Prospective Validation of the PERSEVERE-II AKI Model for Acute Kidney Injury Prediction in Pediatric Septic Shock

Natalja L. Stanski, MD[1] and Stuart L. Goldstein[1]
[1]Cincinnati Children's Hospital Medical Center

Introduction

- Severe acute kidney injury (AKI) impacts 1 in 5 children with septic shock and is associated with increased morbidity and mortality
  - >5x adjusted odds of mortality (Stanski et al, ICM 2020)
  - Worse health related quality of life at 3 months in survivors (Starr et al, PCCM 2022)
- Early prediction of patients at highest risk for new or persistent severe sepsis associated-AKI (SA-AKI) may facilitate targeted proactive intervention, resource allocation, and clinical trial enrollment to improve outcomes
- Consideration of the dysregulated sepsis-induced host inflammatory response is important when considering risk for sepsis-induced organ injury like SA-AKI. As such, we previously derived the PERSEVERE-II AKI Model (**Figure 1**) using CART methodology for prediction of severe AKI prediction at Day 3 of pediatric septic shock.
  - Incorporated the PERSEVERE-II mortality probability (validated multibiomarker tool to estimate 28-day mortality in pediatric septic shock which includes platelet count and the PERSEVERE biomarkers (C-C chemokine ligand 3, heat shock protein 70 kDa 1B (HSPA1B), IL-8, granzyme B (GZMB), matrix metallopeptidase-8
  - Also incorporated Day 1 KDIGO stage and individual PERSEVERE biomarker values

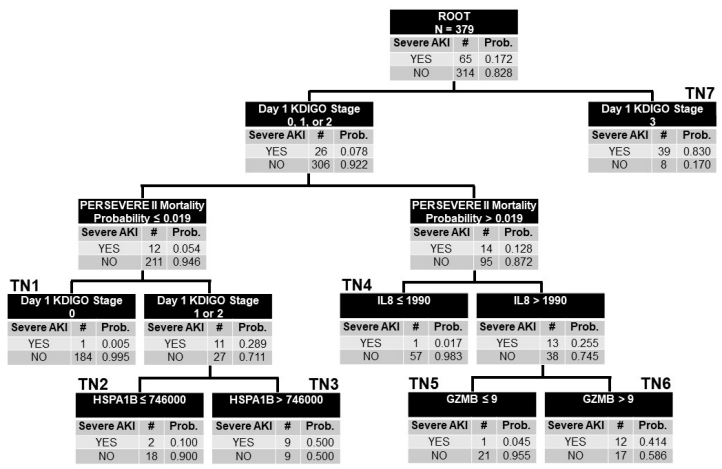

Figure 1. The PERSEVERE-II AKI Model. TN1,2,4 and 5 are low risk (predicted not to have Day 3 severe AKI; TN3,6,7 are high risk (predicted to have Day 3 severe AKI); all biomarker values in pg/ml

- **Model Performance for Day 3 Severe AKI Prediction:**
  - AUC 0.95 (0.92-0.98)
  - Sensitivity 92%, Specificity 89%, PPV 84%, NPV 98%
  - 10-fold cross validation AUC 0.88
- We sought to prospectively assess the predictive performance of the PERSEVERE-II AKI Model in a separate cohort of children with septic shock.

Methods and Materials

- Secondary analysis of a prospective study of children and young adults aged 0-25 years admitted to 11 PICUs with septic shock from March of 2019 to December 2022
  - Exclusion Criteria: missing creatinine or biomarker data, end stage kidney disease *or* pre-existing kidney disease without a known baseline serum creatinine (SCr)
- Serum collected on Day 1 for PERSEVERE biomarker measurement and platelet count, which were used to assign a PERSEVERE-II mortality probability
- Day 1 KDIGO AKI stage, PERSEVERE-II mortality probability, granzyme B, heat shock protein 70 kD 1B, and IL-8 concentrations were used to assign a Day 3 severe AKI probability using the PERSEVERE-II AKI Model (**Figure 1**)
- Model performance was assessed using area under the receiver operating curve (AUROC), sensitivity, specificity, PPV and NPV, and was compared to degree of Day 1 SCr elevation alone.

