Severe Acute Kidney Injury Prediction in the Pediatric Intensive Care Unit

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Background

- Approximately 27% of patients within the pediatric intensive care unit (PICU) will develop severe acute kidney injury (sAKI) during their clinical course[1]
- Both the Renal Angina Index (RAI) and the urinary biomarker neutrophil gelatinase-associated lipocalin (NGAL) are independently associated with the development of pediatric sAKI[2]
- The integration of RAI and NGAL into an algorithm may better assist clinicians in identifying the patients most at risk for developing sAKI in real-time

Methods

- Observational study of clinical decision algorithm (CDA) used as standard of care in PICU
  - Exclusions: < 3 months of age, chronic kidney disease (CKD) ≥ Stage 4, acute kidney disease requiring renal replacement therapy (RRT) prior to admission
  - CDA use began in 2018, and data collection for research will continue through 2021

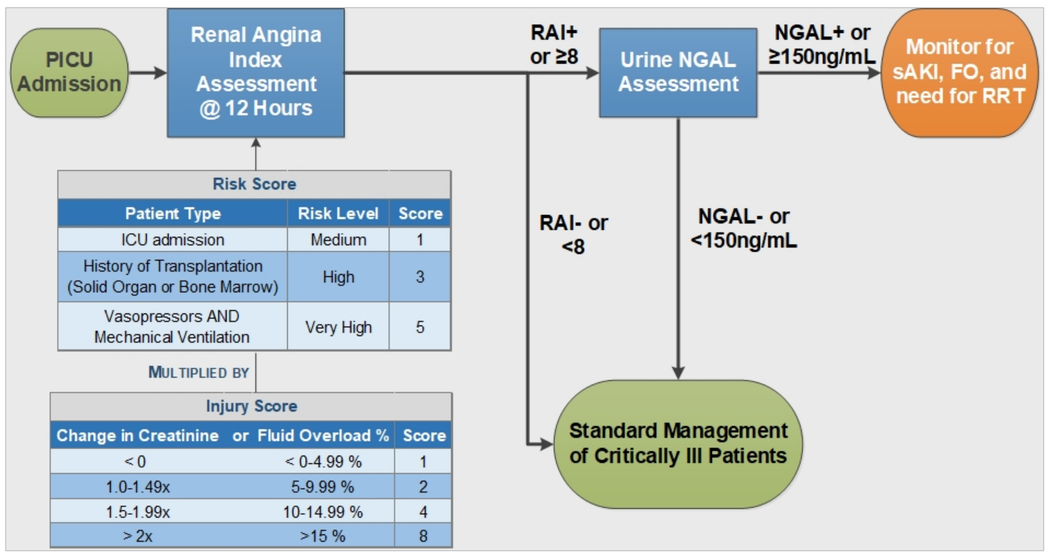

Figure 1. Clinical Decision Algorithm (CDA) Incorporating RAI and NGAL in the PICU

- RAI is automated within the electronic health record (EHR) and results for clinician view
- Urinary NGAL order included in admission orders, for conditional release is RAI ≥ 8 (RAI+)
  - NGAL performed by clinical lab, results in EHR ~ 2 hours after collection
- RAI+NGAL+ patients are hypothesized to be the most at risk for developing PICU Day 2-4 sAKI, as defined as KDIGO Stage 2-3 based on serum creatinine criteria
  - RAI- patients are predicted to be at low risk for sAKI
- Other outcomes measured include need for renal replacement therapy (RRT), more than 10% fluid overload (FO), PICU length of stay (LOS), hospital LOS, and mortality at Day 28
- Outcomes difference between RAI/NGAL groups are assessed by Pearson chi-square, Fisher's exact, or Mann-Whitney tests, with p-value<0.05 considered significant

Results

- 1,614 RAIs resulted between July 2018 and June 2019 and are included in analyses
  - An additional 1,198 patients discharged or deceased prior to PICU Day 2 are excluded from analysis
- RAI+ accounted for 150 (10.2%) of all RAIs
  - The RAI+ cohort was sicker than the RAI- cohort, with median PRISM 9 vs 2 (*p<0.001*) and PIM 2 risk of mortality 1.12 vs 0.83 (*p<0.001*)
- PICU Day 2-4 sAKI developed in 37.3% of RAI+ patients vs 1.7% in RAI- (*p<0.001*)

