Published in final edited form as:

Pediatr Crit Care Med. 2016 December ; 17(12): 1157–1169. doi:10.1097/PCC.0000000000000970.

The Incidence of Acute Kidney Injury and its Effect on Neonatal and Pediatric ECMO Outcomes: A multicenter report from the KIDMO Study Group

Geoffrey M. Fleming, MD¹, Rashmi Sahay, PhD², Michael Zappitelli, MD³, Eileen King, PhD², David J. Askenazi, MD⁴, Brian C. Bridges, MD¹, Matthew L. Paden, MD⁵, David T. Selewski, MD⁶, and David S. Cooper, MD⁷

¹Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee USA

²Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio USA

³Department of Pediatrics, McGill University Health Centre, Montreal, Canada

⁴Department of Pediatrics, University of Alabama Birmingham, Birmingham, Alabama USA

⁵Department of Pediatrics, Emory University, Atlanta, Georgia USA

⁶Department of Pediatrics and Communicable Diseases, University of Michigan School of Medicine, Ann Arbor, Michigan USA

⁷Department of Pediatrics, The Heart Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio USA

Abstract

Objective—In a population of neonatal and pediatric patients on extracorporeal membrane oxygenation (ECMO); to describe the incidence and timing of acute kidney injury (AKI) utilizing a consensus AKI definition and investigate the association of AKI with outcomes (length of ECMO and mortality).

Design—Multicenter retrospective observational cohort study

Setting—Six pediatric ECMO centers

Patients—Pediatric patients (age <18 years) on ECMO at six centers during a period of January 1, 2007 to December 31, 2011.

Interventions—None

Measurements and Main Results—Complete data were analyzed for 832 patients on ECMO. Sixty percent of patients had AKI utilizing the serum creatinine KDIGO criteria (AKI^{SCr}) and

Corresponding Author: Geoffrey M. Fleming, 5112 DOT, 2200 Children's Way, Nashville, TN 37232, Geoffrey.fleming@vanderbilt.edu, Tel: (615) 936-1302.

Conflict of Interest: 1) The authors report no conflict of interest with funding support for RedCap

2) Dr Askenazi reports no conflict of interest with funding support as these sources were not used directly in the execution of this study.

74% had AKI using the using the full KDIGO criteria including renal support therapy (AKI^{SCr+RST}). Of those who developed AKI, it was present at ECMO initiation in a majority of cases (52% AKI^{SCr}) (65% AKI^{SCr+RST}) and present by 48 hours of ECMO support in 86% (AKI^{SCr}) and 93% (AKI^{SCr+RST}). When adjusted for patient age, center of support, mode of support, patient complications and pre-ECMO pH, the presence of AKI by either criteria was associated with a significantly longer duration of ECMO support (AKI^{SCr} 152 vs 110 hours, AKI^{SCr+RST} 153 vs 99 hours) and increased adjusted-odds of mortality at hospital discharge (AKI^{SCr} OR 1.77, 1.22 – 2.55, AKI^{SCr+RST} OR 2.50, 1.61 – 3.90). With the addition of RST to the model, AKI was associated with a longer duration of ECMO support (AKI^{SCr} 149 vs 121 hours) and increased risk of mortality at hospital discharge (AKI^{SCr} OR 1.52, 1.04 – 2.21).

Conclusion—AKI is present in 60-74% of neonatal-pediatric patients supported on ECMO and is present by 48 hours of ECMO support in 86-93% of cases. AKI has a significant association with increased duration of ECMO support and increased adjusted odds of mortality at hospital discharge.

Keywords

ECMO; Acute Kidney Injury; Acute Renal Failure; Renal Dialysis

Introduction

Extracorporeal membrane oxygenation (ECMO) provides short-term support for patients with refractory cardiac or pulmonary failure. Acute Kidney Injury (AKI) in the critically ill population has been repeatedly demonstrated to be associated with adverse outcomes[1-11]. Children treated with ECMO who develop AKI are at increased risk for adverse outcomes with mortality rates ranging from 47-100% with a graded increase by stage of AKI [12-26].

The Extracorporeal Life Support Organization (ELSO) collects outcome data for patients supported by ECMO [27]. The definition of “renal complication” or AKI used by the registry includes the need for renal support therapy (RST) or a threshold serum creatinine (SCr) > 1.5 mg/dL [27]. The published proportion of neonatal AKI from the registry ranges from 10% to 22% using SCr data [15, 28-30]. The most recent ELSO International Data Summary suggests the proportion of neonatal and pediatric AKI ranges from 1.3% -13% using a SCr definition, rising to 20%-43% when RST is included [27].

The Kidney Disease Improving Global Outcomes (KDIGO)[31] consensus definition utilizes a staged severity classification referenced to change from baseline function or the need for RST to characterize the severity of AKI. These criteria have been shown to predict morbidity and mortality in a stepwise fashion in critically ill children and are suggested to be the standard definition [9, 32]. Utilizing older consensus definitions, the single center incidence of AKI in ECMO has been reported to be as high as 72%, with the highest incidence in those infants and neonates with congenital cardiac disease and those with congenital diaphragmatic hernia [25, 26, 33]. The incidence of AKI in single center studies of pediatric ECMO patients has been reported to be as high as 58% in broader pediatric populations [20, 22, 34]. To date there has not been a large multicenter study evaluating the KDIGO AKI definition in a broad neonatal and pediatric ECMO population.

The current study is a systematic evaluation of ECMO data from six centers with three specific aims: (1) describe the incidence and timing of AKI utilizing the KDIGO AKI definition, (2) evaluate the impact of the inclusion of RST in the definition on the proportion of patients with AKI, and (3) investigate the association of AKI with outcomes (length of ECMO and mortality) in a multicenter pediatric ECMO population. We hypothesized that AKI defined by the KDIGO AKI criteria would be more prevalent than previously reported and be associated with increased length of ECMO support and mortality.

Methods

Study Design

Study design is a retrospective observational cohort study of all pediatric patients (age <18 years) on ECMO at six centers from January 1, 2007 to December 31, 2011. Investigational Review Board (IRB) approval for data collection and study was obtained and maintained at each individual participating center.

Data Sources

Data sources for this study included the ELSO Registry (ELSO, Ann Arbor Michigan) and data from individual study sites. Individual study sites collected data retrospectively from medical charts and electronic medical records for data not included in the ELSO database, which was entered into a REDCap™ [35] database. The final data set for the cohort was created by merging data utilizing a 4 point matching scheme (ELSO ID, date of birth, date ECMO initiation, and date ECMO discontinuation).