Results

Cohort Demographics:

- 363 of 384 patients included after exclusion criteria applied
- 79 of 363 (22%) had severe SA-AKI at Day 3

	Entire Cohort
Age, years	9.6 (3.3-16.3)
Male sex, n (%)	187 (52)
PRISM III	8 (5-13)
PERSEVERE-II Mortality Probability	0.007 (0.007-0.189)
Day 1 Vasoactive Medications, yes (%)	268 (74)
Day 1 Mechanical Ventilation, yes (%)	202 (56)
Day 1 KDIGO AKI, yes (%)	152 (42)

Day 3 Severe SA-AKI Risk Estimation:

- Patients assigned to 1 of 7 TNs based on previous model (**Figure 2**)

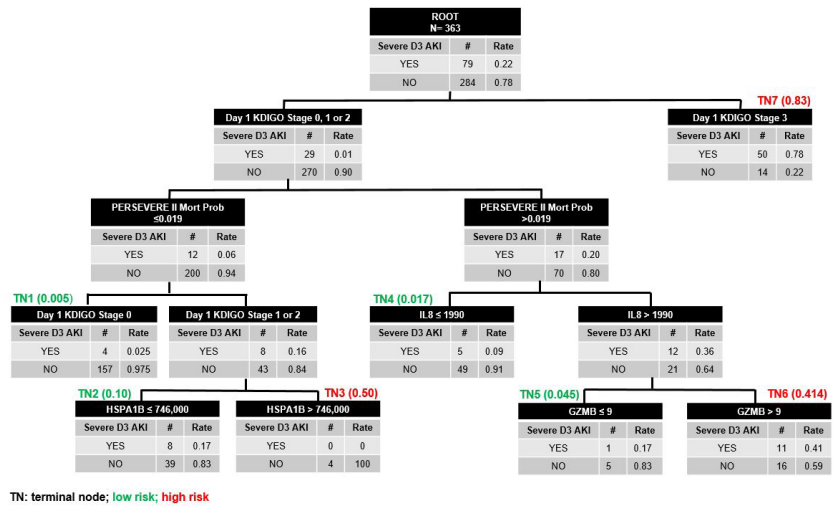

Figure 2. Patient assignment based on the PERSEVERE-II AKI Model. TN1,2,4 and 5 are low risk (predicted not to have Day 3 severe AKI; TN3,6,7 are high risk (predicted to have Day 3 severe AKI); all biomarker values in pg/ml

Comparison to Context-Free SCr Elevation:

	PERSEVERE-II AKI Model Predicted	Day 1 SCr-Based AKI	*p*-value
N (%cohort)	94 (26)	152 (42)	--
Day 3 Severe AKI, n (%)	61 (65)	69 (45)	0.003
Day 3 Severe AKI Prediction			
AUROC	0.89 (0.85-0.93)*	0.82 (0.76-0.88)**	0.004
Sensitivity, %	77 (66-86)	87 (78-93)	
Specificity,%	88 (84-92)	71 (65-76)	
PPV, %	65 (54-74)	45 (37-54)	
NPV, %	93 (89-96)	95 (91-98)	
+LR	6.6 (4.7-9.4)	3.0 (2.4-3.6)	
-LR	0.3 (0.2-0.4)	0.17 (0.1-0.3)	
Day 1-7 RRT, n (%)	38 (40)	40 (26)	0.021
Day 1-2 AKI, n (%)	82 (87)	152 (100)	--
Day 3 Renal Recovery, n (%)	30 (37)	80 (53)	0.019
PICU-free days	13.5 (0-23)	20.5 (0-25)	0.012
Vasopressor-free days	25 (19.5-26)	26 (23-27)	0.016
28-day mortality, n (%)	13 (14)	13 (8.6)	0.19

*AUROC AKI Prediction Mode; **AUROC for degree of SCr above baseline.

Conclusions

- We have prospectively validated the PERSEVERE-II AKI Model for prediction of Day 3 severe SA-AKI
- This tool outperforms context-free SCr elevation, with high specificity and PPV
- The vital next step to translation this tool to the bedside to assess impact on care and outcomes is timely biomarker availability.

THE 29TH INTERNATIONAL CONFERENCE ON
ADVANCES IN CRITICAL CARE NEPHROLOGY
AKI & CRRT 2024
MARCH 12-15, 2024 SAN DIEGO, CALIFORNIA