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Impact of Continuous Renal Replacement Therapy on Oxygenation in Children with Acute Lung Injury after Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract

Background—Acute lung injury (ALI) continues to carry a high mortality rate in children after allogeneic hematopoietic stem cell transplant (HSCT). Continuous renal replacement therapy (CRRT) is often used for these patients for various indications including renal failure and fluid overload, and may have a beneficial effect on oxygenation and survival. Therefore, we sought to determine the effect of CRRT on oxygenation in mechanically ventilated pediatric allogeneic HSCT patients with ALI, and to document survival to intensive care unit discharge in this at-risk population receiving both mechanical ventilation and CRRT.

Procedure—Retrospective analysis of a pediatric allogeneic HSCT cohort admitted to intensive care unit of a single pediatric oncology center from 1994 to 2006 who received CRRT during a course of mechanical ventilation for ALI.

Results—Thirty post-HSCT mechanically ventilated children with ALI who underwent CRRT were included. There was a significant improvement in PaO_2/FiO_2 with median increase of 31 and 43 in the 24 and 48 hour intervals after initiation of CRRT compared with the 24 hour interval before CRRT (p = 0.0008 and 0.0062, respectively). This improvement in PaO_2/FiO_2 correlated significantly with reduction of fluid balance achieved after initiation of CRRT (p=0.0001). There was a trend not reaching statistical significance in improvement in mean airway pressure 48 hours after CRRT in survivors compared to non-survivors.

Conclusions—CRRT improved oxygenation in mechanically ventilated pediatric allogeneic HSCT patients with ALI.

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Keywords

Hematopoietic stem cell transplantation; Critically ill; Acute lung injury; Pediatrics; Renal replacement therapy; Oxygenation

Introduction

Acute lung injury (ALI) is characterized by acute lung inflammation with alveolar leukocyte infiltration and protein-rich pulmonary edema, resulting in acute respiratory failure [1, 2]. Although mortality associated with ALI has declined with implementation of protective lung strategies such as use of lower tidal volume and plateau pressure, it is still considerably high in the pediatric population [3–5]. Mechanically ventilated pediatric HSCT patients continue to have higher risk of mortality [6] that may be attributed to conditioning with irradiation, prior chemotherapy, and/or inherent immune dysregulation associated with the transplant process. Among pediatric HSCT patients admitted to the intensive care unit (ICU), Lamas et al. reported a mortality rate of 76.5% in those requiring mechanical ventilation [7]. Therefore, this at-risk population represents a specific opportunity for outcome improvement. DiCarlo et al. [8] suggested that one form of continuous renal replacement therapy (CRRT), continuous veno-venous hemofiltration (CVVH), may improve survival from acute respiratory distress syndrome after pediatric bone marrow transplantation (BMT) or chemotherapy. However, other groups have noted consistently poor survival in pediatric HSCT patients requiring both mechanical ventilation and dialysis [9–11].

In most instances at our institution, as well as others [12], CRRT is initiated for control of fluid balance or support of renal failure and/or electrolyte disarray. Maintaining fluid balance is challenging in HSCT patients because they often require intense medication support, and fluid overload may occur even in the context of adequate urine output because of necessarily excessive fluid intake. Multi-organ dysfunction is associated with high mortality in pediatric HSCT patients [6,7] and, therefore, measures aimed at reducing fluid overload and/or improving oxygenation may be helpful in this setting [13]. The question of whether CRRT improves oxygenation remains controversial. Some reports have indicated that CRRT improves oxygenation in patients with acute renal failure and respiratory failure [14–16], while others have failed to show similar improvement [17]. Thus, the objectives of our study were to determine the effect of CRRT on oxygenation in mechanically ventilated pediatric allogeneic HSCT patients with ALI, and to document survival to ICU discharge in this at-risk population receiving both mechanical ventilation and renal replacement therapy. We also sought to document potential complications related to the initiation of CRRT.