Cohort

Inclusion criteria were all patients < 18 years of age at the time of ECMO initiation at the participating institutions during the study period. Patients with multiple runs of ECMO, defined as two ECMO support events > 24 hours apart, were excluded from analysis due to the potential co-linearity of AKI developed during the initial run which may have affected the need for a second ECMO run and/or ultimate survival outcome. Patients with fewer than 4 variable field matching at data merge were excluded from analysis.

Data Collection

Data collected included age at ECMO initiation, weight at hospital admission, gender, and center of ECMO support were collected. Age was categorized as neonates (0 to 30 days) and pediatric (31 days to 18 years). Pre-ECMO variables included serum pH, need for vasoactive medication, and oxygenation index (OI). ECMO variables collected included indication for ECMO, Support Mode (veno-venous (VV) or veno-arterial (VA)) with sub-classification of VA if any component of the cannulation included an arterial cannula (VAV, VVA etc.), duration of ECMO, and number of non-renal complications. Date of ECMO initiation and decannulation were used to calculate duration of ECMO, as time difference in hours between ECMO initiation date-time stamp and the date-time stamp for decannulation. Renal specific variables included serum creatinine at baseline, lowest SCr from hospitalization to ECMO initiation, SCr at ECMO initiation, first recorded value daily for the first 21 days of ECMO, and at RST initiation. Baseline serum creatinine was defined as the lowest recorded

value in the chart for up to 90 days prior to ECMO initiation. RST included intermittent hemodialysis, peritoneal dialysis, continuous renal replacement therapy or slow continuous hemofiltration. Date of RST initiation and discontinuation were collected.

Definition of AKI

AKI was assessed at three time points: Pre-ECMO, ECMO initiation to 48 hours, > 48 hours on ECMO. AKI was defined using both the serum creatinine criteria (AKI^{SCr}) of the KDIGO definition[31] OR the addition of renal support therapy (AKI^{SCr+RST}) as follows:

- Stage 0: Increase SCr < 0.3mg/dL from baseline **AND** SCr < 1.5 times baseline
- Stage 1: (0.3 mg/dL increase SCr from baseline < 4mg/dL **AND** SCr < 1.5 times baseline) **OR** (increase SCr < 4mg/dL from baseline **AND** SCr 1.5 times baseline **AND** SCr < 2.0 times baseline)
- Stage 2: Increase SCr < 4 mg/dL from baseline **AND** SCr 2.0 times baseline **AND** SCr < 3.0 times baseline)
- Stage 3: Increase SCr 4 mg/dL from baseline **OR** SCr 3.0 times baseline **OR** need for Renal Support Therapy (AKI^{SCr+RST})

A patient was categorized for AKI using serum creatinine in the AKI^{SCr} cohort and by the need for RST in the AKI^{SCr+RST} cohort with a concomitant automatic classification of Stage 3 disease.

AKI in the neonatal cohort was adjudicated by two members of the research team with expertise in Pediatric Nephrology and AKI (DJA, MZ); any discrepancy was reviewed with a third team member team (DTS). This was done due to difficulties establishing a baseline SCr in the neonatal population [36]. The adjudication used the following step-wise criteria based on local expert opinion to define the baseline SCr: 1) lowest SCr prior to maximum SCr, 2) lowest SCr during hospitalization including those measured after maximum SCr, and 3) normative published values for age.

Outcomes

Outcomes included ECMO duration, mortality at ECMO decannulation and mortality at hospital discharge. Mortality at ECMO decannulation was defined as death within 24 hours post-decannulation. Mortality by hospital discharge included mortality at ECMO decannulation as well as survival through the ECMO decannulation period but death by hospital discharge.

Statistical Analysis

Data was summarized for entire cohort and by status and stages of AKI defined by AKI^{SCr} and AKI^{SCr+RST} criteria. Continuous variables were presented as median and inter-quartile range (IQR) and Wilcoxon rank-sum was used to test for differences between the groups (AKI vs. no-AKI) and Kruskal-Wallis test for differences between the stages of AKI. Categorical variables were presented as frequency counts and percentages, and differences between the groups were tested using Chi-square/Fisher's exact test. Overall incidence of AKI, by the two definitions, was examined at ECMO initiation, 48hours of ECMO, and > 48 hours of ECMO by mode of ECMO and ECMO support type. Univariate linear regression models were developed to identify potential factors associated with ECMO duration, after log-transformation of ECMO duration due to positive skewness. Least square (LS) means of the log transformed data and 95% confidence intervals (CI) for the LS mean

were back-transformed resulting in an estimate of the median (95% CI) on the original measurement scale. Significant factors from univariate analysis were then entered into a multivariable analysis to evaluate the association between AKI/no-AKI with ECMO duration. Mode of ECMO support and pH were considered to be important covariates in multivariable analyses. Although renal support therapy (yes/no) had a significant effect in univariate analysis it was included only in the multivariable model examining the effect of AKI^{SCr} due to its inclusion in the definition of AKI^{SCr+RST}. Although reported in demographic data, oxygenation index (OI) was not examined as a covariate due to significant amount of missing data. Association between AKI/no-AKI and mortality at ECMO decannulation (yes versus no) and between AKI/no-AKI and mortality at hospital discharge (yes versus no) was examined using univariate and multivariable logistic regression analysis with and without RST adjustment, as applicable. Results were presented as odds ratio (OR) and 95% CI. All analyses were two-sided and p-value 0.05 was considered statistically significant. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used to conduct all analyses.

Results

Study population

During the study period 1,009 patients underwent ECMO, and complete data were analyzed for 832 patients (Figure 1). The majority of patients were neonates (60%), had a pulmonary indication for ECMO support (56%) with the most common mode of support being veno-arterial (73%) [Table 1]. The severity of illness in the cohort was substantial with a pre-ECMO oxygenation index median (IQR) of 45 (28-67), pH 7.2 (7.1-7.3) and 86% requiring vasoactive support. Nearly 89% of patients had a non-renal complication as tracked in the ELSO registry and had a median (IQR) of 143 (75-260) hours on ECMO. Renal support therapy was provided in 48% (401/828) of the cohort of whom 97% (389/401) received RST during ECMO and 3% (12/401) prior to ECMO. Of those receiving RST, 23% was delivered via CRRT machine and 73% via inline hemodiafilter [Table 1].

