean gradient estimates.

In the biomarker analysis (taken ~9.5 years before cMRI), we observed an association of apolipoprotein B (ApoB) (0.033 SD increase per SD, P=3.1 x 10^{-12}) and lipoprotein a (Lp (a)) (0.027 SD increase, P=4.8 x 10^{-7}) with higher peak velocity. Using Mendelian Randomization, we found genetic evidence that Lp(a) causally contributes to higher peak velocity (β=0.04, P=6.4 x 10^{-10}) and smaller AVA (β=-0.056, P=1.3 x 10^{-4}). Similarly, ApoB causally contributes to higher peak velocity (β=0.072, P=1.3 x 10^{-6}) and smaller AVA (β=-0.065, P=1.3 x 10^{-5}) in Mendelian Randomization.

Peak velocity was strongly associated with incident AV surgery (N=72, Hazard ratio [HR] 2.40 per SD, P=2.6 x 10^{-11}) and AS (N=123, HR 2.10, P=7.7 x 10^{-13}). The predictive power for AS was higher when using the top 10% vs the remaining 90% of distribution for mean gradient (N in top 10% with event=87, HR 24.91, P=2.4 x 10^{-43}) and peak velocity (N=92, HR 33.01, P=3.0 x 10^{-43}). After excluding individuals with at least mild aortic stenosis (peak velocity >2m/sec, mean gradient >20mmHg, AVA >1.5 cm²) the top 10% of the remaining population was still highly predictive for AS using mean gradient (N=30, HR 8.90, P=9.4 x 10^{-15}) and peak velocity (N=35, HR 13.15, P=1.6 x 10^{-18}).

Conclusion: We found both epidemiological and causal genetic evidence that elevated ApoB and Lp(a) cause a reduction in AVA. Even aortic velocities below the threshold for mild AS were predictive of future clinical disease, suggesting that there may be a role for monitoring at AVA below the current threshold for mild AS. Future work is needed to understand whether clinical outcomes are better predicted by universal or sex-specific cutoffs.
Figure 1: Workflow of deep learning mode
HR of incident valvular disease