KSN SEOUL, KOREA 2023
April 27(Thu) - 30(Sun), 2023
Coex, Seoul, Korea

Abstract Type : Poster
Abstract Submission No. : 1353

Polygenic Risk Score for CKD: Association between Dyslipidemia and the Risk of Incident CKD Affected by Genetic Susceptibility

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Objectives: Polygenic risk score (PRS) provides information of the overall contribution of numerous genetic variants on disease outcomes. The effect of dyslipidemia on kidney disease outcome has been inconsistent and yet needs to be clarified. We aimed to investigate the genetic effect on the association between dyslipidemia and risk of CKD using PRS.

Methods: We analyzed data from 373,523 participants of UK biobank aged 40 to 69 and without history of chronic kidney disease. The PRS for incident CKD was constructed using GWAS summary statistics of CKDGen overall European ancestry (n=480,697). The impacts of lipids and PRS on incident CKD were assessed using Cox proportional hazard model. To investigate the interaction between lipids and genetic factor on incident CKD, we introduced multiplicative interaction terms between them to multivariable analysis model and performed subgroup analysis stratified by PRS tertiles.

Results: A total of 4,424 participants developed CKD. In multivariate analysis, the PRS was significantly predictive of the risk of incident CKD (continuous variable; HR, 1.075; 95% CI, 1.043-1.109). 1-SD lower levels of total cholesterol (HR, 0.898; 95% CI, 0.867-0.931), LDL-C (HR 0.899, 95% CI; 0.931), HDL-C (HR, 0.877; 95% CI, 0.841-0.914), and higher triglyceride (HR, 1.078; 95% CI, 1.048-1.109) were significantly associated with the risk of incident CKD. The interactions between triglyceride and intermediate (HR, 1.122; 95% CI, 1.026-1.228) and high PRS (HR, 0.932; 95% CI 0.872-0.995) were significant, and the interactions were inversely associated with the risk of incident CKD. Similar relationship between triglyceride and PRS were observed in subgroup analysis stratified by PRS tertiles.

Conclusions: The PRS for incident CKD presented significant predictive power for incident CKD. Higher triglyceride, lower total cholesterol, lower LDL-C, and lower HDL-C increased the risk of incident CKD. There were interactions between triglyceride and genetic factor, and the interaction weakened the impact of triglyceride on renal outcome.

Figure 1. Study design