Acute Kidney Injury Incidence and Demographics

Using the AKI^{SCr} definition, 502 (60%) patients had AKI (169/502 (34%) stage 1, 164/502 (33%) stage 2 and 169/502 (34%) stage 3 disease). Table 2 contains patient and ECMO variables associated with AKI. Patients with AKI^{SCr} were significantly older with greater body weight. Severity of illness pre-ECMO was not significantly different between the groups as measured by pH and the need for vasoactive support. Patients with AKI^{SCr} were more likely to require ECMO support for cardiac or ECPR indications, have more complications, receive ECMO for a longer duration and receive RST. There was no association between pre-ECMO severity of illness measures (pH, vasoactive medication) and worsening stage of AKI^{SCr}. Patient and ECMO variables associated with AKI^{SC} by stage of disease are presented in Supplemental Digital Content 1.

Using the AKI^{SCr+RST} definition 615 (74%) patients had AKI (89/615 (14%) stage 1, 65/615 (11%) stage 2 and 461/615 (75%) stage 3 disease). Table 2 contains patient and ECMO variables associated with AKI. Patients with AKI^{SCr+RST} were significantly older

and had greater body weight than the group with no AKI. Severity of illness pre-ECMO was not significantly different between the groups as measured by the need for vasoactive support and not clinically different as measured by pH. Patient and ECMO variables associated with AKI^{SCr+RST} by stage of disease are presented in Supplemental Digital Content 2.

Timing of Acute Kidney Injury

The cross-sectional incidence of AKI at ECMO initiation in the pediatric cohort ranged from 50% (AKI^{SCr}) to 62% (AKI^{SCr+RST}), 66% to 82% at 48 hours and 77% to 88% at > 48 hours. New episodes of AKI occurred between initiation and 48 hours of ECMO in 16% (AKI^{SCr}) and 20% (AKI^{SCr+RST}) of cases, and 11% (AKI^{SCr}) and 6% (AKI^{SCr+RST}) at > 48 hours. Timing of acute kidney injury varied by stage and ECMO support indication or ECMO mode for both definitions in the pediatric cohort (Table 3a, 3b). Timing of AKI analysis was not undertaken for the neonatal cohort due to the adjudication process in the definition of AKI and the need to use post-ECMO creatinine as the baseline comparative level.

Association of AKI with ECMO Outcomes

The overall median (IQR) duration of ECMO was 143 (74,260) hours for the cohort. Duration of ECMO support was significantly longer in patients with AKI regardless of the definition used. In those with AKI^{SCr} the median duration of ECMO was 141.5 hours (95% CI 129.3 - 154.9) vs. 115.4 (95% CI 103.1 - 129.2) [p=0.006] for those without AKI. In patients with AKI^{SCr+RST} the median duration was 137.8 hours (126.9 - 149.6) vs. 111.3 (96.6 - 128.2) [p=0.01] in those without AKI. Univariate analysis for the association of AKI and non-AKI variables with duration of ECMO are presented in Table 4.

Death occurred for 44% (368/830) of the total cohort by hospital discharge, of whom 27% (225/830) died at ECMO decannulation, and 17% (143/830) survived ECMO decannulation but died by hospital discharge. Unadjusted mortality at decannulation and mortality by hospital discharge were significantly increased in patients with AKI regardless of the definition used. The unadjusted OR (95% CI) for mortality at decannulation as compared to no AKI was 1.75 (1.26 - 2.43) for AKI^{SCr} and 2.55 (1.68 - 3.88) for AKI^{SCr+RST}. The unadjusted OR (95% CI) for mortality by hospital discharge as compared to no AKI was 2.14 (1.60 - 2.86) for AKI^{SCr} and 3.07 (2.16 - 4.36) for AKI^{SCr+RST}. RST had a significant effect on mortality at both decannulation 2.21(1.61 – 3.02) and discharge 2.79(2.10 – 3.71). Univariate analysis of AKI and non-AKI variables for the association with mortality at decannulation and by hospital discharge are presented in Table 5.

In multivariable analyses, the association of AKI with outcomes was evaluated, adjusting for age, center of support, mode of support, non-renal complications, and pre-ECMO pH. In addition, presence of RST was modelled for AKI^{SCr} analysis. The presence of AKI by AKI^{SCr} and AKI^{SCr+RST} criteria showed association with duration of ECMO, even when adjusted for covariates. (Table 6) Using AKI^{SCr+RST} criteria the odds for mortality at decannulation with AKI was 1.9 times higher [OR 1.92 (1.15 - 3.23), p=0.01] than those without AKI. The presence of AKI using either definition significantly increased the odds of

mortality by hospital discharge [OR 1.77 (1.22-2.55), $p=0.002$] for AKI^{SCr} and [OR 2.50 (1.61-3.90), $p<0.0001$] for AKI^{SCr+RST}, compared to no AKI. These results did not change after further adjustment for RST when examining AKI^{SCr}.

Discussion

This study systematically evaluates the KDIGO AKI definition in a broad multicenter cohort of pediatric ECMO patients. There are three important findings from this study. First, the incidence of AKI in the neonatal and pediatric ECMO population is high and affects a majority of ECMO patients with incidence ranging from 60 to 74 % depending on the definition used. Second, AKI occurs early in the ECMO course of the pediatric patient, with the majority of those with AKI identified at ECMO initiation and 93% of those identified with AKI by 48 hours. Third, the presence of AKI is associated with a longer duration of ECMO and increased mortality both at ECMO decannulation and by hospital discharge.

The evolution of consensus criteria for the clinical definition of AKI has affected reported incidence in many pediatric scenarios. The previously used “one size fits all” threshold creatinine level definition does not account for age related variables, nor the prior organ function of an individual patient. In prior data collection by ELSO, AKI was identified as a serum creatinine 1.5 mg/dL or the need for RST. For the pediatric and neonatal population, this definition under estimates AKI, as significant injury may occur and the SCr remain below the threshold of 1.5 mg/dL. The 2015 ELSO International Summary reports an incidence of 1.3-11% in using serum creatinine, and 21-43% by the need for RST.[27] In the current study, the KDIGO AKI^{SCr} definition identified 60% of the cohort as having renal dysfunction and the addition of RST to the definition increased the incidence to 74%. AKI severity was significant, stage 2-3 in 86% of cases for the entire cohort and 91% of non-neonatal pediatric cases identified by both definitions across the three time periods studied.

