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Implementation of polygenic risk score in new onset diabetes mellitus after transplantation: results from KOTRY

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Polygenic risk score (PRS) is derived from a set of risk variants based on the summary statistics from genome wide association studies. PRS is typically constructed as the weighted sum of a collection of genetic variants, usually single nucleotide polymorphisms (SNPs) defined as single base-pair variations from the reference genome. Because current PRS is based on the derivation from case-control approach of GWAS, validation in the cohort study is very important.

New onset diabetes mellitus after transplantation (NODAT) is one of the important complications after solid organ transplantation. NODAT can be a mediator for the post-transplant cardiovascular disease, a second leading cause of death among kidney transplant recipients in Asian kidney transplant recipients. Although the usage of calcineurin inhibitor, especially tracrolimus, is one of the risk factor for NODAT, individual prescription of calcineurin inhibitor depending on the prior probability have not been attempted.

To address the clinical utility of PRS, many challenges lies to be overcome. The limitation of current PRS approach includes 1) limited predictability of PRS compared to conventional risk factors 2) unknown information from incompleted genetics or unmodelled environments, 3) applicability of PRS to transethnic group, 4) paucity of elaborate phenotype association such as behavioral intervention or pharmacological intervention [1]

In this lecture, study results of the first PRS application to predict NODAT in Korean Organ Transplantation Registry (KOTRY) will be introduced. Different PRS based on various ethnicities (Asian, Transethnic, European) were applied to KOTRY recipient datasets, and its predictability compared. Mechanism specific PRS were investigated between incident type 2 diabetes from the general population genetic cohort (KoGES) and NODAT in KOTRY.

1. Cathryn M Lewis et al, Genome Medicine (2020) 12:44