Coronary artery disease & genetic susceptibility

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Background

- CAD: a complex etiology → a combination of:
  - lifestyle-related factors and
  - genetic predisposition

- Hereditary influence on CAD susceptibility accounts for 40%-50% of cases

- Genome-wide association studies (GWAS) → large number of variants contributing to CAD aetiology detected

Milestones in cardiovascular genome research from 2007 and beyond

163 CAD risk loci and pathophysiological pathways in atherosclerosis

Circosplot showing 163 risk loci for CAD under the chromosomes, where they are located

Polygenic risk scores for CAD

- the value of individual common variants very limited for risk prediction
- polygenic risk scores (PRSs) (summing the number of risk variant alleles in each individual weighted by the impact of each allele on disease risk) perform better than individual variants
- individuals with a high PRS have a larger benefit from statin treatment than those with low scores
- PRS can identify a four-fold increased risk for CAD in 2.5% of the population

Khera AV et al. Genome-wide polygenic score to identify a monogenic risk-equivalent for coronary disease. bioRxiv 2017;
Genetic SYNTAX score (GESS) study
clinicaltrials.gov ID: NCT03150680
The goal of the research project is to investigate the potential association of 228 SNPs (127 genes) with:

- the complexity and the severity of CAD (SYNTAX score)
- the clinical presentation of CAD (stable CAD vs acute coronary syndrome)
Purpose of the study

The combination of:

• Genetic
• Pharmaco-genetic
• Clinical
• Laboratory parameters

in order to

• develop an algorithm for the prediction of cardiovascular risk (GEneric Syntax Score-GESS)
• Facilitate a personalized approach for patients with CAD
Study population

• INCLUSION CRITERIA
  ➢ all comers, who are admitted in the Department of Cardiology, and undergo coronary angiography for clinical purposes
  ➢ Patients with a previous history of coronary artery disease are excluded.

• SAMPLE SIZE
  ➢ 1000 patients

• FOLLOW-UP FOR MACE
  ➢ 12 months

• DATA COLLECTION
  ➢ Peripheral blood sample (for DNA extraction),
  ➢ Coronary angiography data,
  ➢ Echocardiographic parameters.
DNA isolation and GRS calculation

DNA isolation & handling of DNA extracts
• DNA extraction from peripheral blood sample
• Polymerase chain reaction (PCR) amplification
• Next Generation Sequencing (MiniSeq, Illumina)

Genetic Risk Score Calculation (GRS)
• the weighted sum of alleles of 228 single nucleotide polymorphisms previously associated with CAD
Endpoints

• Relationship between genetic risk score and the SYNTAX score

• Predictive value of combining a Genetic Risk Score, SYNTAX score, clinical variables and echocardiographic parameters for the prediction of 1-year MACCEs

• Prognostic model for the prediction of bleeding complications combining Genetic Risk Score, SYNTAX score and clinical variables
Barplot of the top 15 enriched Disease Ontology terms - Analysis was performed using the tools clusterProfiler and DOSE
Gene-concept network of the top 15 enriched Disease Ontology terms - Analysis was performed using the tools clusterProfiler and DOSE
Baseline patient characteristics

- 792 patients already enrolled
- Mean age: 64.34±12.53
- 40.8% presented with acute coronary syndrome (54 with STEMI, 187 with NSTEMI and 82 patients with unstable angina)

Medical history:
- Hypertension 54.79% of patients
- Diabetes 26% of patients
- Dyslipidemia 38.69% of patients
- Smoking 42.41% of patients
**Initial results: Effect of Type of Polymorphisms on Total Syntax Score**

<table>
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<tr>
<th>Comparison</th>
<th>Method</th>
<th>Statistic</th>
<th>p-value</th>
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Initial results: Effect of Type of Polymorphism on ACS

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Collaborators

- First Department of Cardiology A.P.TH., AHEPA University Hospital
  - Study co-ordinator: Prof. Sianos

- School of Pharmacy A.P.TH.

- A’ First Department of Microbiology, Medical School, A.P.TH.

- LABNET IAE - Private Reference Diagnostic Laboratory
Study funding

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THANK YOU FOR YOUR ATTENTION!