The use of RST as a defining condition of AKI in the KDIGO criteria must be tempered with the knowledge that it is a physician derived variable rather than patient derived variable and there was no standard indication across centers to trigger initiation of therapy. As a result we systematically evaluated the contribution of RST to the incidence and outcomes by evaluating the incidence of AKI with and without RST as part of the Stage 3 definition. A number of patients previously classified as stage 0 moved to stage 3 with the addition of RST to the definition and the incidence of AKI increased from 60 to 74%, with no appreciable impact on outcomes. This may be reflective of differences in practice patterns about RST utilization in children on ECMO previously reported by our group based on survey data and will be the subject of future studies [37]. RST was noted to have an effect on both duration of ECMO and survival in unadjusted analysis, but when added to the multivariable model for the effect of AKI, the results were similar to the model without RST. Further study will be required to understand the complex effect of RST on outcomes.

Limited prior data has been published beyond case reports on the timing of AKI during ECMO. Early neonatal respiratory studies identified an initial period of low urine output and fluid changes, but no data are collected in the ELSO registry to identify the timing of AKI [38]. In the current study, AKI developed early in the course of ECMO, with 51-64% of AKI

present at ECMO initiation and 86-93% of all cases of AKI identified by 48 hours. These data suggest that AKI risk factors are likely present prior to initiation of ECMO, rather than exposure to extracorporeal therapy. Pre-ECMO severity of illness measures (pH and need for Vasoactive agents) used in this study are convenience surrogate measures, but despite this limitation were not associated with the risk for AKI to allow for identification of specific risk variables. Some authors have suggested that the need for cardiac mechanical support and non-pulsatile flow may be associated with the development of AKI [39], yet reduced urine output and positive fluid balance have also been reported in the VV ECMO population, suggesting lack of pulsatility is not the only variable associated with AKI on ECMO [40].

In the current study, the presence of AKI was associated with a significantly increased duration of ECMO and reduced survival to hospital discharge after controlling for patient and support variables previously associated with these outcomes. This finding is consistent with previous reports in other critically ill pediatric populations [9, 10]. Acute kidney injury is associated with increasing severity of illness in most critically ill populations, yet it is unknown if its presence in the ECMO population is a marker of severity of illness or a driver of mortality. Prior studies have suggested that return to pre-ECMO dry weight is associated with separation from support in the neonatal population [12, 14, 38], hence renal dysfunction and subsequent fluid overload may be a direct contributor to the increase in duration of ECMO support seen in this study. Regardless of the etiology, the finding that AKI is associated with a longer ECMO course and increased mortality risk are important both for clinical practice as well as further study.

This study has limitations predominantly related to the data set used for analysis. The retrospective study design limits findings to association rather than causality. Data were not collected for the calculation of previously validated severity of illness adjustments for outcomes. The neonatal cohort are problematic in the definition of AKI due to the natural history of SCr in the immediate birth period. This known limitation in defining neonatal AKI likely leads to an imprecise identification of AKI in neonates. The adjudication of neonatal AKI requires identification of the baseline SCr, and utilization of the convalescent lowest SCr may potentially under-estimate AKI if this value were higher than published norms by age. This study was undertaken across 6 separate ECMO centers likely potentially with patients from varied socio-economic and ethnic backgrounds with no protocolized indication for ECMO or RST support, which will potentially affect outcomes. Although general ECMO and RST practices are similar among these centers, there was no protocol or equipment standardization leading to the potential for the introduction of bias into the study. Finally, the study centers may represent a practice bias toward the application of RST that would potentially affect the incidence of AKI^{SCr+RST}, but should not bias the incidence of AKI by serum creatinine measures only.

Conclusions

Utilizing the KDIGO AKI definitions we found a pediatric AKI incidence during ECMO higher than reported to date that allows for a more precise baseline understanding required to design intervention trials. The increase in reported incidence is valuable to the clinician as AKI onset is associated with adverse outcomes including longer duration of ECMO and

reduced survival to hospital discharge. AKI occurs early in the course of ECMO, with a majority of cases identified at ECMO initiation and 86-93% of AKI acquired by 48 hours of support. Additional studies should attempt to elucidate the potentially modifiable factors associated with the development of AKI both before and during ECMO. Further studies in this cohort will evaluate the contribution of fluid overload to outcomes and the practices around the modality and timing of RST initiation and its effect on outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Elaine Cooley (University of Michigan), Heart Institute Research Core (CCHMC)

Funding Support: 1) RedCap is supported: UL1 TR000445 from NACTS/NIH

2) Dr. Askenazi receives funding from the NIH (R01 DK13608-01) and the Pediatric and Infant Center for Acute Nephrology (PICAN), which is sponsored by Children's of Alabama and the University of Alabama at Birmingham (UAB) School of Medicine, as well as by the Department of Pediatrics, and Center for Clinical and Translational Science (CCTS) under award number UL1TR00165.

References

1. Bailey D, Phan V, Litalien C, et al. Risk factors of acute renal failure in critically ill children: A prospective descriptive epidemiological study. *Pediatr Crit Care Med*. 2007; 8:29–35. [PubMed: 17251879]
2. Chang JW, Tsai HL, Wang HH, et al. Outcome and risk factors for mortality in children with acute renal failure. *Clin Nephrol*. 2008; 70:485–489. [PubMed: 19049704]
3. D'Onofrio A, Cruz D, Bolgan I, et al. RIFLE criteria for cardiac surgery-associated acute kidney injury: risk factors and outcomes. *Congest Heart Fail*. 2010; 16(Suppl 1):S32–36. [PubMed: 20653709]
4. Lassnigg A, Schmid ER, Hiesmayr M, et al. Impact of minimal increases in serum creatinine on outcome in patients after cardiothoracic surgery: do we have to revise current definitions of acute renal failure? *Crit Care Med*. 2008; 36:1129–1137. [PubMed: 18379238]
5. Moghal NE, Brocklebank JT, Meadow SR. A review of acute renal failure in children: incidence, etiology and outcome. *Clin Nephrol*. 1998; 49:91–95. [PubMed: 9524778]
6. Uchino S, Bellomo R, Goldsmith D, et al. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med*. 2006; 34:1913–1917. [PubMed: 16715038]
7. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005; 294:813–818. [PubMed: 16106006]
8. Symons JM, Chua AN, Somers MJ, et al. Demographic characteristics of pediatric continuous renal replacement therapy: a report of the prospective pediatric continuous renal replacement therapy registry. *Clin J Am Soc Nephrol*. 2007; 2:732–738. [PubMed: 17699489]
9. Selewski DT, Cornell TT, Heung M, et al. Validation of the KDIGO acute kidney injury criteria in a pediatric critical care population. *Intensive care medicine*. 2014; 40:1481–1488. [PubMed: 25079008]
10. Alkandari O, Eddington KA, Hyder A, et al. Acute kidney injury is an independent risk factor for pediatric intensive care unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: a two-center retrospective cohort study. *Critical care*. 2011; 15:R146. [PubMed: 21663616]
11. Schneider J, Khemani R, Grushkin C, et al. Serum creatinine as stratified in the RIFLE score for acute kidney injury is associated with mortality and length of stay for children in the pediatric intensive care unit. *Crit Care Med*. 2010; 38:933–939. [PubMed: 20124891]

