# Optimal Timing of Continuous Renal Replacement Therapy Initiation from Initial Renal Insult

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## Introduction

- In the Pediatric Intensive Care Unit (PICU), acute kidney injury (AKI) is common. For those with severe AKI, continuous renal replacement therapy (CRRT) is often the preferred modality to help stabilize metabolic abnormalities as well as manage optimal hemodynamic, and fluid status.
- The optimal timing of CRRT initiation in patients without immediate life-threatening complications of AKI is unclear.
- Earlier initiation of CRRT from severe AKI onset may allow for early removal of toxins, management of acidosis, and reversal of fluid overload. However, many with severe AKI may recover spontaneously, making delayed initiation preferable.
- In the adult literature, the AKIKI and STARRT-AKI trials demonstrated no mortality difference between early or delayed initiation of RRT.
- We investigated, in a pediatric population, how the length of time between initial renal insult and CRRT initiation impacts midterm renal outcomes

## Methods and Materials

- Single center cohort study of pediatric CRRT patients between 2/2014 to 2/2020.
- Inclusion Criteria:
  - Age < 18 years of age at CRRT start
  - Admitted to the Texas Children's pediatric, cardiac or neonatal intensive care units
- Exclusion Criteria:
  - Age ≥ 18 years of age at CRRT start
  - Patients with end stage renal disease, chronic kidney disease, inborn errors of metabolism, or ingestions
- Onset of renal injury was defined as AKI-Cr (≥ 2x baseline creatinine), AKI-UOP (<0.5ml/kg/hr for 24h), and/or fluid overload (FO) >15% in the seven days prior to CRRT start.
- Fluid overload was defined as cumulative intake minus output divided by weight at ICU admission.
- Primary outcome was CRRT-free days, defined as the number of days not on CRRT censored at 30 days.

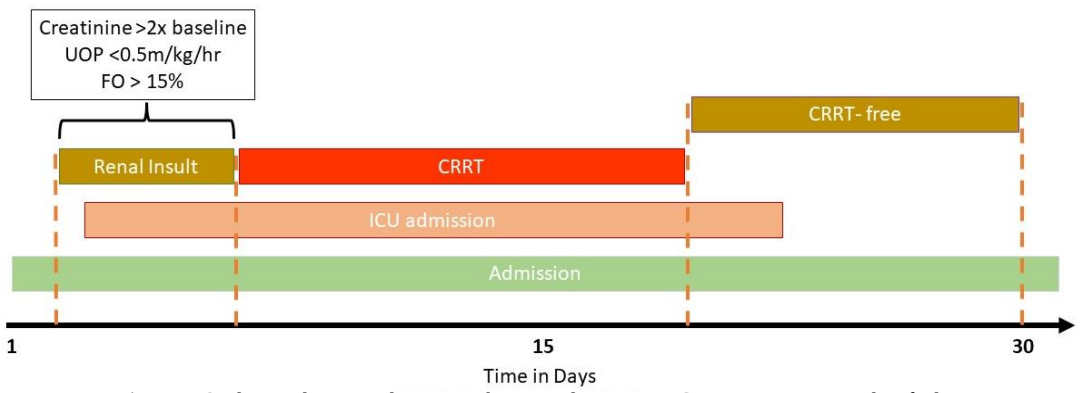


**Figure 1.** Study Timeline: Renal injury in the seven days prior to CRRT initiation was identified in patients admitted to the pediatric ward or PICU. CRRT-Free days were then defined as the number of days not on CRRT at 30 days.