Table 1. Performance of RAI in Predicting sAKI

	Value	95% CI
Sensitivity	69.1%	57.9 – 78.9%
Specificity	93.9%	92.6 – 95.0%
Positive Predictive Value	37.3%	31.8 – 43.2%
Negative Predictive Value	98.3%	97.7 – 98.8%

- No difference in the incidence of FO through PICU Day 7 (32.0% vs 30.7%, *p=0.7*)
- In addition, no difference in duration of FO, with both groups observed to have a median of 4 days of FO (*p=0.7*)

Results

- Of the 150 RAI+ patients, 55 were RAI+NGAL+ (36.7%) and 40 were RAI+NGAL- (26.7%)
  - The remaining 55 RAI+ patients did not have a urine NGAL collected by bedside staff
- PICU Day 2-4 sAKI developed in 61.8% of RAI+NGAL+ patients compared to 2.4% of RAI- and RAI+NGAL- patients combined (*p<0.001*)

Table 2. Performance of RAI and NGAL Combined in Predicting sAKI

	Value	95% CI
Sensitivity	48.6%	36.4 – 60.8%
Specificity	98.6%	97.9 – 99.1%
Positive Predictive Value	61.8%	49.8 – 98.1%
Negative Predictive Value	97.6%	97.0 – 98.1%

- RAI+NGAL+ patients are not at higher risk of developing FO (32.7% vs 30.9%, *p=0.8*) or longer duration of FO once it develops (median 4 days both groups, *p=0.7*)

Renal Replacement Therapy

- RAI+ patients were at a higher risk of needing RRT (10.7% vs 0.3%, *p<0.001*)
- Adding NGAL into the prediction model continues to show significance (27.3% vs 0.4% of RAI- and RAI+NGAL- patients combined, *p<0.001*)

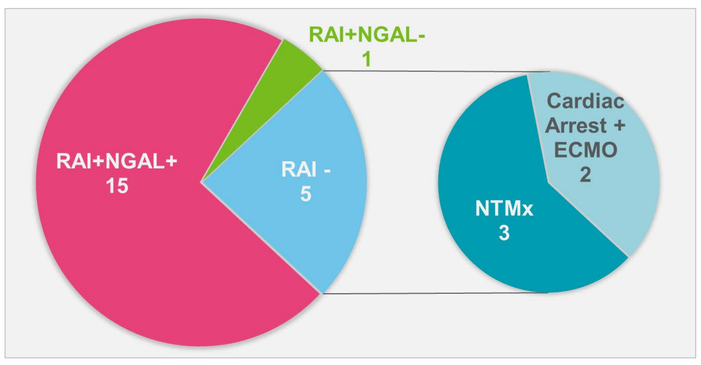

Figure 2. RRT for sAKI by RAI and NGAL Assessment

- 1 RAI+NGAL- was admitted for minocycline induced DRESS requiring RRT
- 3 RAI- patients had high exposures to nephrotoxic medications
- 2 RAI- patients had cardiac arrest >12 hours into their PICU admission, resulting in VA ECMO for return of circulation

PICU and Hospital Outcomes

- RAI was predictive of worse outcomes at PICU and hospital discharge
- RAI alone was a significant for the failure to resolve sAKI at PICU discharge (DC), but RAI+NGAL+ status was not significant in predicting the failure to resolve AKI (*p=0.4*)

Table 3. PICU and Hospital Outcomes by RAI Status at PICU Admission

	AKI Resolved @ PICU DC	PICU LOS	Hospital LOS	PICU Mortality	Day 28 Mortality
RAI+	27 of 56 sAKI (48.2%)	5.5 (3.0, 9.9)	14.7 (8.5, 25.0)	10.7%	10.7%
RAI-	20 of 26 sAKI (76.9%)	3.7 (2.6, 7.6)	7.7 (4.6, 18.7)	1.6%	2.3%
p-value	*0.014*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

Conclusion

- The use of RAI and NGAL to screen patients at high risk for the development of sAKI continues to show clinical promise
- More research is needed into the contribution of nephrotoxic medication exposure after PICU admission to sAKI development in lower risk groups
  - Explore whether RAI should be adjusted to account for nephrotoxic exposures

References

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