Materials and Methods

Patients

Patients in this study were admitted to the ICU at St. Jude Children's Research Hospital, a tertiary-care pediatric oncology center, with ALI requiring mechanical ventilation and subsequently requiring CRRT. Study patients were identified by screening an ICU admission database followed by review of individual patient charts. Inclusion criteria were: 1) age, newborn to 19 years; 2) admission to the ICU between 1994 and 2006; 3) allogeneic HSCT; 4) diagnosis of ALI according to the American-European Consensus Conference (acute onset, $PaO_2/FiO_2 < 300$, and bilateral pulmonary infiltrates on chest radiography without evidence of left atrial hypertension) [1]; 5) need for mechanical ventilation; 6) initiation of CRRT. Patients who underwent continuous arterio-venous hemofiltration (CAVH) were excluded.

Methods

Data collection—After approval by the St. Jude institutional review board, which waived the need for informed consent, the following data were extracted from the ICU and transplant databases and from patient medical records: demographic variables, oncologic diagnosis, transplant data including conditioning chemotherapy, acute graft versus host disease (aGVHD) prophylaxis, the grade of aGVHD if it occurred, use of adjunctive therapies for ALI (such as inhaled nitric oxide), ICU length of stay (LOS), survival to ICU discharge, duration of mechanical ventilation (MV), and duration of CRRT. Fluid balance was defined as: [fluid in]-[fluid out] (in ml). The percentage of fluid overload (FO) was calculated based on the formula described by Goldstein: % FO= {[Fluid in]−[Fluid out](in liters)/[admission weight](in kilograms)}×100 for the 24 hrs before and 24 and 48 after initiation of CRRT [18]. The following variable data were collected at 6 hour intervals from 24 hours before, to 48 hours after initiation of CRRT: arterial blood gas results, ventilator settings including FiO_2, peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), tidal volume, and mean airway pressure (MAP), and laboratory values for blood urea nitrogen (BUN), creatinine, and C-reactive protein (CRP). Hemodynamic variables including heart rate and blood pressure were also recorded, as well as the administration of vasopressors.

CRRT in these mechanically ventilated patients was initiated secondary to acute renal failure or fluid overload unresponsive to intermittent dosing or continuous infusion of diuretics. CRRT was performed with a flow-controlled blood roller pump machine. Polyacrylonitrile filters were primarily used until 2006, when they were replaced with polysulfone filters. The blood pump flow rate was usually 2–5 ml/kg/min. Dialysate fluid rate was calculated using the following formula: (2000 ml/h × BSA)/1.73 m^2. Anticoagulation was achieved with a heparin protocol until 2002 when it was replaced by a citrate protocol. Fluid removal rate was determined by the ICU physician depending on the clinical condition and fluid status of the patient.

Statistical analysis—The baseline value for each variable 24 hours before CRRT was calculated by averaging the measurements at 24, 18, 12, and 6 hours prior to starting CRRT. The value for each variable 24 hours after CRRT was calculated by averaging the measurements at 6, 12, 18, and 24 hours after onset of CRRT. The value for each variable 48 hours after CRRT was calculated by averaging the measurements at 30, 36, 42, and 48 hours after onset of CRRT. Changes of each variable were calculated based on paired data in each patient from baseline (24 hours prior) to 24 and 48 hours after onset of CRRT. The signed-rank test (univariate procedure, SAS v 9.1.3, SAS Institute Inc., Cary, NC, USA) was applied to determine whether the median change was 0 for each measurement in the study cohort. Significance was set at a p value < 0.05. A general linear mixed model was applied to test the association of PaO_2/FiO_2 and fluid balance/wt. The compound symmetry covariance was applied to take patient intra correlation into account. In this model, PaO_2/FiO_2 was considered as the dependent variable and fluid balance/wt as the independent variable. Mean CRP levels were compared by applying 2 sample t-test. Based on a previous study demonstrating the advantage of < 10% FO on survival, FO was analyzed as a categorical variable of equal or greater than 10% and was compared between survivors and non-survivors using Fisher's exact test [19]. Potential associations between various clinical variables and survival were assessed using the Wilcoxon-rank sum test.

