Visual Abstract

Hemorrhoids disease (HEM)

ICD10 I84, ICD9 455, self-reported

GWAS meta-analysis

23andMe
UK Biobank
EGCUT
MG1
GERA
5 study cohorts: 218,920 cases, 725,213 controls

Results

102 novel genome-wide significant loci with 819 candidate genes

100 prioritized genes > based on tissue and pathway enrichment, as well as gene expression, analyses

Two missense variants; functional effects observed *in vitro* for F6085 (rs2186797) in AM1 protein

Polygenic risk score analysis

(Genetic) correlation analyses with other diseases/traits

Background

Hemorrhoidal disease affects a large and silently suffering fraction of the population but its etiology, including suspected genetic predisposition, is poorly understood. No genome-wide significant association has been described until today.

Conclusion:

Hemorrhoids disease has a genetic component that compares to that of other complex diseases and that predisposes to smooth muscle, epithelial, and connective tissue dysfunction. Patients with a very high polygenic risk score have an increased risk for recurrent invasive procedures and a younger age of onset.