Conclusion: These results suggest that RORalpha protects kidney from I/R damage through transcriptional activation of HIF-1 and represents a potential therapeutic target for AKI.

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0028
Optimal Transplantation Timing of Mesenchymal Stem Cell in Rat Model of Renal Ischemia Reperfusion Injury
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Objective: Cell therapy in renal ischemia-reperfusion injury (IRI) is currently limited by low rates of cell engraftment after systemic delivery. In this study, we investigated whether timing of mesenchymal stem cells (MSCs) transplantation can determine the survival and therapeutic potential of MSCs in ischemic kidney.

Methods: The model of renal I/R injury was induced by the release of bilateral renal pedicle clamps following 60 min of occlusion. Six rats per group were sacrificed per time point, at 0 h, 1 h, 12 h, 24 h, 48 h, 72 h and 1 week post-I/R respectively. MSCs were cultured with different time points kidney homogenate supernatants. The animals were sacrificed 48 h after reperfusion and 24 h after MSCs transplantation.

Results: The serum creatinine level peaked at 24 h of reflow and NGAL peaked at 12 h. The highest expression of inflammatory factor was in 12 h and 24 h groups, and the lower was in -1 h, 0 h and 1 w groups. In vitro, there was lower cell apoptosis and higher proliferation in -1 h and 0 h groups compared with other groups. Significant kidney function and histological damage improvement was observed after the treatment of MSCs in -1 h and 0 h groups. Meanwhile, the expression of proinflammatory factor significantly decreased and anti-inflammatory factor significantly decreased in -1 h and 0 h groups compared with other point time groups and control group. In addition, we also observed more obvious inhibition of renal tubular cell apoptosis and promotion of proliferation in -1 h and 0 h groups compared with other groups. Consistent with the improvement above, the viability of implanted MSCs also increased in -1 h and 0 h groups.

Conclusion: MSCs transplanted 1 h before reperfusion or immediately after reperfusion produce the most dramatic improvement in renal function and morphology in rat model of renal I/R injury. It is the optimal timing to transplant MSCs in IRI before the inflammatory response is established.

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0029
Changes in Epidemiology and Influencing Factors of Acute Kidney Injury After Cardiac Surgery: A 5-year Study from 2009 to 2013
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Objective: We collected the epidemiological data of patients with AKI from 2009 to 2013 in order to explore the influencing factors of changes of epidemiology after cardiac surgery.

Methods: Clinical data, which included demographic data of preoperative, intraoperative, postoperative, were prospectively collected in our hospital from January 2009 to December 2013. The main endpoint was poor prognosis including overall mortality and abandon of treatment. The second point was renal outcome.

Results: A total of 11693 patients enrolled, including 6637 males and 5056 females. The overall AKI incidence was 34.5%. The AKI incidence increased during the five years from 34.2% to 36.5% (P < 0.05). There was no significantly statistical differences in AKI-RRT incidences during the 5 years (P = 0.360). The hospital mortality of AKI decreased from 6.3% in 2009 to 3.8% in 2013. The incidence of poor prognosis in AKI were 8.3%, 7.5%, 6.8%, 5.1%, 8.0% (P = 0.196). The mortality of AKI-RRT decreased from 47.1% in 2009 to 29.5% in 2013 (P = 0.230). The incidence of poor prognosis in RRT decreased from 66.7% to 57.4% (P = 0.825). Multivariate logistic regression analysis showed that male, old age, body mass index (every additional 5 kg/m²), hypertension, chronic heart failure, pre-operative serum creatinine (> 115 µmol/L), CPB (every additional 30 minutes) were the risk factors of AKI after cardiac surgery.

Conclusion: The incidence of AKI after cardiac surgery increased from 2009 to 2013 and the rate of poor prognosis did not change.

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0030
Effect of Fluid Overload in Different Periods on Outcome Among Acute Kidney Injury Patients Receiving Renal Replacement Therapy After Cardiac Surgery
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Objective: We explored the effect of fluid overload in different periods on the outcome among acute kidney injury (AKI) patients receiving renal replacement therapy (RRT) after cardiac surgery to guide the fluid management strategy.

Methods: Clinical data of patients who developed AKI and received RRT after cardiac surgery from January 2009 to April 2014 in our hospital were prospectively analyzed. The absolute fluid overload (FO) = fluid in (L) — fluid out (L). Percent fluid overload (%FO) = [(fluid in — fluid out)/admission weight × 100]. %FO > 10% baseline weight was defined as fluid overload. AKI was diagnosed according to the KDIGO guideline standard.
Results: A total of 297 patients were enrolled. The hospital mortality was 64.7%. The %FO at RRT initiation and at the end of RRT in the death group was significantly higher than in the survival group [5.0 [2.4, 9.3] vs. 2.5 [0.2, 5.8%]; 8.4 [3.6, 14.2] vs. 3.9 [0.4, 9.2%]; P < 0.05]. Among AKI-RRT patients, the incidence of low cardiac output syndrome (LCOS) in the death group was significantly higher than in the non-LCOS group (81.9% vs. 56.7%, P < 0.001). Hospital mortality in the LCOS group was significantly higher than in the non-LCOS group (P < 0.05). The %FO at RRT initiation and at the end of RRT in the LCOS group were higher than in the non-LCOS group (>0.05).

Conclusion: Among AKI-RRT patients after cardiac surgery, absolute FO and %FO in the death group were higher than in the survivor group. Fluid overload and LCOS increased the risk of mortality.