Results

Between 1994 and 2006, fifty-two pediatric allogeneic HSCT patients underwent CRRT in the ICU. Of the 52 patients who underwent CRRT, 30 had ALI and were receiving mechanical ventilation at the time of initiating CRRT, meeting inclusion criteria.

Patient characteristics

Table I lists the characteristics of the study population. Nineteen (63%) were male; median age was 11 years (range 0.5–18.5). Most common oncologic diagnosis was AML (37%), and 13% received allogeneic HSCT for non-oncologic diagnosis. Most common conditioning chemotherapy regimen was cyclophosphamide and cytarabine and antithymocyte immunoglobulin in 23% of the patients. Prophylaxis for GVHD was achieved most commonly with cyclosporine (23%), or with cyclosporine and cellcept (17%), or with cyclosporine and cellcept and methotrexate combination (17%). Seven patients (23%) had aGVHD GIII-IV. Twenty-six (87%) patients underwent continuous veno-venous hemodialysis (CVVHD), whereas 4 (13%) had CVVH. The median duration of MV was 21 days (range, 3–105 days); the median duration of CRRT was 15 days (range, 1–60 days). The median duration of MV before initiation of CRRT therapy was 3 days (range, 0–50 days). The median length of stay in the ICU was 28 days (range, 3–117 days). Five (17%) patients in this cohort survived to ICU discharge. Median % fluid overload (FO) 24 hours before initiation of CRRT was 3.6% (range −11.6–+16%). One survivor out of 5 versus 4/25 non-survivors had % FO >10%.

Effect of initiation of CRRT on oxygenation

Using baseline values 24 hours prior to onset of CRRT, median changes in respiratory, ventilator, hemodynamic and laboratory data for 24 hours and 48 hours after onset of CRRT are shown in Tables II and III respectively. PaO_2/FiO_2 improved significantly after the start of CRRT. There was a significant median change of PaO_2/FiO_2 of 30.51 (range, −37.08 to 140.98) from 24 hours before to 24 hours after the start of CRRT ($p = 0.0008$; Table II). This change persisted for 48 hours after the start of CRRT with a median change of 43 (range, −88.61 to 264.91; $p = 0.0062$; Table III).

Effect of CRRT on ventilator settings and laboratory values

The median BUN and creatinine dropped significantly after CRRT (Table II and III). FiO_2 dropped significantly 48 hours after initiation of CRRT (Table II and III). There was no significant change in the mean CRP level 2 days prior to CRRT compared to the mean CRP level at 48 hours after initiation of CRRT (11.9 ± 9.4 pre-CRRT compared to 6.4 ± 5.5 after CRRT, $p = 0.13$).

Effect of CRRT on fluid balance

The median fluid balance/wt every 6 hours dropped from a net positive of 8.03 mL/kg 24 hours before the start of CRRT (range, −29.2 to +57 mL/kg) to a net negative of 6.87 mL/kg 24 hours after (range, −47.1 to + 2.16mL/kg) and net negative of 4.9 mL/kg 48 hours after initiation of CRRT (range, −89.3 to +25.73 mL/kg). These fluid balance changes were significant, with a median change of −14.74 mL/kg 24 hours after (range, −90.94 to +5.31 ml/kg; $p < 0.0001$) and −12.47 mL/kg 48 hours after initiation of CRRT (range, −121.96 to +30.14 mL/kg; $p < 0.0001$; Tables II and III). There was significant negative association between PaO_2/FiO_2 and fluid balance/wt ($p = 0.0001$), and therefore, negative fluid balance was associated with significant improvement in the PaO_2/FiO_2.

