Resuscitation Bundle in Pediatric Shock Decreases Acute Kidney Injury and Improves Outcomes

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Objective To investigate the impact of an early emergency department (ED) protocol-driven resuscitation (septic shock protocol [SSP]) on the incidence of acute kidney injury (AKI).

Study design This was a retrospective pediatric cohort with clinical sepsis admitted to the pediatric intensive care unit (PICU) from the ED before (2009, PRE) and after (2010, POST) implementation of the SSP. AKI was defined by pRIFLE (pediatric version of the Risk of renal dysfunction; Injury to kidney; Failure of kidney function; Loss of kidney function, End-stage renal disease creatinine criteria).

Results A total of 202 patients (PRE, n = 98; POST, n = 104) were included (53% male, mean age 7.7 ± 5.6 years, mean Pediatric Logistic Organ Dysfunction [PELOD] 8.9 ± 12.7, mean Pediatric Risk of Mortality score 5.3 ± 13.9). There were no differences in demographics or illness severity between the PRE and POST groups. POST was associated with decreased AKI (54% vs 29%, $P < .001$), renal-replacement therapy (4 vs 0, $P = .04$), PICU, and hospital lengths of stay (LOS) (1.9 ± 2.3 vs 4.5 ± 7.6, $P < .01$; 6.3 ± 5.1 vs 15.3 ± 16.9, $P < .001$, respectively), and mortality (10% vs 3%, $P = .037$). The SSP was independently associated with decreased AKI when we controlled for age, sex, and PELOD (OR 0.27, CI 0.13-0.56). In multivariate analyses, the SSP was independently associated with shorter PICU and hospital LOS when we controlled for AKI and PELOD ($P = .02$, $P < .001$, respectively).

Conclusion A protocol-driven implementation of a resuscitation bundle in the pediatric ED decreased AKI and need for renal-replacement therapy, as well as PICU and hospital LOS and mortality. *(J Pediatr 2015;167:1301-5)*.

Septic shock affects almost more than 50 000 children annually[1-4] and is the leading cause of acute kidney injury (AKI) in the pediatric intensive care unit (PICU).[5] One recent point prevalence study in 26 nations found that 8% of children in PICUs met the criteria for severe sepsis.[2] Mortality rates of up to 25% have been reported in both industrialized and developing nations.[2] Standardized definitions and stratification schemes[6] for AKI have greatly improved our understanding of the epidemiology and impact of AKI. Despite increased awareness and detection through the widespread use of standardized AKI definitions, AKI remains an independent mortality and morbidity risk for hospitalized patients. Twenty-five percent of patients in the PICU are discharged with AKI, and follow-up frequently is sporadic.[7,8] Repeated episodes of AKI, especially in these with chronic conditions, are now recognized to lead to the development of chronic kidney disease (CKD).[9-14]

Patient outcomes have improved consistently in the PICU during the last 3 decades; however, despite advances in renal support, little has changed in the outcome of critical illness–associated AKI. Furthermore, AKI already is present on admission to the PICU in up to 30% of patients.[15] Because a significant percentage of AKI already is established on admission to the PICU, we hypothesized that early intervention before admission to the PICU would reduce the incidence of AKI. Texas Children's Hospital implemented a protocol-driven sepsis resuscitation bundle (septic shock protocol [SSP]) in the emergency department (ED) in 2010, resulting in earlier recognition of shock and significant improvements in time-to-critical interventions such as fluid resuscitation with normal saline and appropriate intravenous antibiotics.[16] Given the poor outcomes once AKI is established and the frequency of association with sepsis, we wanted to investigate the incidence of AKI in children receiving protocolized resuscitation in the pre-PICU setting to see whether AKI could be prevented before arrival to the PICU.

AKI	Acute kidney injury
CKD	Chronic kidney disease
ED	Emergency department
ESRD	End-stage renal disease
LOS	Length of stay
PELOD	Pediatric logistic organ dysfunction
PICU	Pediatric intensive care unit
RRT	Renal-replacement therapy
SSP	Septic shock protocol

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Methods

We performed a retrospective review of patients with clinical septic shock admitted to the PICU from the ED in the 12 months before (2009; PRE) and the 6 months immediately after institution of the SSP (POST) in 2010. AKI was defined a priori as one of the clinical outcomes to be tracked after the implementation of the quality improvement project and was defined by pediatric version of the Risk of renal dysfunction; Injury to kidney; Failure of kidney function; Loss of kidney function, End-stage renal disease (ESRD) creatinine criteria (Table I).[6,17] Severe AKI was defined as pediatric version of the Risk of renal dysfunction; Injury to kidney; Failure of kidney function; Loss of kidney function, ESRD injury or failure. Outcome criteria of loss and ESRD were not investigated. Because urine output data were not consistently available, this variable was not integrated into the AKI definition. The lowest serum creatinine available in the last 6 months was recorded for each patient to define baseline creatinine clearance. If no baseline creatinine measurement was available, the patient was assumed to have normal renal function (estimated creatinine clearance of 120 mL/min/1.73 m^2).[6] Only the initial admission for shock for each patient was analyzed. Patients with known CKD or ESRD were excluded, as were patients who had no serum creatinine obtained during the index admission. Institutional review board approval was obtained.