12. Adolph V, Heaton J, Steiner R, et al. Extracorporeal membrane oxygenation for nonneonatal respiratory failure. *Journal of pediatric surgery*. 1991; 26:326–332. [PubMed: 2030480]
13. Sell LL, Cullen ML, Whittlesey GC, et al. Experience with renal failure during extracorporeal membrane oxygenation: treatment with continuous hemofiltration. *Journal of pediatric surgery*. 1987; 22:600–602. [PubMed: 3649394]
14. Weber TR, Connors RH, Tracy TF Jr, et al. Prognostic determinants in extracorporeal membrane oxygenation for respiratory failure in newborns. *Ann Thorac Surg*. 1990; 50:720–723. [PubMed: 2241330]
15. Zwischenberger JB, Nguyen TT, Upp JR Jr, et al. Complications of neonatal extracorporeal membrane oxygenation. Collective experience from the Extracorporeal Life Support Organization. *J Thorac Cardiovasc Surg*. 1994; 107:838–849. [PubMed: 8127113]
16. Duncan BW, Hraska V, Jonas RA, et al. Mechanical circulatory support in children with cardiac disease. *J Thorac Cardiovasc Surg*. 1999; 117:529–542. [PubMed: 10047657]
17. Zahraa JN, Moler FW, Annich GM, et al. Venovenous versus venoarterial extracorporeal life support for pediatric respiratory failure: are there differences in survival and acute complications? *Crit Care Med*. 2000; 28:521–525. [PubMed: 10708194]
18. Meyer RJ, Brophy PD, Bunchman TE, et al. Survival and renal function in pediatric patients following extracorporeal life support with hemofiltration. *Pediatr Crit Care Med*. 2001; 2:238–242. [PubMed: 12793948]
19. Shaheen IS, Harvey B, Watson AR, et al. Continuous venovenous hemofiltration with or without extracorporeal membrane oxygenation in children. *Pediatr Crit Care Med*. 2007; 8:362–365. [PubMed: 17545928]
20. Hoover NG, Heard M, Reid C, et al. Enhanced fluid management with continuous venovenous hemofiltration in pediatric respiratory failure patients receiving extracorporeal membrane oxygenation support. *Intensive care medicine*. 2008; 34:2241–2247. [PubMed: 18629472]
21. Askenazi D. Acute Kidney Injury and Renal Replacement Therapy independently predict mortality in neonatal and pediatric noncardiac patients on extracorporeal membrane oxygenation. *Pediatric Critical Care Medicine*. 2011; 12:e1–6. [PubMed: 20351617]
22. Paden ML, Warshaw BL, Heard ML, et al. Recovery of renal function and survival after continuous renal replacement therapy during extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2010; 12:153–158.
23. Selewski DT, Cornell TT, Blatt NB, et al. Fluid overload and fluid removal in pediatric patients on extracorporeal membrane oxygenation requiring continuous renal replacement therapy. *Crit Care Med*. 2012; 40:2694–2699. [PubMed: 22743776]
24. Selewski DT, Cornell TT, Lombel RM, et al. Weight-based determination of fluid overload status and mortality in pediatric intensive care unit patients requiring continuous renal replacement therapy. *Intensive care medicine*. 2011; 37:1166–1173. [PubMed: 21533569]
25. Gadepalli SK, Selewski DT, Drongowski RA, et al. Acute kidney injury in congenital diaphragmatic hernia requiring extracorporeal life support: an insidious problem. *Journal of pediatric surgery*. 2011; 46:630–635. [PubMed: 21496529]
26. Zwiers AJ, de Wildt SN, Hop WC, et al. Acute kidney injury is a frequent complication in critically ill neonates receiving extracorporeal membrane oxygenation: a 14-year cohort study. *Critical care*. 2013; 17:R151. [PubMed: 23883698]
27. ELSO. ECLS Registry Report: International Summary. Extracorporeal Life Support Organization, Ann Arbor MI. 2015:1–26.
28. Haines NM, Rycus PT, Zwischenberger JB, et al. Extracorporeal Life Support Registry Report 2008: neonatal and pediatric cardiac cases. *Asaio J*. 2009; 55:111–116. [PubMed: 19092657]
29. Meyer DM, Jessen ME, Eberhart RC. Neonatal extracorporeal membrane oxygenation complicated by sepsis. Extracorporeal Life Support Organization. *Ann Thorac Surg*. 1995; 59:975–980. [PubMed: 7695427]
30. Rajagopal SK, Almond CS, Laussen PC, et al. Extracorporeal membrane oxygenation for the support of infants, children, and young adults with acute myocarditis: a review of the Extracorporeal Life Support Organization registry. *Crit Care Med*. 2010; 38:382–387. [PubMed: 19789437]