Comparison between survivors and non-survivors

Table IV depicts the comparison of the different clinical variables between survivors and non-survivors. There was no significant difference in % FO at baseline between survivors and non-survivors (0.7, range −11.6–+16, and 4.1, range −1.6–+13, in survivors and non-survivors respectively, p=0.14). CRRT was initiated at <10% FO in the majority of our patients with no significant effect on survival (4/21 non-survivors had %FO>10% versus 1/5 survivors with %FO>10%, p=1). There was a trend of improvement in mean airway pressure at 48 hours after initiation of CRRT when comparing survivors and non-survivors (13, range 8–20 versus 17, range 9–37 in survivors and non-survivors respectively, p=0.099).

Complications after CRRT

Thirteen of the 30 patients required vasopressor support before initiation of CRRT and continued to require this support during CRRT. Six of these 13 patients required increased vasopressor support during the first 48 hours of CRRT, while 4 required less vasopressor support and 3 required no change in vasopressor infusion. Four patients required vasopressors at the time of initiating CRRT, although two of these patients were off vasopressors by hour 18 after starting CRRT. Three patients required vasopressor support at different time intervals after CRRT (at hour 6, hour 12, and hour 24). None of the patients died at initiation of CRRT. Mean arterial blood pressure had no significant median change when comparing 24 hours before start of CRRT to 24 and 48 hours after start of CRRT (Tables II and III). Heart rate significantly improved with CRRT, with a median change of −11.5 (−65–+11.75) and −9 (−61.75–+32.5) at 24 and 48 hours post CRRT respectively.

Discussion

Our data demonstrate that CRRT was associated with improvement of oxygenation in mechanically ventilated pediatric HSCT patients with ALI. As a parameter indicating severity of lung injury, we show that the PaO_2/FiO_2 ratio significantly improved 24 and 48 hours after the initiation of CRRT. Furthermore, CRRT was efficient in fluid removal and resulted in net negative median change in fluid balance of 6.87 mL/kg at 24 hours and an additional 4.9 mL/kg 48 hours after initiation of CRRT compared to the 24 hours preceding the onset of CRRT.

The effect of CRRT on ALI has been controversial. DiCarlo et al. [8] reported improved survival when CVVH was used in pediatric patients with acute respiratory distress syndrome (ARDS) after BMT or chemotherapy. However, the study involved only 10 patients in whom CVVH was initiated 24 hours after the start of mechanical ventilation, regardless of fluid balance and renal function. Eight patients were successfully extubated and survived, but it is not clear whether their survival was causally related to use of CVVH. Several small studies in the 1990s showed benefits of continuous arteriovenous hemofiltration on oxygenation in adult patients with respiratory failure [14–16]. In a larger study involving 37 adult patients, Hoste et al. [17] found no benefit from continuous venovenous hemodiafiltration (CVVHDF) on oxygenation in adult patients with acute renal failure and ALI. From their observations, the PaO_2/FiO_2 ratio 24 hours after initiation of CVVHDF did not change compared with that of the 24-hour period before CVVHDF [17]. However, it is important to note that this study aimed at zero fluid balance, and thus precluded distinct evaluation of the potentially beneficial effect of CRRT on fluid removal.

Managing fluid balance is particularly challenging in allogeneic HSCT patients. On one hand, many of these patients manifest some degree of systemic inflammatory response syndrome (SIRS) after transplantation which may be triggered by conditioning with total

body irradiation and/or chemotherapy. Some patients develop capillary leak syndrome shortly after transplantation, resulting in pulmonary edema that is unresponsive to diuretic therapy and may lead to deterioration of respiratory status [21]. On the other hand, the necessary post-transplant nutritional support and medical regimen frequently requires that HSCT patients receive higher than normal fluid intake. In this setting, even normally adequate urine output of greater than 2 ml/kg/hour becomes insufficient to prevent fluid overload. Therefore, in our experience, some patients undergo CRRT for management of fluid overload even if they have not exhibited signs of renal failure. This practice is similar to that of other institutions and is consistent with a recent report from the prospective pediatric CRRT registry group on patients with stem cell transplantation [12]. According to this registry, the primary reason for initiating CRRT was fluid overload in 39% of the cases.

