Description

Fall_gwas_results_any_chd_tab.txt.gz

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Publication

Fall T, Gustafsson S, Orho-Melander M, Ingelsson E. Genome-wide association study of coronary artery disease among individuals with diabetes: the UK Biobank. Diabetologia. 2018 Jul 12. doi: 10.1007/s00125-018-4686-z

Main findings

Coronary artery disease (CAD) is more common in individuals with diabetes than in those without. Coronary artery disease can manifest as myocardial infarction or as chest pain. It is not well understood why diabetes increases the risk of this disease. Genetic studies could enhance the understanding of the underlying biology, but there are only few inconclusive genetic studies on this topic in this patient group. The key question of our study was to determine the genetic underpinnings of CAD among individuals with diabetes. We studied many gene variants across the genome in UK Biobank participants and found similar effects of genetic variation in several established genetic loci for CAD in the general population as in individuals with diabetes. Hence, our results support that the genetic architecture of CAD is largely similar in individuals with diabetes as in those without. We therefore conclude that novel drugs to prevent CAD based on genetic targets identified in the general population are likely to have similar effects in a diabetes population. We did not identify any diabetes-specific CAD gene variants.

Study

Population: 15,666 non-related individuals of white British ancestry with diabetes at baseline and valid genetic data

Diabetes type

We used the algorithm (Eastwood et al) to define diabetes type among UK Biobank participants at baseline (2006-2010) based on self-reported disease, medication and age of diabetes onset. Out of 24,680 individuals with available genetic data and possible/probable type 1 or type 2 diabetes, we proceeded with 20,644 individuals deemed unrelated and passing quality control (Bycroft et al). Of these, 4,978 individuals of non-white non-British ancestry were excluded from main analyses. Hence, the main data set contained 15,666 individuals of white British ancestry.

Coronary artery disease

CAD was defined as having a recorded death or hospitalization with primary or secondary diagnosis recorded with the International Statistical Classification of Diseases and Related Health Problems (ICD) version 10 codes I20, angina pectoris; I21, acute myocardial infarction; 122 subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; I23, certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; I24, other acute ischemic heart diseases; or I25, chronic ischemic heart disease. The event was considered bith if it happened before or after diabetes diagnosis. We further considered the

following ICD-9 codes: 410, acute myocardial infarction; 411, other acute and subacute forms of ischemic heart disease; 412, old myocardial infarction or 413 angina pectoris. We also considered those individuals as CAD that had the following surgical intervention recorded: K40, saphenous vein graft replacement of coronary artery; K41, other autograft replacement of coronary artery; K42, allograft replacement of coronary artery; K43 prosthetic replacement of coronary artery; K44, other replacement of coronary artery; K45, connection of thoracic artery to coronary artery; K46, other bypass of coronary artery; K49, transluminal balloon angioplasty of coronary artery; K50, other therapeutic transluminal operations on coronary artery; K75, percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery. Further, individuals were classified as CAD if they reported angina pectoris or myocardial infarction at the verbal interview. If the participant was uncertain of the type of illness they had had, then they described it to the interviewer (a trained nurse) who attempted to place it within the coding tree. If the illness could not be located in the coding tree, the interviewer entered a free-text description of it. These free-text descriptions were subsequently examined by a doctor and, where possible, matched to entries in the coding tree. Free-text descriptions which could not be matched with very high probability have been marked as "unclassifiable". Individuals not fulfilling the above criteria were defined as not having CAD.

Methods

Quality control and imputation using the Haplotype Reference (HRC) was conducted centrally at the UK Biobank, yielding a total of about 39 million single-nucleotide polymorphisms (SNPs).

The association between any_chd and each variant with a minor allele count >= 30 and an imputation quality metric r2 >= 0.8 was tested in a logistic (Firth in case of non-convergence) regression:

any_chd ~ SNP + age + pc1 + pc2 + pc3 + pc4 + pc5 + pc6 + pc7 + pc8 + pc9 + pc10 + pc11 + pc12 + pc13 + pc14 + pc15 + pc16 + pc17 + pc18 + pc19 + pc20 + sex.l2 + array.l2 + array.l3

The association tests were performed in PLINK v2.00aLM 64-bit Intel (28 Nov 2017) using dosages (additive coding), including a total of 9,087,334 markers.

Column names

chr	chromosome
pos	position (hg19)
snpid	chromosome and position
effect_allele	effect allele
other_allele	other allele
eaf	effect allele frequency
ntotal	n contributing to analysis
beta	effect
se	standard error
p_value	p
rsq	MACH imputation quality
merged	coded 3 for HRC panel (this column can be disregarded)