31. Acute Kidney Injury Work Group. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int*. 2012; 2:1–138.
32. Fortenberry JD, Paden ML, Goldstein SL. Acute kidney injury in children: an update on diagnosis and treatment. *Pediatric clinics of North America*. 2013; 60:669–688. [PubMed: 23639662]
33. Smith AH, Hardison DC, Worden CR, et al. Acute renal failure during extracorporeal support in the pediatric cardiac patient. *ASAIO J*. 2009; 55:412–416. [PubMed: 19381083]
34. Zwiers AJ, Cransberg K, de Rijke YB, et al. Urinary Neutrophil Gelatinase-Associated Lipocalin Predicts Renal Injury Following Extracorporeal Membrane Oxygenation. *Pediatr Crit Care Med*. 2015; 16:663–670. [PubMed: 26121099]
35. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009; 42:377–381. [PubMed: 18929686]
36. Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. *Current opinion in pediatrics*. 2012; 24:191–196. [PubMed: 22227783]
37. Fleming GM, Askenazi DJ, Bridges BC, et al. A multicenter international survey of renal supportive therapy during ECMO: the Kidney Intervention During Extracorporeal Membrane Oxygenation (KIDMO) group. *ASAIO J*. 2012; 58:407–414. [PubMed: 22588147]
38. Anderson H, Coran A, Drongowski R, et al. Extracellular fluid and total body water changes in neonates undergoing extracorporeal membrane oxygenation. *Journal of pediatric surgery*. 1992; 27:1003–1008. [PubMed: 1403525]
39. Adademir T, Ak K, Aljodi M, et al. The effects of pulsatile cardiopulmonary bypass on acute kidney injury. *Int J Artif Organs*. 2012; 35:511–519. [PubMed: 22466997]
40. Roy BJ, Cornish JD, Clark RH. Venovenous extracorporeal membrane oxygenation affects renal function. *Pediatrics*. 1995; 95:573–578. [PubMed: 7700761]

Figure 1. Flow diagram for study patients

Table 1
Patient and ECMO demographic data for the entire cohort, data presented as n (%)
unless otherwise specified

Variable	n	Data
Age, days (median, IQR)	832	9 (1 - 221.5)
Age category (%)	832	
Neonates		502 (60.3)
Pediatric		330 (39.7)
Gender (%)	827	
Males		487 (58.9)
Females		340 (41.1)
Admission weight (kg) Median IQR	830	3.6 (3 - 7)
Center (%)	832	
A		213 (25.6)
B		89 (10.7)
C		107 (12.9)
D		183 (22)
E		226 (27.2)
F		14 (1.7)
Pre-ECMO		
Oxygenation Index (OI) Median (IQR) *	542	45.4 (28.0 - 66.7)
pH Median (IQR)	766	7.2 (7.1 - 7.3)
Inotropes (% Y)	832	712 (85.6)
ECMO indication (%)	832	
Pulmonary		468 (56.3)
Cardiac		217 (26.1)
ECPR		147 (17.7)
ECMO Mode (%)	832	
VV		214 (25.7)
VA		608 (73.1)
Other		10 (1.2)
ELSO Non Renal Complication (% Y)	832	739 (88.8)
ECMO duration (hours) Median, IQR	832	143 (74.5 - 260)
Mortality (% Y)		
At ECMO Decannulation	830	225 (27.1)
By Hospital Discharge	830	368 (44.3)
RST Performed (%)	828	
Yes		401 (48.4)
No		427 (51.6)
RST Mode (%)	822	
CRRT		94 (11.4)
Inline Hemodiafilter		293 (35.6)

Variable	n	Data
Intermittent Hemodialysis		3 (0.4)
Peritoneal Dialysis		5 (0.6)
None		427 (51.6)
Timing of RST (%)	828	
None		427 (51.6)
During ECMO		389 (47)
Pre-ECMO		12 (1.5)

*
33% of data points for OI are missing

Table 2

Demographic data for patients by presence of AKI

	no-AKI ^{SCr}		AKI ^{SCr}		p	no-AKI ^{SCr+RST}		AKI ^{SCr+RST}		p
	(n=323)	(n=502)	(n=502)	(n=615)		(n=207)	(n=615)			
Age, days median (IQR)	2 (1 - 18)	31 (6 - 415)		20 (4 - 333)	<.0001	2 (1 - 9)				<.0001
Age category (%)					<.0001					<.0001
Neonates	247 (49.6)	251 (50.4)		328 (66.1)		168 (33.9)				
Pediatric	76 (23.2)	251 (76.7)		287 (88.0)		39 (12.0)				
Gender (%)					0.03					0.18
Males	205 (42.4)	278 (57.6)		351 (73.0)		130 (27.0)				
Females	117 (34.7)	220 (65.3)		259 (77.1)		77 (22.9)				
Missing =12										
Admission weight (kg) Median (IQR)	3.3 (2.9 - 4.3)	3.9 (3 - 9)		3.8 (3.0 - 8.4)	<.0001	3.3 (2.9 - 4.1)				<.0001
Center City (%)					<.0001					<.0001
A	45 (21.2)	167 (78.8)		177 (83.5)		35 (16.5)				
B	27 (31.0)	60 (69.0)		64 (75.3)		21 (24.7)				
C	72 (67.3)	35 (32.7)		41 (38.3)		66 (61.7)				
D	72 (40.2)	107 (59.8)		160 (89.4)		19 (10.6)				
E	103 (45.6)	123 (54.4)		161 (71.6)		64 (28.4)				
F	4 (28.6)	10 (71.4)		12 (85.7)		2 (14.3)				
Pre-ECMO										
pH Median(IQR)	7.2 (7.1 - 7.3)	7.2 (7.1 - 7.3)		7.2 (7.1 - 7.3)	0.40	7.2 (7.1 - 7.3)				0.05
Inotropes (% Y)	284 (87.9)	423 (84.3)		522 (84.9)	0.14	183 (88.4)				0.21
ECMO Indication (%)					<.0001					<.0001
Pulmonary	247 (52.9)	220 (47.1)		297 (64.0)		167 (36.0)				
Cardiac	50 (23.5)	163 (76.5)		187 (87.8)		26 (12.2)				
ECPR	26 (17.9)	119 (82.1)		131 (90.3)		14 (9.7)				
ECMO Mode (%)					<.0001					<.0001
VV	128 (60.1)	85 (39.9)		129 (61.1)		82 (38.9)				
VA	192 (31.9)	410 (68.1)		477 (79.4)		124 (20.6)				