There is increasing evidence that the percent of fluid overload before starting CRRT also affects survival. In critically ill children who received CVVH, Foland et al. [20] found survivors to have a significantly lower percentage of fluid overload before starting CVVH compared with non-survivors. Goldstein et al. [13] suggested a significant improvement in survival when CRRT was initiated with less than 20% cumulative fluid overload in patients with multi-organ system failure. Similarly, in pediatric stem cell transplant patients with acute renal failure, survivors had significantly <10% fluid overload compared to non-survivors [19]. In our cohort, only 5 patients had %FO>10% and none had >20%. This may explain why there % FO was not significantly different between survivors and non-survivors since CRRT was initiated at earlier stages and is consistent with the recent report from the prospective CRRT registry group on CRRT after stem cell transplantation [12]. In the present study, our patients had a median fluid balance/wt of positive 8.03 mL/kg on the day before initiating CRRT, and significant fluid removal was achieved at 24 and 48 hours after starting CRRT correlating directly with improvement in the PaO_2/FiO_2 ratio. However, this improvement in oxygenation didn't translate to improved survival as there was no significant difference in the fluid balance/weight between survivors and non-survivors after 24 and 48 hours after initiating CRRT. There was a trend of significant improvement in mean airway pressure at 48 hours after CRRT in survivors compared to non-survivors. This trend may have gained more significance as time moved forward beyond the 48 hours after initiation of CRRT. The prospective CRRT registry group have shown that mean airway pressure was significantly less at the end of CRRT therapy in survivors versus non-survivors after stem cell transplantation; however, the days of CRRT therapy varied from one day to 52 days and thus a longer interval was used in that study to assess the effect of mean airway pressure on survival [12].

Mechanisms other than fluid overload have been considered in an attempt to explain the beneficial effect of CRRT on ALI. Some believe that CVVH is beneficial in removing inflammatory cytokines that contribute to the pathophysiology of ALI [8]. In porcine [22] and canine [2] models, investigators have found that hemofiltration results in improvement in oxygenation and lung mechanics. Although there is an early reduction in cytokine levels after initiation of conventional hemofiltration in human studies, these levels return to baseline within hours, a pattern which may be related to initial adsorption of cytokines onto the membrane which then becomes saturated [23,24]. High volume hemofiltration at rates ≥35ml/kg/min has been efficient in cytokine removal and appears to improve outcome in adult patients with refractory septic shock [25]. However, this technique is associated with practical difficulties including machinery, cost, and accurate safety monitoring systems. It is possible that the observed benefit of CRRT on oxygenation in our cohort may have resulted in part from an attenuated inflammatory response, however, mean CRP levels did not change significantly in the 48 hours following CRRT initiation. In addition, the majority (87%) of our patients underwent the diffusive modality of CVVHD, which is less effective

in clearing medium sized inflammatory molecules [12], therefore, we suspect that effective fluid removal was the primary beneficial effect of CRRT on oxygenation.

Recent reports indicate that survival ranges from zero to 13% in post-HSCT pediatric patients who require both mechanical ventilation and dialysis [9–11]. Although our retrospective, single-institution data span a twelve-year period, and they include patients with acute lung injury, we observed an encouraging 17% rate of survival to ICU discharge. Whether this survival rate can improve further with other modalities of CRRT such as CVVHDF is not fully known. The prospective pediatric CRRT registry group reported a better survival rate in stem cell pediatric patients who underwent convective therapies (CVVH or CVVHDF) as compared with those who received diffusive therapy (CVVHD) [12].

