Urinary Biomarkers and the Progression from Pediatric AKI to CKD

Kelli A Krallman MS BSN RN, Alexandra Schmerge BA, Stuart L Goldstein MD

Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Background

- Children with a history of acute kidney injury (AKI) are at an increased risk of developing chronic kidney disease (CKD)[1,2]
- Urinary biomarkers have been shown to be increased in AKI[1,3]
- Elevated levels of urinary biomarkers are known to be associated with worsening CKD[1]
- There is a need for identifying biomarkers that can assist in predicting a patient's trajectory between AKI, acute kidney disease (AKD), and CKD[4]
- We assessed for an association between urinary biomarker levels and the progression from AKI to CKD over 1 year
- Biomarkers of interest include:
  - Kidney injury molecule-1 (KIM-1)
  - Liver-type fatty acid-binding protein (L-FABP)
  - Neutrophil gelatinase-associated lipocalin (NGAL)

Methods

- Prospective, observational study of pediatric patients with severe, persistent AKI
  - KDIGO Stage 2 or 3 by serum creatinine criteria lasting at least 48 hours
- Urine collection attempted at each study visit within the first year
  - Visits included: Enrollment/AKI, Day 14, Day 30, Month 3, Month 6, and Year 1
- The outcome of interest is MAKE365 – major adverse kidney events within the first year following the first AKI event (includes development of CKD, kidney transplant, or death)
- Biomarker concentrations are described with median and interquartile ranges and assessed by the Mann-Whitney U test; area under the curve (AUC) is assessed by a receiver operating characteristic (ROC) curve

Results

- Of the 208 patients enrolled in the observational study, 111 (53.4%) had at least one urine sample over the first year after AKI
- The most common reasons urine samples were missed included delayed consent, no urine output during clinic visits, and missed study visits

Table 1. Available Urine Samples by Time Point and MAKE365

	AKI	Day 14	Day 30	Month 3	Month 6	Year 1
No MAKE365	8	10	21	22	22	31
MAKE365	11	17	23	23	20	21
Total	19	27	44	45	42	52

- Of the 111 contributing samples, 41 developed CKD, 1 required a kidney transplant, and 14 patients were deceased by Year 1 (MAKE365 n=56, 50.5%)
- Urinary KIM-1 results were not significantly different at any time point

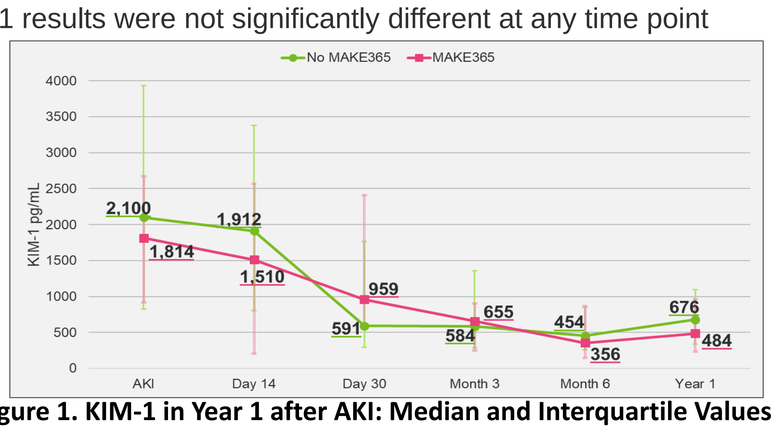


Figure 1. KIM-1 in Year 1 after AKI: Median and Interquartile Values

- Urinary NGAL was significantly higher at Day 30 in patients with MAKE365 (*p=0.005*)

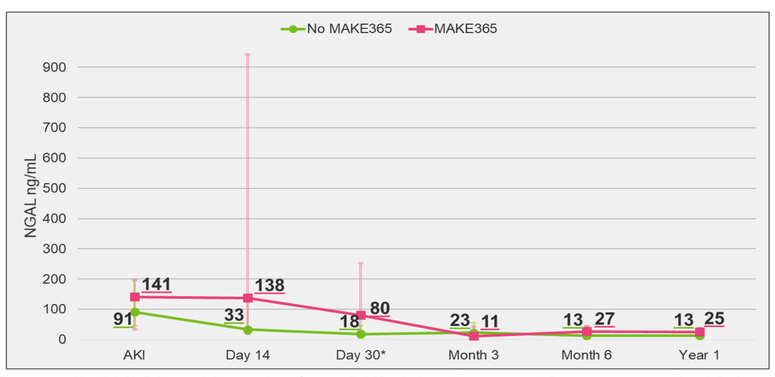


Figure 2. NGAL in Year 1 after AKI: Median and Interquartile Values

Results

- L-FABP was significantly higher at time of AKI (*p=0.04*), Day 14 (*p=0.006*), and Day 30 (*p=0.001*) after AKI in patients with MAKE365

