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Impact of Aging on Repair Process of Renal Ischemia-Reperfusion Injury

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Introduction:

Immune cells regulate organ repair from ischemia-reperfusion injury (IRI), which affects outcomes after deceased donor organ transplantation. With a rising number of organs from elderly donors, there is an increasing recognition of senescence immune response, but it is less clear in kidney transplantation. We hypothesized that immune responses in IRI repair are affected by aging.

Methods:

Renal IRI surgery with 45 min unilateral ischemia was performed in C57BL/6 mice of three different age groups (7 weeks, 6 months, and 12 months). The mice were followed up with measuring serum creatinine, and kidneys and spleens were collected after 4 weeks. Lymphocytes were analyzed using flow cytometry. Cytokine expression in kidneys was measured using multiplex protein assay.

Results:

Serum creatinine levels were higher in older mice at 4 weeks from IRI (7-week-old, 0.25±0.05; 6-month-old, 0.41±0.04, P=0.01; 12-month-old, 0.39±0.02 mg/dL, P<0.01). NK T cells and Tregs were lower in ischemic kidneys from 12-month-old mice than those from 7-week-old mice (NK T cells, 6.27±0.5 vs 2.51±0.3%, P<0.01; Tregs, 13.42±1.1 vs 7.87±0.5%, P<0.01). There were more activated B cells in ischemic kidneys from older mice (10.00±1.1; 16.37±2.0, P=0.04; 19.77±1.7%, P<0.01) as well as in contralateral kidneys (2.78±0.2; 6.52±1.1, P<0.01; 7.81±0.4%, P<0.01).Spleens from older mice had less Tregs after IRI. There was a downregulation of IL-10 in both ischemic (7-week-old vs 12-month-old, 4.06±2.4 vs 1.27±0.6pg/mg, P<0.01) and contralateral (2.49±0.5 vs 1.80±0.1pg/mg, P<0.01) kidneys from 12-month-old mice, whereas MCP-1 (16.86±3.1 vs 25.42±4.5pg/mg, P<0.01) and RANTES (15.54±3.8 vs 26.92±8.5pg/mg, P<0.01) were upregulated in contralateral kidneys.

Conclusion:

Kidneys from older mice exhibited accelerated proinflammatory and diminished anti-inflammatory responses during IRI repair phase. Age-dependent abnormal immune responses could be a potential mechanism of inferior graft outcomes from elderly donors and may be a promising therapeutic target to improve the quality of organs for transplantation.