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The Protective Effect of Interleukin-1 Receptor Antagonist on Kidney Function: A Mendelian Randomization Study

Jeong Min Cho[1], Jeong Hoon Ko[1], Semin Cho[2], Soojin Lee[3], Dong ki Kim[1], Sehoon Park[1]
[1]Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Chung-Ang University Hospital, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, Eulji University School of Medicine, Korea, Republic of

Objectives: Interleukins (ILs), key cytokine family of inflammatory response, are closely associated with kidney function. However, the causal effect of various ILs on kidney function needs further investigation.

Methods: We performed two-sample summary-level mendelian randomization (MR) analysis. Genetic variants with strong association with serum IL levels were obtained from a previous genome-wide association study meta-analysis. Summary-level data for eGFR were obtained from CKDGen database. A replication analysis was performed in the independent UK Biobank data. As a main MR analysis, multiplicative random-effect inverse-variance weighed method was performed. Pleiotropy-robust MR analysis, including MR-Egger with bootstrapped error and weighed-median methods, were also implemented.

Results: We tested the causal estimates from nine ILs on eGFR traits. Among the results, higher genetically predicted serum IL-1ra level was significantly associated with higher eGFR values, both in the CKDGen and the UK Biobank data (Figure 1). In addition, the result was consistent towards eGFR decline phenotype of the outcome database. Otherwise, nonsignificant association was identified between other genetically predicted ILs and eGFR outcome (Figure 2).

Conclusions: These findings support the clinical importance of IL-1 associated pathway in relation to kidney function in the general individuals, particularly highlighting the importance of IL-1ra.

Figure 1. Mendelian randomization plots of the causal effect of serum interleukin-1 receptor antagonist (IL-1ra) level on kidney function.