Editorial

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Is immunosenesence good for kidney injury?

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The incidence of acute kidney injury (AKI) has increased as the population has aged [1]. Aging is an independent risk factor for AKI [2]. AKI that develops in the elderly is more severe and the patient is less likely to recover [3]. Although AKI has emergent problems, there is no specific therapeutic agent and it is difficult to develop new drugs for AKI.

The high incidence of AKI in the elderly might be attributed to age-dependent structural and functional alterations, comorbidities that accumulate with age, and aggressive procedures including surgery and nephrotoxic agents [3]. The pathophysiology of AKI is multifactorial and complicated and is divided into renal structural injury and immunological disorders. The target of structural injury in AKI is considered to be proximal tubular cells. Cell death including necrosis, necroptosis, and apoptosis during AKI might increase as aging progresses. The basal levels of pro-apoptotic factors including cytosolic cytochrome C and active caspase-3/9 was elevated and tubular cell apoptosis increased more significantly in aged rats than in young rats after renal ischemia/reperfusion (I/R) [4], suggesting aged tubular cells might be susceptible to ischemic injury. Autophagy in proximal tubular cells plays a role in protecting against AKI [5]. Autophagic activity has been shown to be diminished in aging tubular cells [6], suggesting less autophagy function can amplify tubular injury in the aged kidney. In terms of inflammation, aging may act in good and/or bad directions with respect to AKI. Aging is associated with chronic inflammation, which is characterized by progressive accumulation of lymphocytes and macrophages in the renal interstitium [7]. A higher influx of lymphocytes and macrophages was detected in aged kidneys following transient ischemic injury [8]. On the other hand, immunosenescence, which is an age-related change affecting the immune system, leads to increased vulnerability to infectious diseases. Various immune system components including innate and adaptive immunity are less functional during immunosenescence. Various anti-inflammatory strategies for AKI are straightforward and have been reported. But, the effects of immunosenescence on AKI development remain unknown.

Lee et al [9] clearly showed the advantage of immunosenesence on AKI by using chimeric mice. Less renal function deterioration, tubular injury, infiltration of macrophages to the renal interstitium, and renal interleukin-12 were identified after renal I/R in young mice transplanted with old bone marrow cells compared to young mice transplanted with young bone marrow cells. Monocytes go into the renal interstitium shortly after neutrophils at 24 hours after renal I/R and differentiate into macrophages, which mainly act as an M1 subset (classically activated pro-inflammatory) [10]. Macrophage ablation before renal I/R injury maintained renal function [11]. Thus, macrophage immunosenescent macrophages might contribute to the deterioration of AKI. Macrophages also play an important role in AKI recovery. The polarization from M1 to M2 (classically activated anti-inflammatory) contributes to resolution of renal inflammation during AKI. Lee et al [9] showed that argi-

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nase-1, an M2 marker, was less expressed 24 hours after reperfusion in mice transplanted with aged bone marrow cells compared to mice transplanted with young bone marrow cells, but not significantly. This suggested that macrophage immunosenesence might support recovery from AKI although the timing to evaluate the M2 marker was too early.

In summary, the immunosenescence-reduced renal inflammations induced by AKI and aging macrophages are candidates that may contribute to AKI improvement.

This discovery may influence therapeutic strategies for the young and elderly suffering from AKI. We should consider the distinct targets of young and elderly patients suffering from AKI. In the case of elderly patients who have immunosenescence, the main therapeutic target might be inhibition of renal tubular cell death. In the case of young patients, it could be reduction of renal inflammation. It is necessary to develop specific new drugs aimed at appropriate patients and therapeutic targets.

Conflicts of interest

The author has no conflicts of interest to declare.

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