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만성신장병이 급성신손상의 중등도와 회복에 미치는 영향

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The Impact of Preexisting Chronic Kidney Disease on the Severity and Recovery of Acute Kidney Injury

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Recent observational studies have shown that a substantial proportion of patients with AKI have often progression to chronic kidney disease (CKD). Among several risk factors for the development of CKD after AKI, decreased baseline glomerular filtration rate (GFR) represents an important risk factor. However, precise mechanisms involved in the development of fibrosis after AKI with preexisting CKD have not been completely ascertained. Here in this study, we assessed the impact of preexisting CKD on the severity and recovery of AKI in mouse model of 5/6 nephrectomy. Male CD-1 mice underwent 5/6 nephrectomy or sham operation, and 6 weeks later ischemia reperfusion injury (IRI) was performed. On day 1, 7 and 28 after IRI, functional, histological, and molecular parameters were compared between them. Twenty five minutes clamping of renal pedicle in 5/6 nephrectomized mice did not provoke more severe functional, histological deterioration compared to normal mice on day 1 and 7. Similar elevations in SCr were observed in both groups until day 7 after IRI; however, SCr remained higher on day 28 in 5/6 nephrectomized mice compared to normal mice, suggesting that preexisting CKD does not modify severity of AKI but adversely affect the recovery process. From day 7 to 28, mRNA expression of p21, and protein level of pH3, both representing cell cycle arrest were significantly increased in 5/6 nephrectomized mice (CKD+AKI) compared to sham (sham+AKI). Treatment with p53 inhibitor after IRI resulted in not only decreased p21 and pH3 protein level, but also fibrosis in CKD+AKI mice, suggesting that epithelial cell cycle arrest is partially responsible for impaired recovery from AKI in 5/6 nephrectomized mice. Taken together, reduced nephron mass do not seem to increase severity of AKI, but have negative effect on repair process, leading to development of fibrosis.

Key Words: 급성신손상, 만성신장병, 세포주기억류
Acute Kidney injury, Chronic kidney disease, Cell cycle arrest