

## 3.2 First Genome-Wide Association Study of Cardiovascular Magnetic Resonance Derived Aortic Distensibility Reveals 7 Loci

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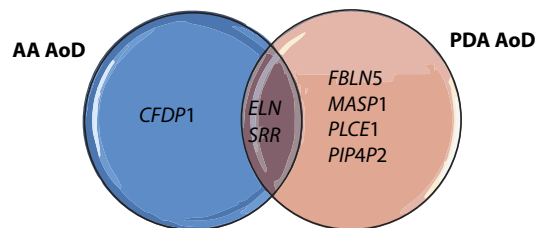
### ABSTRACT

**Background:** Although arterial stiffness has demonstrated moderate heritability, our knowledge of the genes modulating arterial stiffness is still limited. We conducted genome-wide association studies (GWASs) of aortic distensibility (AoD) in both ascending (AA) and proximal descending aorta (PDA) to discover novel genetic loci.

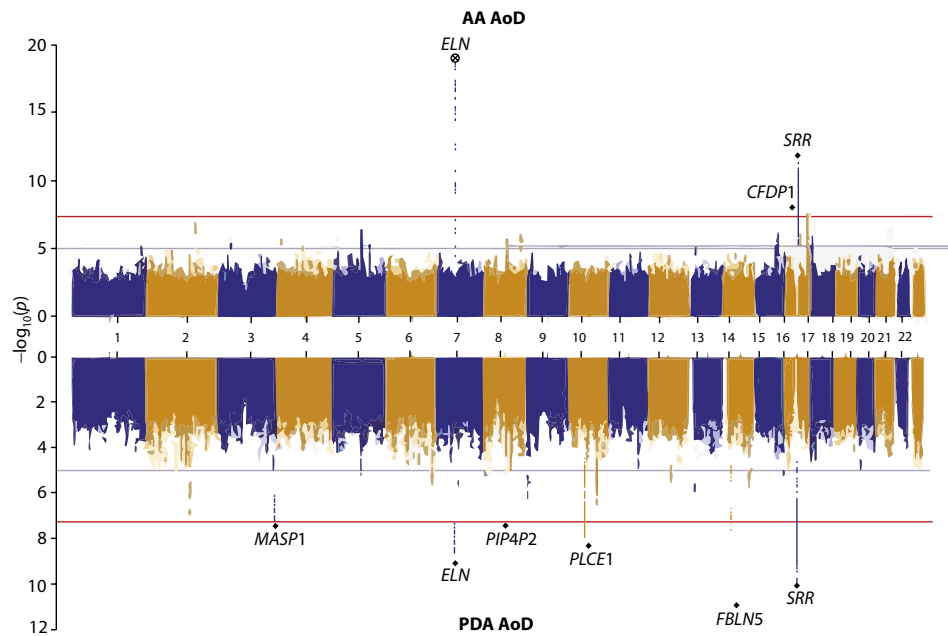
**Methods:** Our study included ~14,500 European-ancestry participants in the UK Biobank study. AoD in AA and PDA were assessed at the level of pulmonary artery bifurcation using transverse cine images obtained from 1.5 Tesla cardiovascular magnetic resonance scanners<sup>1</sup>. Relative cross-sectional aortic area change was calculated using an automated tool<sup>2</sup>. GWASs were performed in a discovery cohort ( $n = 3,841$ ), with replication in 9,630 individuals. We also performed GWASs for each trait in the combined cohort ( $n = 14,596$ ). All GWASs were performed under a linear mixed model and adjusted for age, sex, height, weight, systolic blood pressure, diabetes, smoking, genotype array type and the first ten principal components.

**Results:** We found three significant loci ( $p < 5 \times 10^{-8}$ ) for AA AoD and six for PDA AoD (Figure 1A). The ELN locus was discovered and replicated for AA AoD, and was significantly associated with PDA AoD in the combined cohort (Figure 1B). ELN encodes elastin a central component of elastic fibres in the heart and blood vessels. The most significant locus for PDA AoD was FBLN5; FBLN5 encodes fibulin 5 which is vital for elastic fibre formation.

**Conclusions:** In the first GWAS of AoD, we discovered seven unique loci. These results enhance our understanding of the biological processes underlying arterial stiffness.



**Figure 1A** | Venn diagram of the 7 genome-wide significant loci from our study.



**Figure 1B** | Miami plot of distensibility in the ascending (AA) and proximal descending aorta (PDA) in the combined cohort. Quartered cross symbol denotes locus was also genome-wide significant in discovery and replication cohorts.

## REFERENCES

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