This study has several limitations. First, it is a retrospective, single center report with the inherent limitations of retrospective case series, including the potential for selection bias. However, all mechanically ventilated patients who received CRRT during the study period were screened to determine if study inclusion criteria were met, and the study inclusion criteria were relatively strict and straightforward. Secondly, the primary end-point for assessing changes in oxygenation, the PaO_2/FiO_2 ratio, is a relatively crude measure. However, it is a simple and well-accepted measure of the severity of lung injury in the critical care literature and is included in internationally accepted definitions of acute lung injury and ARDS. Third, the study spans a 12 year period during which there were changes in strategies of mechanical ventilation with the introduction of protective lung strategy and weaning protocol that were not present in the earlier years of the study before 2000. Finally, while it is prudent and important to determine what factors influenced survival, the small number of 5 survivors in our study makes it hard to draw solid conclusions about these factors.

We report here the largest series of CRRT in the context of pediatric acute lung injury after allogeneic HSCT. We demonstrate that CRRT is associated with improvement in oxygenation 24 and 48 hours after its initiation in mechanically ventilated post-HSCT children. However, it is unknown whether this effect on oxygenation is sustained for the long term, or whether it would positively affect survival. Our data suggest that the beneficial effect of CRRT is likely due to efficient management of fluid balance, although favorable clearance of inflammatory mediators was not assessed. To more definitively evaluate these possibilities, large multi-institutional studies are now needed to make further recommendations as to the optimal use of CRRT in this high risk population.

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Table I

Characteristics of study patients

***n* = 30**	**Number**	**Percent of total**
Demographics		
Sex (male/female)	19/11	63.3/36.7
Median Age (yr)	11 (range 0.5–18.5)	
Disease		
AML	11	37
ALL	7	23
CML/JCML	4	13
Neuroblastoma	2	7
NHL	1	3
Histiocytosis	1	3
Non malignant	4	13
aGVHD GIII-IV	7	23
NO	11	33
ICU survivors	5	16.7
	Median	**Range**
Clinical data		
CRRT (days)	15	1–60
Intubation to CRRT (days)	3	0–50
Duration of MV (days)	21	3–105
ICU LOS (days)	28	3–117
BUN at start of CRRT (mg/dl)	79	32–102
Cr at start of CRRT (mg/dl)	1	0–4
PaO_2/FiO_2 24 hours pre-CRRT	156	78–293
% FO 24 hours pre-CRRT	3.6	−12—+16
Baseline Ventilator settings		
PIP(cm H_20)	32	24–54
PEEP(cm H_20)	9	5–18
Paw(cm H_20)	19	13–34
FiO_2	0.46	0.3–0.8

AML, acute myelocytic leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myelogenous leukemia; JCML, juvenile chronic myelogenous leukemia; NHL, non-hodgkin lymphoma; aGVHD, acute graft versus host disease; NO, inhaled nitric oxide; ICU, intensive care unit; CRRT, continuous renal replacement therapy; MV, mechanical ventilation; ICU LOS, intensive care unit length of stay; BUN, blood urea nitrogen; Cr, creatinine; FO, fluid overload; PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure; Paw, mean airway pressure;. FiO_2, fraction of inspired oxygen.

Table II

Median change in respiratory, ventilator, hemodynamic, and laboratory values 24 hours before and 24 hours after CRRT

Measurement	n[1]	Median Change	Range	p[2]
$PaCO_2$ (torr)	30	+ 0.40	(−38.13 to +12.71)	0.74
PaO_2 (torr)	30	+8.62	(−19.25 to +73.00)	0.0373
PaO_2/FiO_2	30	+30.51	(−37.08 to +140.98)	0.0008
FiO_2	30	−0.01	(−0.21 to +0.15)	0.25
PIP (cm H_20)	25	−1.75	(−13.00 to +10.25)	0.19
PEEP (cm H_20)	25	+0.25	(−7.00 to +6.00)	0.75
Paw(cm H_20)	29	0.00	(−7.25 to +10.25)	0.51
Fluid balance/wt (mL/kg)	29	−14.74	(−90.94 to +5.31)	<0.0001
Mean BP (mmHg)	30	+1.42	(−28.50 to +19.00)	0.43
Heart Rate	30	−11.50	(−65.00 to +11.75)	<0.0001
BUN (mg/dl)	29	−8.75	(−66.50 to +24.00)	0.0085
Creatinine (mg/dl)	29	−0.22	(−1.23 to +0.45)	0.0002
HCO_3 (mmole/l)	30	+1.22	(−8.02 to +60.43)	0.17
pH	30	+0.04	(−0.12 to +0.20)	0.0333

[1] Number of patients with available data;

[2] *p* value from signed rank test.