	AKI ^{SCr}		AKI ^{SCr+RST}		p
	no-AKI ^{SCr} (n=323)	AKI ^{SCr} (n=502)	no-AKI ^{SCr+RST} (n=207)	AKI ^{SCr+RST} (n=615)	
Other					
ELSO Non Renal Complication (% Y)	3 (30)	7 (70)	1 (10)	9 (90)	
ECMO duration (hours) Median (IQR)	257 (79.6)	477 (95.0)	148 (71.5)	583 (94.8)	<.0001
Mortality (% Y)	122 (70 - 233)	162 (88 - 272)	120 (70 - 209)	156 (82 - 267)	0.0006
At ECMO Decannulation	66 (20.4)	155 (31.0)	31 (15.0)	190 (31.0)	<.0001
By Hospital Discharge	107 (33.1)	257 (51.4)	52 (25.1)	311 (50.7)	<.0001
RST performed (%)					
Yes	114 (28.4)	287 (71.6)	-	-	<.0001
No	207 (49.2)	214 (50.8)	-	-	
RST Mode (%)					
CRRT	21 (22.3)	73 (77.7)	0 (0)	94 (15.4)	<.0001
Inline Hemodiafilter	89 (30.4)	204 (69.6)	0 (0)	293 (48.1)	
Intermittent Hemodialysis	2 (66.7)	1 (33.3)	0 (0)	3 (0.5)	
Peritoneal Dialysis	1 (20.0)	4 (80.0)	0 (0)	5 (0.8)	
None	207 (49.2)	214 (50.8)	207 (100)	214 (35.1)	

Chi-square test/fisher's exact test used to test for difference in categorical variables between groups

Wilcoxon Rank Sum test used to test for difference in continuous variables between groups

Table 3a
Proportions of AKI by stage and ECMO support type in the pediatric cohort

		Stage 0	Stage 1	Stage 2	Stage 3
	n examined	n(%)	n(%)	n(%)	n(%)
All Support types (n=330)					
Pre-ECMO (at Init)					
AKI ^{SCr}	314	152 (48.4)	55 (17.5)	58 (18.5)	49 (15.6)
AKI ^{SCr+RST}	310	109 (35.2)	38 (12.3)	37 (11.9)	126 (40.7)
On-ECMO (48 Hr)					
AKI ^{SCr}	312	129 (41.4)	53 (17.0)	72 (23.1)	58 (18.6)
AKI ^{SCr+RST}	309	64 (20.7)	23 (7.4)	30 (9.7)	192 (62.1)
On-ECMO (> 48Hr)					
AKI ^{SCr}	248	83 (33.5)	46 (18.6)	56 (22.6)	63 (25.4)
AKI ^{SCr+RST}	245	31 (12.7)	20 (8.2)	18 (7.4)	176 (71.8)
Pulmonary (n=162)					
Pre-ECMO (at Init)					
AKI ^{SCr}	159	98 (61.6)	25 (15.7)	21 (13.2)	15 (9.4)
AKI ^{SCr+RST}	156	71 (45.5)	13 (8.3)	11 (7.1)	61 (39.1)
On-ECMO (48 Hr)					
AKI ^{SCr}	153	78 (51.0)	23 (15.0)	30 (19.6)	22 (14.4)
AKI ^{SCr+RST}	151	37 (24.5)	7 (4.6)	11 (7.3)	96 (63.6)
On-ECMO (> 48Hr)					
AKI ^{SCr}	135	48 (35.6)	21 (15.6)	30 (22.2)	36 (26.7)
AKI ^{SCr+RST}	133	18 (13.5)	10 (7.5)	7 (5.3)	98 (73.7)
Cardiac (n=94)					
Pre-ECMO (at Init)					
AKI ^{SCr}	88	32 (36.4)	18 (20.5)	22 (25.0)	16 (18.2)
AKI ^{SCr+RST}	88	23 (26.1)	16 (18.2)	16 (18.2)	33 (37.5)
On-ECMO (48 Hr)					
AKI ^{SCr}	92	30 (32.6)	21 (22.8)	23 (25.0)	18 (19.6)

	Stage 0	Stage 1	Stage 2	Stage 3
	n (%)	n (%)	n (%)	n (%)
AKI ^{SCr+RST}	92	15 (16.3)	11 (12.0)	55 (59.8)
On-ECMO (> 48Hr)				
AKI ^{SCr}	71	18 (25.4)	22 (31.0)	13 (18.3)
AKI ^{SCr+RST}	71	7 (9.9)	9 (12.7)	6 (8.5)
ECPR (n=74)				
Pre-ECMO (at Init)				
AKI ^{SCr}	67	22 (32.8)	12 (17.9)	15 (22.4)
AKI ^{SCr+RST}	66	15 (22.7)	9 (13.6)	10 (15.2)
On-ECMO (< 48 Hr)				
AKI ^{SCr}	67	21 (31.3)	9 (13.4)	19 (28.4)
AKI ^{SCr+RST}	66	12 (18.2)	5 (7.6)	8 (12.1)
On-ECMO (> 48Hr)				
AKI ^{SCr}	42	17 (40.5)	3 (7.1)	13 (31.0)
AKI ^{SCr+RST}	41	6 (14.6)	1 (2.4)	5 (12.2)

Table 3b
Proportions of AKI by stage and ECMO mode type in the pediatric cohort

	n examined	Stage 0	Stage 1	Stage 2	Stage 3
		n(%)	n(%)	n(%)	n(%)
Overall (n=330)					
Pre-ECMO (at Init)					
AKISCr	314	152 (48.4)	55 (17.5)	58 (18.5)	49 (15.6)
AKISCr+RST					
	310	109 (35.2)	38 (12.3)	37 (11.9)	126 (40.7)
On-ECMO (< 48 Hr)					
AKISCr	312	129 (41.4)	53 (17.0)	72 (23.1)	58 (18.6)
AKISCr+RST	309	64 (20.7)	23 (7.4)	30 (9.7)	192 (62.1)
On-ECMO (> 48Hr)					
AKISCr	248	83 (33.5)	46 (18.6)	56 (22.6)	63 (25.4)
AKISCr+RST	245	31 (12.7)	20 (8.2)	18 (7.4)	176 (71.8)
Venoarterial (n=239)					
Pre-ECMO (at Init)					
AKISCr	225	94 (41.8)	43 (19.1)	47 (20.9)	41 (18.2)
AKISCr+RST	222	69 (31.1)	32 (14.4)	31 (14)	90 (40.5)
On-ECMO (< 48 Hr)					
AKISCr	226	83 (36.7)	44 (19.5)	54 (23.9)	45 (19.9)
AKISCr+RST	224	45 (20.1)	21 (9.4)	25 (11.2)	133 (59.4)
On-ECMO (> 48Hr)					
AKISCr	170	55 (32.4)	35 (20.6)	34 (20.0)	46 (27.1)
AKISCr+RST	168	23 (13.7)	14 (8.3)	13 (7.7)	118 (70.2)
Venovenous (n=83)					
Pre-ECMO (at Init)					
AKISCr	81	53 (65.4)	11 (13.6)	9 (11.1)	8 (9.9)
AKISCr+RST	81	36 (44.4)	6 (7.4)	6 (7.4)	33 (40.7)
On-ECMO (< 48 Hr)					

