Assessing the Efficacy of Various Kidney Injury Parameters in Predicting Acute Kidney Injury Outcomes (Using Rodent Acute Kidney Injury Models)

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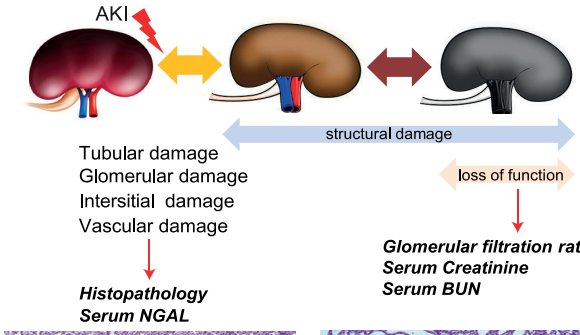
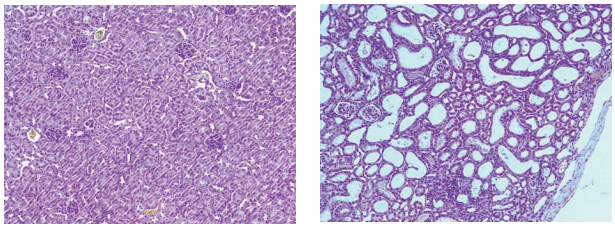
Introduction and Aim

Ferroptosis is a prominent form of renal cell death in acute kidney injury (AKI). The tools of rapid AKI *in vivo* assessment vary, and their robustness as predictors of AKI outcome remains questionable. So, the identification of correlations between kidney injury parameters assessed through various AKI models in rodents, aiming to pinpoint the most effective markers for injury outcome assessment, was aimed to be discovered.



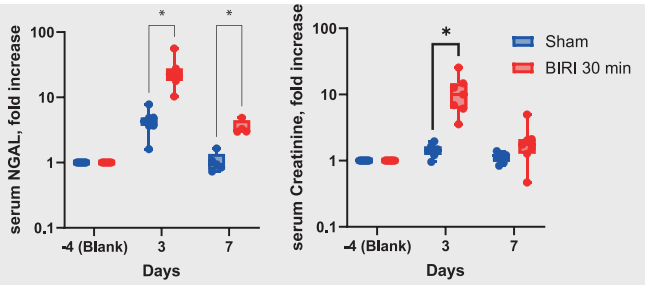


Kidneys of animals subjected to Sham (left) and UIRI (right) surgeries, 7th day post-AKI. Ischemic kidneys demonstrate tubular apparatus violation, interstitial inflammation, necroses and renal parenchyma replacement with connective tissue. H&E, ×100

Methods

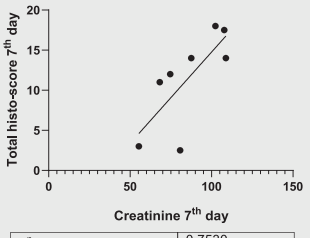
Three AKI models were employed: bilateral ischemia-reperfusion (BIRI), unilateral ischemia-reperfusion injury with contralateral nephrectomy 7 days post-injury (UIRI-Nx), and Cisplatin (CisPt)-induced AKI. Indirect markers (Creatinine, Urea, and Neutrophil gelatinase-associated lipocalin - NGAL) were measured on specific days post-AKI induction, and kidney histopathology scores were taken at the terminal points. Pearson correlation coefficients were calculated, considering only strong (r>0.7) and statistically significant (p<0.05) correlations.

Results



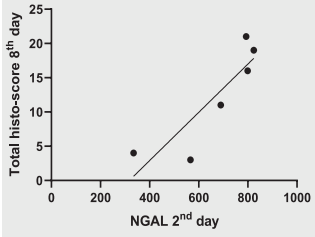
Serum NGAL and Creatinine dynamics (left) and correlations between NGAL and total histo-scores on different post-AKI days (right) in animals subjected BIRI-induced AKI

r	0.8130
95% confidence interval	0.2537 to 0.9649
R squared	0.6610

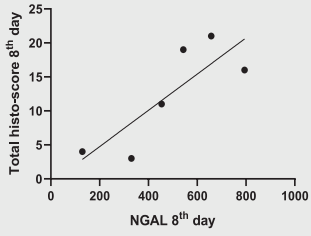


r	0.7530
95% confidence interval	0.1029 to 0.9523
R squared	0.5670

Creatinine and Urea peaked on the 3rd day post-AKI, showing a strong correlation. NGAL, with a higher increase and reduced variability, emerged as a more sensitive marker, especially with early assessments. Both Creatinine/Urea and NGAL collected at any post-AKI timepoint strongly correlated with terminal Histopathology scores, with NGAL demonstrating superior correlation coefficients (r=0.82-0.87 for NGAL vs 0.7-0.81 for Creatinine/Urea). In CisPt-induced and UIRI-Nx-induced AKI, correlations between NGAL and Histopathology scores were stronger that those between Creatinine/Urea and Histo-scores, suggesting its utility as a more indicative marker for kidney injury assessment and prediction.



r	0.8722
95% confidence interval	0.2077 to 0.9859
R squared	0.7608



r	0.8264
95% confidence interval	0.04515 to 0.9804
R squared	0.6830

Conclusions

Serum biochemical and NGAL values correlated strongly with kidney injury severity at terminal points. Using "fold increase" values for NGAL could mitigate individual variability. NGAL appeared to be a robust indicator and predictor of kidney injury outcome.

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References

1. Li J. *et al. Cell Death and Disease* **2020**: *11* 88.
2. Lv J. *et al. Journal of Multidisciplinary Healthcare* **2022**:*15* 2261–2275.
3. Feng Q. *et al. Front. Pharmacol.* **2022**: *13*:858676.