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0038
Protective Role of Smad7 in Acute Kidney Injury (AKI)
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Objective: Recent studies indicate that Smad7 plays a protective role in many chronic kidney diseases by attenuating both renal fibrosis and inflammation. However, role of Smad7 in acute kidney injury (AKI) remains unclear, which was investigated in this study in a mouse model of AKI induced in Smad7 knockout (KO) mice.

Methods: Ischemia/reperfusion mouse model of AKI was induced in Smad7 KO mice and their WT (wild type) littermates by bilaterally clamping their renal arteries with vascular clip for 45 min. In addition, a rescued study was also performed in Smad7 KO mice by Smad7 gene transfer locally into renal arteries with vascular clip for 45 min. In day1, day2 and day7, sham-operated mice were used as control. Serum creatinine (Scr), tubular epithelial cell necrosis, MIF and NF-κb signaling, and renal inflammation including F4/80+ macrophage infiltration and MCP-1 expression were examined.

Results: Compared to WT mice, Smad7 KO mice developed more severe renal damage as demonstrated by a significant increase in serum creatinine and tubular necrosis at 48 hour. Further study revealed that cell proliferation, detected by BrdU incorporation and PCNA expression, was greatly suppressed in Smad7 KO mice after AKI. This was associated with enhanced activation of Smad3 and up-regulation of CDK inhibitor p21 and p27, resulting in inactivation of cell cycling by suppressing CDK2 and Cyclin E. In contrast, restored Smad7 locally in the kidney of Smad7 KO mice attenuated the progression of AKI by reversing Smad3-dependent p21/p27-induced inhibition of CDK2/Cyclin E-mediated tubular cell proliferation.

Conclusion: Smad7 plays a protective role in the recovery process of AKI via mechanism of inactivating TGF-β/Smad3-p21/p27-dependent inhibition of CDK2/Cyclin pathway. Thus, Smad7 may be a novel therapeutic agent for AKI.

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0042
Aldosterone Induced NRK Cells Apoptosis in AKI via rno-miR-203
Hypermethylation and Kim-1 Upregulation
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Acute kidney injury is defined by an acute reduction in kidney function as identified by an increase in the serum creatinine and reduction in urine output. Kidney injury molecule-1 (Kim-1) is the hallmark of kidney diseases which is normally not detectable in non-injured kidney but up-regulated and shed into the urine during the AKI. Aldosterone (Aldo) is an important mediator of the renin-angiotensin-ALD system (RAAS) and plays a pivotal role in the regulation of salt and extracellular fluid metabolism. It was found that RAAS induced the Kim-1 expression of proximal tubule epithelial cells and the kidney injury while when treated with Aldo receptor antagonist, the Kim-1 expression decreased and kidney injury was eased. These results suggested that Aldo is related with the expression of Kim-1 during AKI. Until now there is few molecular mechanism reported about the mediation of Aldo to the Kim-1 expression.

In this research, we found that Aldo induced NRK cells apoptosis in AKI via rno-miR-203 hypermethylation and Kim-1 upregulation, Kim-1 is a target gene of rno-miR-203 in NRK cells. When cells were co-treated with pre-miR-203 and spironolactone, cell apoptosis induced by Aldo reduced significantly when compared with only treated with spironolactone. These results may provide likely promising diagnostic marker or new therapeutic target of acute kidney injury.

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0070
Macrophage Migration Inhibitory Factor Promotes Acute Kidney Injury by Amplifying NF-κB-dependent Inflammation
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Objective: Inflammation is a key feature of acute kidney injury (AKI). Macrophage migration inhibitory factor (MIF) is known as an upstream regulator of immune and inflammatory responses. However, its role in AKI remains unclear, which was examined in this study.

Methods: An ischemia/reperfusion mouse model of AKI was induced in MIF knockout (KO) and wild-type (WT) mice and groups of 8 mice were sacrificed at day1, day2 and day7. Sham-operated mice were used as control. Serum creatinine (Scr), tubular epithelial cell necrosis, MIF and NF-κb signaling, and renal inflammation including F4/80+ macrophage infiltration and MCP-1 and TNF-α expression were examined.

Results: Compared to sham-operated mice, MIF WT model mice developed severe AKI including a significant increase in serum creatinine and tubular necrosis, which was associated with upregulation of MIF signaling such as upregulation of MIF and its receptor CD74 and activation of NF-κB signaling, resulting in many macrophage infiltration and marked upregulation of MCP-1 and TNF-α. In contrast, MIF KO mice were protected against the development of AKI by lowering serum creatinine with less extent of tubular necrosis. These protective effects were associated with suppression of NF-κB-dependent renal inflammation including fewer macrophages and inhibition of MCP-1 and TNF-α expression in the AKI kidney (all p < 0.01).

Conclusion: MIF plays a pathogenic role in AKI. Enhanced CD74-NF-κB-driven renal inflammation may be a key mechanism by which MIF mediates AKI.

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0137
NMM, a NAD+ Precursor, Can Rescue Age-associated Susceptibility to Cisplatin-Induced Acute Kidney Injury in a SIRT1-dependent Manner
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Objective: AKI is a common critical condition, the incidence of which increases with age. SIRT1, a NAD+-dependent deacetylase, has been shown to have beneficial effects on both life span and renal health. NMM is a NAD+ precursor involved in NAD+ recycle and thereby SIRT1 activity. This study explores the role of SIRT1 and NMM in age-associated AKI, and mechanism by which SIRT1 deficiency aggravates AKI.