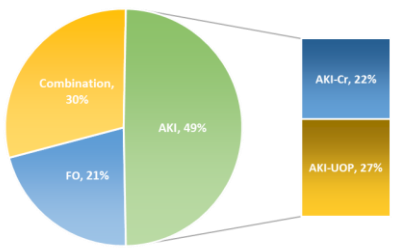


**Figure 2.** Breakdown of patients with renal injury at 24 hours to seven days prior to CRRT start (n=198).

## Results

- 233 patients, 53% male, with a median age of 55 months (IQR 11.5-155).
  - Median duration of CRRT was 13 days (IQR 5-27).
  - 85% of patients had renal injury in the seven days prior to CRRT start.
  - Onset of initial renal injury was median 4 (IQR 1-7) days prior to CRRT start.
  - 65% of patients were on vasoactive medications at CRRT start and PELOD -2 score at CRRT start was 8 (IQR 7-10).
  - Median CRRT-free days was 17 (IQR 3-25).
- Renal injury (AKI-Cr, AKI-UOP, and FO) in seven days prior to CRRT start was associated with fewer CRRT-free days.
- Every additional day between initial injury (AKI-Cr, AKI-UOP, as well as FO) and CRRT start resulted in fewer CRRT-free days.
- Duration between any initial injury to CRRT start was associated with less CRRT-free days (ß -0.9, p<.001).

**Table 1** CRRT-Free Days (Unadjusted)

| Covariate | β coefficient | 95%CI | P value |
|---|---|---|---|
| Primary Diagnosis | 0.10 | -0.67 – 0.48 | 0.74 |
| Gender | -0.92 | -3.69 – 1.85 | 0.51 |
| Age at Hospitalization (months) | .01 | -0.01 – 0.029 | 0.25 |
| PELOD-2 score at ICU admission | 0.12 | -0.22 – 0.47 | 0.49 |
| **PELOD-2 score at CRRT start** | **-0.50** | **-0.22 – -0.05** | **0.03** |
| **Vasoactive Inotropic Score** | **0.08** | **<0.01 – 0.15** | **0.04** |
| **AKI-Cr Present (Yes)** | **-3.76** | **-6.54 – -0.99** | **0.01** |
| **AKI-Cr to CRRT start (Day)** | **-0.99** | **-1.5 – -0.48** | **<0.01** |
| **AKI-UOP to CRRT start (Day)** | **-0.95** | **-1.45 – -0.45** | **<0.01** |
| **FO >15% to CRRT start (Day)** | **-0.45** | **-0.9 – -0.01** | **0.05** |
| **Initial Injury to CRRT start (Day)** | **-0.85** | **-1.29 – -0.40** | **<0.01** |

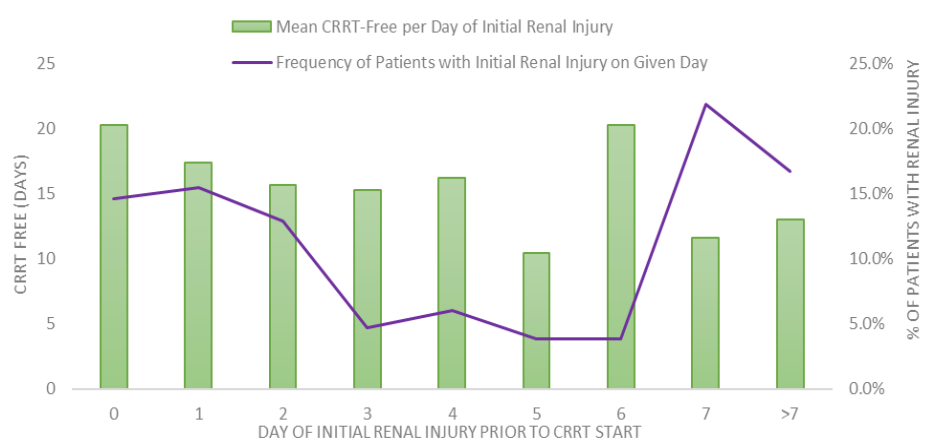


**Figure 3.** Association of day of initial renal injury preceding CRRT start with mean CRRT-free days as well as with frequency of renal injury. % of patients with initial renal insult on given day

## Conclusions

- Illness severity was associated with fewer CRRT free days.
- Earlier initiation of CRRT from AKI or development of fluid overload in pediatric patients without underlying kidney disease was associated with more CRRT-free days.
- Further studies should investigate the optimal timing of CRRT initiation in pediatric CRRT.

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