CRRT, continuous renal replacement therapy; pts, patients; $PaCO_2$, carbon dioxide pressure; PaO_2, oxygen pressure; FiO_2, fraction of inspired oxygen; PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure; Paw, mean airway pressure; BP, blood pressure; BUN, blood urea nitrogen.

Table III

Median change in respiratory, ventilator, hemodynamic, and laboratory values 24 hours before and 48 hours after CRRT

Measurement	n[1]	Median Change	Range	p[2]
$PaCO_2$ (torr)	29	+0.77	(−37.05 to +83.25)	0.49
PaO_2 (torr)	29	+ 0.97	(−29.83 to +54.00)	0.08
PaO_2/FiO_2	29	+ 43.00	(−88.61 to +264.91)	0.0062
FiO_2	29	−0.05	(−0.33 to +0.28)	0.0495
PIP (cm H_20)	25	−1.50	(−17.50 to +15.50)	0.09
PEEP (cm H_20)	25	0.00	(−8.00 to +7.75)	0.60
Paw (cm H_20)	28	−0.75	(−7.53 to +16.25)	0.50
Fluid balance/wt (mL/kg)	29	−12.47	(−121.96 to +30.14)	<0.0001
Mean BP (mmHg)	29	−4.25	(−26.67 to +81.75)	0.63
Heart Rate	29	−9.00	(−61.75 to +32.50)	0.0126
BUN (mg/dl)	29	−10.33	(−109.25 to +23.25)	0.0001
Creatinine (mg/dl)	29	−0.35	(−1.25 to +14.70)	0.0002
HCO_3 (mmole/l)	29	+ 0.38	(−7.61 to +19.87)	0.27
pH	29	+0.01	(−1.36 to +0.23)	0.70

[1] Number of patients with available data;

[2] *p* value from signed rank test.

CRRT, continuous renal replacement therapy; pts, patients; $PaCO_2$, carbon dioxide pressure; PaO_2, oxygen pressure; FiO_2, fraction of inspired oxygen PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure; Paw, mean airway pressure; BP, blood pressure; BUN, blood urea nitrogen.

Table IV

Clinical variables and survival

		Median (Range)		
Variable	**Time Point**	**Survivors (5)**	**Non-survivors (21)**	***P***
Mean airway pressure(cm H_20)	Pre 24 hours	18.75 (13.00–27.60)	18.13 (12.50–33.50)	0.841
	Post 24 hours	14.50 (13.50–21.40)	18.75 (11.15–33.00)	0.231
	Post 48 hours	13.00 (8.50–20.08)	17.42 (9.00–37.00)	0.099
Fluid Balance/weight (ml/kg)	Pre 24 hours	−1.73 (−29.20—+40.24)	10.24 (−1.96–+57.00)	0.089
	Post 24 hours	−0.17 (−47.06—+ 0.89)	−6.90 (−34.88—+ 2.16)	0.411
	Post 48 hours	−1.03 (−4.90—+ 3.75)	−6.21 (−89.34—+ 25.73)	0.205
Age at ICU admission (yr)		15.48 (1.56–17.16)	9.64 (0.52–18.77)	0.475
Weight at ICU admission (kg)		54.00 (13.00–72.00)	32.00 (7.00–76.00)	0.201
%Fluid overload		0.70 (−11.60–16.00)	4.10 (−1.60–13.00)	0.139