Abstract ID:- 238

Abstract Topic:- Molecular effects of genetic variation

Abstract Title:- Unraveling the genetic determinants of aortic distensibility and their impact on the cellular composition of the aorta

Presenting author name :- Mehak Chopra

Presenting author institute:- School of Mathematical & Statistical Sciences, University of Galway, Ireland

Co-authors name:- Niamh Hynes, Cathal Seoighe

Co-authors institute:-CORRIB-CURAM-Vascular Group and Department of Vascular Surgery and Endovascular Surgery, Galway Clinic, University of Galway, Galway, Ireland, School of Mathematical & Statistical Sciences, University of Galway, Ireland

Aims:-Aortic distensibility is a risk factor underlying several cardiovascular events, however the contributing genetic factors remain unknown. This study aimed to understand the genetics of aortic distensibility utilizing genotypic and cardiovascular magnetic resonance images (CMRI) data from the UK Biobank (UKBB). Moreover, novel deconvolution methods will be explored to investigate the age-associated changes in the cellular composition of aortic samples obtained from GTEx and whether these changes are associated to GTEx genotypic data.

Methods:- To find the aortic distensibility, an existing deep learning convolutional neural network (CNN) was applied on 62,497 CMRI from the UKBB. Further, quality checks allowed us to exclude the CMRI which may affect the segmentation accuracy and measurement of distensibility. Following quality checks, GWAS was carried out on the aortic distensibility of 56,765 participants. To examine the cellular mechanism and age-related shifts in cellular proportions, we utilized CIBERSORTx deconvolution on aortic gene expression data from 432 GTEx participants. In the future, we plan to test whether any of the genetic variants identified through GWAS also show an association with the cell-type composition of aortic tissues in the GTEx samples.

Results:- Aortic distensibility is a direct measure of aortic stiffness that can be accurately obtained from CMRI. Distensibility can predict adverse cardiovascular events and shed light on the relationships between imaging phenotypes and aortic disorders. The CNN network enabled us to calculate the distensibility for 56,765 subjects from CMRI. Furthermore, a two-stage GWAS on distensibility helped us grasp the significance of incorporating variables in the research to minimize erroneous positives. The significant SNPs were tested against the GTEx genotypic data. To understand the changes in the cellular composition of aorta and to shed light on some of the associations observed, the deconvolution method enabled us to identify changes in cellular composition of the aorta associated with aging.

Conclusions:- To the best of our knowledge, this is one of the largest studies conducted until now utilizing UKBB data, that helped us to identify the SNPs associated with the distensibility. The deconvolution approach on GTEx samples allowed us to uncover the changes in cellular composition in aortic samples. Further, the association of the genetic variants with the cell-type composition of aortic tissues will enable us to assess whether variation in cell-type composition could help to explain some of the genetic variation in this important physiological phenotype.

Keywords:- Distensibility, CMRI, CNN, GWAS, Deconvolution