	Stage 0	Stage 1	Stage 2	Stage 3
	n (%)	n (%)	n (%)	n (%)
AKISCr	78 41 (52.6)	9 (11.5)	15 (19.2)	13 (16.7)
AKISCr+RST	78 17 (21.8)	2 (2.6)	5 (6.4)	54 (69.2)
On-ECMO (> 48Hr)				
AKISCr	70 24 (34.3)	9 (12.9)	21 (30)	16 (22.9)
AKISCr+RST	70 7 (10.0)	5 (7.1)	5 (7.1)	53 (75.7)
Other modes (n=8)				
Pre-ECMO (at Init)				
AKISCr	8 5 (62.5)	1 (12.5)	2 (25)	0 (0)
AKISCr+RST	7 4 (57.1)	0 (0)	0 (0)	3 (42.9)
On-ECMO (48 Hr)				
AKISCr	8 5 (62.5)	0 (0)	3 (37.5)	0 (0)
AKISCr+RST	7 2 (28.6)	0 (0)	0 (0)	5 (71.4)
On-ECMO (> 48Hr)				
AKISCr	8 4 (50.0)	2 (25.0)	1 (12.5)	1 (12.5)
AKISCr+RST	7 1 (14.3)	1 (14.3)	0 (0)	5 (71.4)

Table 4
Univariate analysis examining study variables in relation to ECMO duration (hours)

Variable	Median (95% CI) [¶]	p
AKI ^{SCr}		0.006
AKI absent	115.4 (103.1 - 129.2)	
AKI present	141.5 (129.3 - 154.9)	
AKI ^{SCr+RST}		0.01
AKI absent	111.3 (96.6 - 128.2)	
AKI present	137.8 (126.9 - 149.6)	
Age		0.04
Neonatal	135.0 (122.7 - 148.4)	
Pediatric	115.6 (102.8 - 130.0)	
Patient Complications		0.05
Yes	130.2 (120.4 - 140.9)	
No	103.4 (82.9 - 129.0)	
ECMO Mode		0.10
VV	141.2 (122.1 - 163.4)	
VA	121.4 (111.4 - 132.4)	
other	194.1 (98.9 - 380.7)	
Center		<.0001
A	120.0 (104.3 - 138.1)	
B	135.3 (108.9 - 168.1)	
C	265.4 (217.8 - 323.5)	
D	88.3 (75.9 - 102.8)	
E	124.2 (108.4 - 142.4)	
F	114.8 (66.4 - 198.4)	
RST		<.0001
Yes	158.4 (142.8 - 175.8)	
No	103.9 (93.9 - 114.9)	
	Log β -estimate $\pm$ SE	
pH	0.208 $\pm$ 0.195	0.29

[¶]Median is based on back transforming the Least Square means and 95% CI

Table 5
Univariate analysis examining study-variables in relation to mortality

Variable	Mortality at ECMO decannulation		Mortality by hospital discharge	
	OR (95% CI)	p-value	OR (95% CI)	p-value
AKI ^{SCr}				
AKI absent	1		1	
AKI present	1.75 [1.26 - 2.43]	0.0009	2.14 [1.60 - 2.86]	<.0001
AKI ^{SCr+RST}				
AKI absent	1		1	
AKI present	2.55 [1.68 - 3.88]	<.0001	3.07 [2.16 - 4.36]	<.0001
Age				
Neonatal	1			
Pediatric	1.10 [0.81 - 1.50]	0.54	0.80 [0.60 - 1.06]	0.12
Patient Complications				
No	1			
Yes	5.16 [2.35 - 11.33]	<.0001	6.31 [3.38 - 11.76]	<.0001
ECMO Mode				
VA	1		1	
VV	0.22 [0.14 - 0.35]		0.21 [0.15 - 0.31]	
other	0.50 [0.11 - 2.38]	<.0001	0.22 [0.05 - 1.03]	<.0001
Center				
A	1.65 [1.06 - 2.57]		0.96 [0.66 - 1.41]	
B	1.98 [1.14 - 3.43]		2.27 [1.37 - 3.74]	
C	1.18 [0.67 - 2.06]		0.91 [0.57 - 1.47]	
D	1.91 [1.22 - 3.0]		1.81 [1.22 - 2.68]	
E	1		1	
F	3.02 [1.0 - 9.13]	0.02	3.92 [1.19 - 12.88]	<.0001
RST				
No	1		1	
Yes	2.21 [1.61 - 3.02]	<.0001	2.79 [2.10 - 3.71]	<.0001
pH	0.14 [0.06 - 0.34]	<.0001	0.29 [0.13 - 0.61]	0.001

Table 6
Multivariable analysis examining association between AKI and Outcomes

Variable	AKI ^{SCr}		AKI ^{SCr} +RST	
Model 1				
Duration of ECMO (hours)	Median (95%CI) [¶]	P	Median (95%CI) [¶]	p
AKI absent	110.0 (85.1-142.3)	<0.0001	98.5 (75.3-128.9)	<0.0001
AKI present	152.2 (118.3-195.9)		152.8 (119.1-196.2)	
Model 2				
Duration of ECMO (hours)	Median (95%CI) [¶]	P		
AKI absent	120.7 (93.9-155.0)	0.01	~	~
AKI present	149.2 (116.9-190.5)			
Model 1				
Mortality at ECMO decannulation	OR [CI]		OR [CI]	
AKI absent	1		1	
AKI present	1.19 [0.80-1.77]	0.40	1.92 [1.15 - 3.23]	0.01
Model 2				
Mortality at ECMO decannulation	OR [CI]			
AKI absent	1		~	~
AKI present	1.04 [0.69-1.56]	0.86		
Model 1				
Mortality by hospital discharge	OR [CI]		OR [CI]	
AKI absent	1		1	
AKI present	1.77 [1.22-2.55]	0.002	2.50 [1.61-3.90]	<0.0001
Model 2				
Mortality by hospital discharge	OR [CI]			
AKI absent	1		~	~
AKI present	1.52 [1.04-2.21]	0.03		

Model 1 – adjusted for age, center, mode, complications and pH

Model 2 – In addition to model 1 further adjusted for RST

[¶]Median is based on back transforming Least Square means and 95% CI values to the original scale