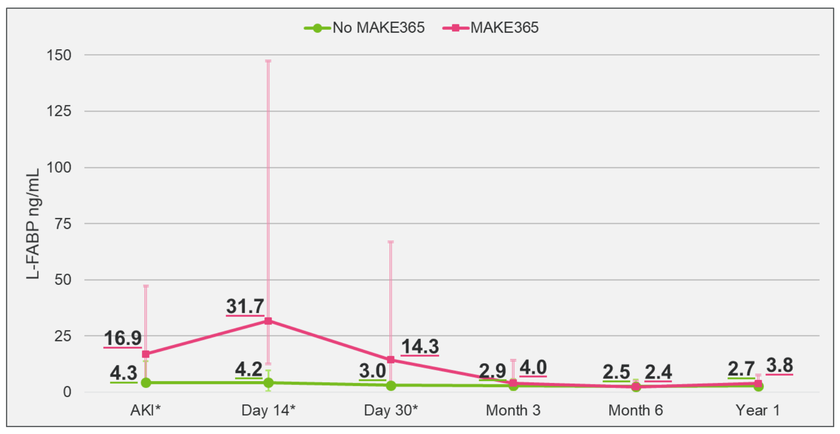


Figure 3. L-FABP in Year 1 after AKI: Median and Interquartile Values

- Examining urinary biomarker results with a ROC curve at Day 30:
  - NGAL AUC = 0.75 (95% CI 0.59, 0.90)

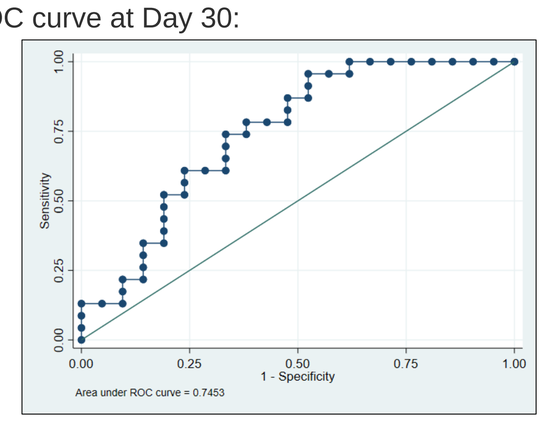
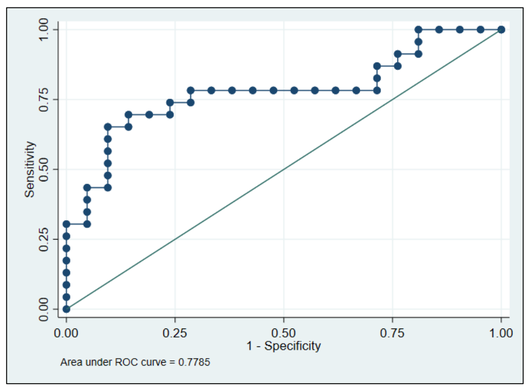


Figure 4. ROC Curve for NGAL at Day 30 Predicting MAKE365



- L-FABP AUC = 0.78 (95% CI 0.63, 0.92)

Figure 5. ROC Curve for L-FABP at Day 30 Predicting MAKE365

Conclusion

- Urinary NGAL and L-FABP concentrations are elevated at Day 30 following severe, persistent AKI in patients who have persistent negative outcomes following the event
- These results show that AKI causing kidney injury that is slow to recover could be a risk factor for the development of CKD
- We may be able to identify patients at high risk for adverse long-term outcomes at the time of AKI or in the immediate follow up time period
- This analysis does not include urine specimen from every enrolled patient at every time point, so the overall sample size at each time point is small and may not reflect a generalizable trend. Additional research is needed

References

1. Devarajan, P. and J.L. Jefferies, Progression of Chronic Kidney Disease after Acute Kidney Injury. Prog Pediatr Cardiol, 2016. 41: p. 33-40.
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4. Chawla, L.S., et al., Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nat Rev Nephrol, 2017. 13(4): p. 241-257.

Acknowledgement

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