Commentary

# Coronary Heart Disease: A Transient Ischemic Stroke

Mehta Cobble[*]

*Department of Cardiology, Emory University, Atlanta, USA*

## DESCRIPTION

Carotid plaque and intima media thickness are indicators of subclinical atherosclerosis linked to coronary heart disease and ischemic stroke. Here, we conduct meta-analyses of genome-wide association studies in cIMT in 71,128 individuals and carotid plaque traits in 48,434 individuals. We discover eight new cIMT susceptibility loci, one new carotid plaque locus, and one independent association at the previously discovered PINX1 locus. Candidate genes at two additional potential loci, ADAMTS9 and LOXL4, are discovered through localization analysis with nearby vascular expression quantitative loci derived from arterial wall and metabolic tissues obtained from patients with CHD. Significant genetic correlations between cIMT and plaque traits, as well as between cIMT and plaque and CHD, any subtype of stroke, and ischemic stroke, are revealed by LD score regression. Our research sheds light on the genes and tissue-specific regulatory systems that link atherosclerosis to both its functional genomic causes and the clinical effects they have on people. In the sub-intimal region of medium and large arteries, atherosclerosis is characterised by an accumulation of lipid-rich and inflammatory deposits. Increased plaque size results in reduced blood flow, organ ischemia, and/or tissue necrosis. Acute vascular occlusion brought on by plaque rupture underlies clinical cardiovascular events like myocardial infarction and ischemic stroke. In the US, stroke and coronary heart disease each cause one in twenty fatalities, respectively.

Due to the lengthy pre-clinical stage of atherosclerosis, early detection of the disease using non-invasive techniques may help identify people who are at risk for developing atherosclerotic clinical events and offer a chance for prevention. By measuring the intima-media thickness or carotid plaques in the common carotid artery using B-mode ultrasound, subclinical atherosclerosis can be identified. Genetic elements in both clinical and subclinical atherosclerosis are well known. Previous genome-wide association studies of subclinical atherosclerosis found two loci associated with common carotid artery plaque at PIK3CG and EDNRA4, and three loci significantly associated with cIMT at ZHX2, APOC1, and PINX1. Significant correlations between cIMT and coronary artery calcification and the APOE 2 allele were found in an exome-wide association study. Since the APOC1 variant and the APOE single nucleotide polymorphism are in linkage disequilibrium, they both represent the same signal. Further GWAS-identified associations for carotid plaque at the 9p21 and SFXN2 loci, as well as for cIMT at the CFDP1-TMEM170A locus, were reported. However, these previous studies had small sample sizes and incomplete genomic coverage, and they did not investigate the potential etiological significance of subclinical atherosclerosis on atherosclerotic clinical events. Here, using 1000 Genomes imputed genotype data from collaborations between the Cohorts for Heart and Aging Research in Genomic Epidemiology consortium and the University College London-Edinburgh-Bristol consortium; we conduct a significant meta-analysis of GWAS of subclinical atherosclerosis. The lack of access to RNA expression data from tissues with relevance to specific diseases is one of the biggest obstacles in the translation of GWAS findings to biological understanding. Therefore, we prioritised candidate genes for known and novel loci of cIMT and carotid plaque using statistical methods for localization in an effort to accurately identify the tissue-specific gene regulatory functions accountable for the GWAS signals.

## CONCLUSION

These techniques combine identified loci with expression quantitative loci inferred from the Stockholm-Tartu Atherosclerosis Reverse Network Engineering Task Study, where arterial wall and metabolic-related RNA samples were obtained from as many as 600 patients with CHD. This study examined the genetics of RNA expression relevant to cardiovascular disease. We also examine the relationships between cIMT and carotid plaque and clinically apparent CHD and stroke using summary data from two sizing consortia. In conclusion, our study evaluates the tissue-specific patterns of gene regulation and the genetic epidemiology that contribute to the development of subclinical atherosclerosis traits across cardiovascular disease-related tissues.

**Correspondence to:** Mehta Cobble, Department of Cardiology, Emory University, Atlanta, USA, E-mail: Mehtacobble@gmail.com