Timing of Continuous Renal Replacement Therapy Initiation and Major Adverse kidney events at 90 days: A retrospective analysis of the WE-ROCK Registry

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Introduction

- Acute kidney injury (AKI) and pathologic fluid overload (FO) are common in critically ill children and young adults.
- CRRT is used for the most severe form of AKI and FO, but there is significant practice heterogeneity across centers.
- Adult studies have not demonstrated no survival benefit for an accelerated vs. delayed strategy of of CRRT initiation.
- There is no consensus on when to start CRRT in children and most studies are retrospective, small and single center in design.

Aim and Hypothesis

- **Aim:** Determine if early vs. late CRRT start is associated with Major Adverse Kidney Events at 90 days (MAKE-90).
- **Hypothesis:** A longer time to CRRT initiation would be associated with worse MAKE-90.

Methods and Materials

- Multi-center retrospective study.
  - 32 Centers, 7 nations
- **Inclusion:** Patients aged 0-25 years treated with CRRT for AKI, and/or FO from 2015-2021.
- **Exclusion**: ESKD, non-AKI/FO indication, concurrent ECMO or use of PD in the same admission prior to CRRT, use of CARPEDIEM™ device.
- **Primary Exposure:** Time to CRRT initiation as a continuous and dichotomous variable (early: ≤48h; late: >48h from ICU admission).
- **Primary Outcome:** MAKE-90 (dialysis dependence, persistent kidney dysfunction defined by >25% decline in eGFR from baseline or death).
  - Time to CRRT start was modeled as restricted cubic splines (3 knots) to allow for potential non-linear associations with outcomes.
  - OR for a unit increase are equal to the interquartile range

Results

- 980 patients included in the analysis.
- MAKE-90 in 618 (63%), of which 51% died.
- Median time to CRRT start among the entire cohort was 2 (IQR: 1,7) days.
- **The odds of MAKE-90 for patients with a CRRT start time of 6 (3rd quartile) days was 1.07 times that of patients with CRRT start of 1 day (1st quartile)**

Comparison of MAKE-90 Outcomes

Variable	No MAKE-90	MAKE-90	P-Value
Age (years)	8.76 (1.97, 14.68)	8.76 (1.10, 15.34)	0.6
Female Sex	286 (47%)	159 (43%)	0.3
Admit Category			<0.001
• **Shock/infxn/Trauma**	235 (38%)	129 (35%)	
• **Respiratory Failure**	84 (14%)	111 (30%)	
• **Post-surgical**	35 (5.7%)	14 (3.8%)	
• **CNS dysfunction**	22 (3.6%)	17 (4.6%)	
• **Pain/sedation**	6 (1.0%)	2 (0.5%)	
• **Primary cardiac**	14 (2.3%)	17 (4.6%)	
• **Primary cardiac (post surgery)**	40 (6.5%)	9 (2.4%)	
• **Heart failure/myopat**	22 (3.6%)	17 (4.6%)	
• **Other**	154 (25%)	52 (14%)	
Primary Comorbidity			
• **None**	152 (25%)	41 (11%)	<0.001
• **Respiratory**	72 (12%)	61 (17%)	0.042
• **Cardiac**	104 (17%)	88 (24%)	0.010
• **Oncologic**	110 (18%)	112 (30%)	<0.001
• **Immunologic**	68 (11%)	85 (23%)	<0.001
Time to CRRT start	2 (1, 5)	3 (1, 10)	<0.001
PELOD-2 CRRT initiation	6 (4, 8)	8 (6, 10)	<0.001
VIS at CRRT start	2 (0, 14)	10 (0, 25)	<0.001
%FO at CRRT initiation	6.97 (2.00, 16.74)	8.59 (3.25, 21.17)	0.01

Multivariable regression for MAKE-90 Outcomes

Variable	Reference	Contrast	OR (95% CI)
Time of CRRT start (days)	1.0	6.0	1.07 (1.01-1.15)
No comorbidities	No	Yes	0.45 (0.32-0.63)
Respiratory comorbidity	No	Yes	0.88 (0.58-1.33)
Cardiac comorbidity	No	Yes	1.25 (0.86-1.81)
Oncologic comorbidity	No	Yes	1.16 (0.84-1.59)
Immunologic comorbidity	No	Yes	2.07 (1.19-3.61)
Sepsis at ICU admission	No	Yes	1.10 (0.77-1.57)
VIS at CRRT initiation	0.0	20.0	1.12 (0.95-1.31)
% FO at CRRT initiation	2.4	18.1	1.06 (0.96-1.17)
CRRT duration (days)	3.0	14.0	1.42 (1.26-1.61)

Conclusions

- Longer time to CRRT start is associated with worse MAKE-90 outcomes
- RCT's in children, like STARRT-AKI are necessary to determine when accelerated vs. delayed start impact outcomes

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