The details of the SSP have been published previously.[16] To summarize, patients who were suspected to have septic shock or severe sepsis were triaged rapidly in the ED and received hemodynamic measure–targeted fluid resuscitation with normal saline, intravenous antibiotics, and, when applicable, vasoactive support and steroids, as part of an institutional protocol. The control cohort (PRE) consisted of patients who were admitted to the PICU from the ED with clinical septic shock in the 12 months preceding institution of shock protocol. Demographics, comorbidities, physiological and laboratory data required for calculation of severity of illness scores, the amount of fluid received in the ED, as well as outcome data (length of PICU and hospital length of stay [LOS, calculated from time of ED triage], 30-day mortality, and use of renal-replacement therapy [RRT]) were recorded.

Continuous data were presented as mean ± SD or median (IQR). Categorical data were presented as percentages. Parametric data were analyzed using the Student t or χ^2 test. Nonparametric data were analyzed by the Kruskal-Wallis or Mann-Whitney U test. Multivariate analyses were performed with linear or logistic regression. All statistical analyses were performed using Stata 11 (Stata, Inc, College Station, Texas).

Results

Of 206 patients identified, 2 each had ESRD or lacked any serum creatinine measurements and were excluded (Table II). There were no differences in age, sex, presence of preexisting conditions, or Pediatric Risk of Mortality or pediatric logistic organ dysfunction (PELOD) scores between PRE and POST SSP. Overall, 83 patients (41%) had AKI (risk = 52 [63%], injury = 23 [28%], failure = 8 [10%]). There were no differences in age, sex, or the proportion of patients with comorbidities between patients with and without AKI. Patients with AKI had greater mortality, greater severity-of-illness scores, and longer PICU and hospital LOS (Table III). The SSP (POST) group in our study had a median time to intervention of 34 minutes. Twenty-six percent of PRE patients got the first antibiotic dose within the first 60 minutes of arrival in the ED compared with 56% of POST patients ($P < .001$). Children without AKI received more fluids than those with AKI, but the differences volume received was unlikely to be of clinical significance (56 mL/kg vs 47 mL/kg, $P = .002$).

Fewer patients developed AKI in the POST group (54% PRE vs 29% in POST, $P < .001$); there also were reductions in mortality, LOS, and use of RRT (Table IV). The stages of AKI were similar in PRE and POST groups. Severe AKI, defined as combination of injury and failure, was greater in the PRE than the POST group (21/98 [21%] vs 10/104 [10%], $P = .01$). POST patients received statistically more fluid then PRE patients in the ED (56 vs 49 mL/kg), but this difference is of minimal clinical significance. In multivariate analyses, the POST period was independently associated with decreased AKI when we controlled for age, sex, and PELOD or Pediatric Risk of Mortality. The shock protocol also was associated with shorter PICU and hospital

Table I. Pediatric version of the Risk of renal dysfunction; Injury to kidney; Failure of kidney function; Loss of kidney function, ESRD (pRIFLE) classification

Category	Definition	Mortality rate (aOR)
R: Risk	Decline in eCCL >25% from baseline	4.3 (2.3-7.8)
I: Injury	Decline in eCCL >50% from baseline	8.1 (4.6-14.3)
F: Failure	Decline in eCCL >75% from baseline	15.6 (9.5-25.6)
L: Loss	Loss of renal function >4 wk	Unknown/not studied
E: ESRD	Complete loss of renal function for >3 mo	Unknown/not studied

eCCL, estimated creatinine clearance.
Pediatric modified RIFLE classification system as per Akcan-Arikan et al[6] and reported mortality rate in terms of aORs and AKI by RIFLE.[17]

Table II. Characteristics of the study population

Variables	PRE control group (n = 98)	POST intervention group (n = 104)	*P* value
Age, y	8.1 ± 5.8	7.3 ± 5.5	.31
Male, n (%)	54 (55)	53 (51)	.29
Previously healthy, n (%)	38 (39)	45 (43)	.56
PRISM score	6.6 ± 14.9	4.2 ± 12.9	.22
PELOD score	7.7 ± 16.1	10.2 ± 8.4	.16
Fluid given, mL/kg	48.7 ± 24.1	55.9 ± 15.7	.01
Time to first bolus, min	65 (29-121)	34 (24-85)	.01
Time to first antibiotic, min	141 (86-199)	54 (41-125)	.001

PRISM, Pediatric Risk of Mortality.
Time to first fluid bolus and first antibiotic is time elapsed from arrival in ED to said intervention.