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Abstract Topic:- Complex traits and polygenic disorders

Abstract Title:- Genome-wide polygenic risk score better predicts multi-vessel coronary artery disease compared to late-onset single vessel disease in the Indian population

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Aims:-To access the predictability of multi-vessel and single vessel coronary artery disease using Polygenic Risk Score

Methods:- Successive patients of premature CAD (<60 years) (n=930) who underwent coronary angiography were recruited. Clinical details were recorded and extent of CAD was evaluated. Recently validated 6.6 million SNP-based GPRS was used to classify patients into average, moderate and high-risk groups. Descriptive statistics are reported. Further we have validated the latest GPSmult model comprising 1.3 million genetic markers in South Asian population comprising of 1800 cases and 1163 controls.

Results:- Genetic data were available for 830 (89.2%). GPRS followed a normal-distribution with mean 0.17+0.97 (range -2.90 to 3.19). Average genetic risk was in 423 (51%), moderate in 246 (30%) and high in 161 (19%). Clinical characteristics in various risk groups are shown in Table. GPRS was significantly higher in younger CAD patients (<50yr) vs others (0.29+0.95 vs 0.08+0.98; p=0.003). Mean GPRS in single, double, and triple vessel CAD were 0.11±0.95, 0.23±0.96 and 0.19±1.01 (p=0.263). The late-onset single vessel CAD cases (age>50 years) had a lower median GPRS compared to the young-onset Single vessel disease (SVD) and multi vessel disease (MVD). The late-onset MVD cases had a median PRS similar to that of young-onset SVD. Although direct correlation of GPRS with extent of CAD was insignificant (Spearman's rho=0.042, p=0.232; Kendall's tau-B=0.033, p=0.226), high-risk GPRS patients had significantly more multivessel CAD ($\chi 2$ test=11.09, p=0.026). Further we have validated the latest GPSmult model containing 1.3 million genetic markers in the South Asian population comprising of 1800 cases and 1163 controls. We observed a significant improvement in the genetic risk prediction compared to the 6.6 million marker model.

Conclusions:- Premature CAD patients in India and those with multivessel disease have higher mean GPRS. Further, GPRS may better predict MVDs and young-onset SVDs. Prospective studies are needed to confirm these observations.

Keywords:- coronary artery disease, Polygenic Risk Score, South Asian, Single vessel disease, multi vessel disease