Epidemiology of Chronic Kidney Disease at One Year Following Pediatric Acute Kidney Injury

Alexandra Schmerge BA, Kelli Krallman RN, Stuart Goldstein MD
Cincinnati Children's Hospital Medical Center, Center for Acute Care Nephrology, Cincinnati, OH

Purpose

- Adults who experience acute kidney injury (AKI) have a 10 times greater risk of developing end stage renal disease (ESRD) within 12 months[1]
- Acute kidney injury has been consistently associated with the development of new chronic kidney disease (CKD), worsening of existing CKD, and heightened long-term risk of ESRD and death[2]
- Over the past 1-2 decades, pediatric AKI (pAKI) causes have shifted from direct renal etiologies, such as hemolytic uremic syndrome, to etiologies including renal ischemia, SIRS/sepsis, nephrotoxin use, and that are cardiogenic in nature[1]
- Recognition of the AKI characteristics associated with CKD development by one year holds great potential to reform pAKI follow-up care

Methods

- Interim analysis at year 1 (Y1) of a 5 year prospective observational study
- Patients were enrolled with the onset of severe AKI (sAKI), defined as KDIGO Stage 2-3, by SCr criteria, for at least 48 consecutive hours
- Elective follow-up for 5 years after the initial AKI
  - Serum creatinine (SCr), Cystatin-C, and urine studies are collected when ordered as standard of care at each visit to assess CKD status
- The primary outcome of the study is the development of CKD
- CKD severity is stratified using the estimated glomerular filtration rate (GFR) using cystatin-C, where available, or the Schwartz formula using Y1 SCr:
  - CKD Stage 1: GFR ≥ 90 ml/min/1.73m² + proteinuria
    - Proteinuria is defined as urine protein to creatinine ratio ≥ 0.2, urine microalbumin to creatinine ratio ≥ 30, or urinalysis with 2+ protein and a specific gravity < 1.020
  - CKD Stage 2: GFR 60-89 ml/min/1.73m²
  - CKD Stage 3: GFR 30-59 ml/min/1.73m²
  - CKD Stage 4: GFR 15-29 ml/min/1.73m²
- Contributing causes of CKD development are reported, including (a) patient demographics, (b) characteristics of initial sAKI, and (c) repeated sAKI events
  - Fluid overload (FO%) = $\frac{\text{net fluid balance (L)}}{\text{admission weight (kg)}}$ x 100%
- Statistical significance was determined by either a Pearson chi square or Mann-Whitney test, where appropriate, with a p-value of ≤0.05 being considered statistically significant

Results

- A total of 208 patients were enrolled. At Y1:
  - 18 patients (8.7%) were deceased
  - 1 patient (0.5%) required a kidney transplant
  - 28 patients (13.5%) missed the Y1 appointment
  - 125 (60%) had appropriate laboratory studies to assess CKD status and were further analyzed
- Of the 125 patients who completed Y1 visits:
  - 75 patients (60%) had normal GFR and no evidence of proteinuria at Y1
  - The remaining 50 patients (40%) developed CKD by Y1

    Stage 1 → 12 (9.6%) Stage 2 → 29 (23.2%)

    Stage 3 → 5 (4%) Stage 4 → 4 (3.2%)
- No significant difference seen in CKD development based on age or gender
- Of the 23 patients with non-kidney transplant history, 17 (73.9%) developed CKD

Table 1. Incidence of CKD at Y1 in accordance with demographics

	CKD (n = 50)	No CKD (n = 75)	*p-value*
Age at Y1	12.5 (5.8,16.6)	13.8 (7.3, 17.6)	0.513
% Male	28 (56%)	33 (44%)	0.189
Heart/Liver Transplant	17 (34%)	6 (8%)	0.000

Results (continued)

- Most common causes of initial AKI included nephrotoxic medication exposure (NTMx), sepsis, and surgical procedures
  - No significant difference in CKD development NTMx or septic AKI
- Mechanical ventilation and intensive care unit (ICU) stay during the initial hospitalization with AKI are significantly more likely to develop CKD at Y1

Table 2. Incidence of Y1 CKD with initial admission characteristics

	CKD (n = 50)	No CKD (n = 75)	*p-value*
Mechanical Ventilation	32 (64%)	22 (29.3%)	0.000
Hospital LOS	29 (13, 70)	15 (8, 35)	0.014
Hospital FO%	18.6 (0.9, 83.1)	9.5 (0, 35.2)	0.159
ICU Admission	36 (72%)	36 (48%)	0.008
→ ICU FO%	16.7 (1.8, 42.1)	8.4 (2.5, 28.1)	0.612

- Renal Replacement Therapy (RRT), including peritoneal dialysis, acute hemodialysis, and continuous RRT, is associated with Y1 CKD

Table 3. Incidence of CKD at Y1 with initial AKI characteristics

	CKD (n = 50)	No CKD (n = 75)	*p-value*
Days of AKI	12.5 (10, 23)	11 (7, 18)	0.064
Days of sAKI	9 (6, 15)	8 (5, 13)	0.257
RRT	20 (40%)	12 (16%)	0.003

- SCr values were available for 123 patients at Y1
  - 55 patients (44.7%) did not return to baseline, defined as SCr within 50% of original baseline value
  - 28 of the 55 (50.9%) who did not return to baseline did not have CKD at Y1
- Blood pressure measurements were available for 109 patients at Y1
  - 34 (31%) had hypertension, defined per AAP or AHA guidelines[3]
  - 21 of the 34 (61.8%) with hypertension did not have CKD at Y1

Table 4. Incidence of CKD at Y1 and other markers of renal recovery

	CKD	No CKD	*p-value*
Return to Baseline	21 (43.8%) n = 48	47 (62.7%) n = 75	0.040
Hypertension	13 (31%) n = 42	21 (31.3%) n = 67	0.966

- The incidence of at least one repeat sAKI episode significantly increases the likelihood of CKD development ($p < 0.000$)
  - 25 of the 38 patients (66%) who experienced at least one repeat sAKI developed CKD within a year
  - 13 of the 87 patients (19.4%) without a repeat episode of sAKI had Y1 CKD

Conclusions

- Intubation, hospital LOS, ICU admission requirement, and RRT requirement are associated with the development of CKD at Y1
- Failure to return to baseline SCr by Y1, as well as repeated sAKI insults are also associated with this development of CKD
- These findings seem to reinforce the importance of preventing AKI reoccurrence
- Patients who experience the aforementioned AKI factors are at an increased risk for CKD and should be followed prospectively
- AKI follow-up care could be customized based on patient-specific risk factors, such as surgical procedures and history of transplant

References

1. Goldstein, S.L. and P. Devarajan, *Acute kidney injury in childhood: should we be worried about progression to CKD?* Pediatr Nephrol, 2011. 26(4): p. 509-22.
2. Chawla, L.S., et al., *Acute kidney injury and chronic kidney disease as interconnected syndromes.* N Engl J Med, 2014. 371(1): p..
3. Flynn, J.T., et al., *Clinical Practice G*58-66*uideline for Screening and Management of High Blood Pressure in Children and Adolescents*. Pediatrics, 2017. 140(3).