Prognostics factors for mortality and renal recovery in critically ill patients with acute kidney injury and renal replacement therapy

ORIGINAL ARTICLE

INTRODUCTION

The incidence of acute kidney injury (AKI) has increased considerably over the last two decades, particularly among inpatients.1-3 Currently, approximately 20% of critically ill patients experience at least one episode of AKI,4-6 of whom requiring renal replacement therapy.5 The mortality rate of critically ill patients receiving renal replacement therapy because of AKI remains high, reaching approximately 50% cases, despite the growing understanding of the pathophysiology of AKI, the development of renal replacement therapy methods, the optimization of fluid resuscitation, and the choice of amine therapy.6 Incomplete renal function recovery is also common5 and has a significant effect on morbidity and mortality rates, quality of life, and healthcare costs.7

ABSTRACT

Objective: Identify prognostic factors related to mortality and non-recovery of renal function.

Methods: A prospective single-center study was conducted at the intensive care medicine department of a university hospital between 2012 and 2015. Patients with acute kidney injury receiving continuous renal replacement therapy were included in the study. Clinical and analytical parameters were collected, and the reasons for initiation and discontinuation of renal replacement therapy were examined.

Results: A total of 41 patients were included in the study, of whom 43.9% had sepsis. The median Simplified Acute Physiology Score II (SAPSII) was 56 and the mortality was 53.7%, with a predicted mortality of 59.8%. The etiology of acute kidney injury was often multifactorial (56.1%). Survivors had lower cumulative fluid balance (median = 3,600mL, interquartile range [IQR] = 1,175 - 8,025) than non-survivors (median = 12,000mL, IQR = 6,625 - 17,875; p = 0.004). Patients who recovered renal function (median = 51.0, IQR = 45.8 - 56.2) had lower SAPS II than those who do not recover renal function (median = 73, IQR = 54 - 85; p = 0.005) as well as lower fluid balance (median = 3,850, IQR = 1,425 - 8,025 versus median = 11,500, IQR = 6,625 - 16,275; p = 0.004).

Conclusions: SAPS II at admission and cumulative fluid balance during renal support therapy were risk factors for mortality and non-recovery of renal function among critically ill patients with acute kidney injury needing renal replacement therapy.

Keywords: Acute kidney injury; Renal insufficiency; Insufficiency renal, chronic; Renal replacement therapy; Intensive care

Conflicts of interest: None.

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The prevalence of incomplete renal function recovery varies considerably across the studies published in the scientific literature.\(^6,8\) One possible explanation for this variation refers to the absence of a clear definition of renal function “recovery”. Consequently, different definitions are used, and different prevalence rates are reported in turn. However, the possibility that certain therapeutic strategies, including the choice of renal replacement therapy, its start time, or the anticoagulant used, interfere with renal function recovery cannot be excluded.

The present study aimed to identify the prognostic factors related to mortality or renal function non-recovery in critically ill patients with AKI and renal replacement therapy.

**METHODS**

A prospective single-center study was conducted in an intensive care unit (ICU) of a university hospital between 2012 and 2015. The Ethics Committee of Centro Hospitalar Sáo João approved this study, and all participants or their family members signed an informed consent document. To be included in this study, the patients were between 18 and 90 years old, diagnosed with AKI, and were on continuous renal replacement therapy. The reasons for renal replacement therapy initiation were identified in a predefined multiple-choice table featuring items such as electrolyte disturbance, metabolic disorder, hypervolemia, oliguria/anuria, increased urea/creatinine, sepsis, and other, in which more than one option could be checked. The intensive care physicians made the decision to initiate continuous renal replacement therapy according to the standard of care practice, usually after considering the existence of hemodynamic instability requiring amine therapy, liver failure, or severe brain injury. The AKI classification stage was recorded using the Risk, Injury, Failure, Loss, and End-stage (RIFLE)\(^9\) criteria when renal replacement therapy was initiated. During the renal replacement therapy, patients were able to switch to intermittent renal replacement therapy according to the usual practices of the unit, usually after considering the absence of hemodynamic instability requiring amine therapy, liver failure, or severe brain injury.

The etiology of AKI was recorded based on the following options: sepsis, cardiogenic shock, hypovolemia, drug-induced nephrotoxicity, major surgery, use of contrast, obstructive uropathy, or other. More than one option could be selected. Patients were monitored based on the standard of care practice. Systolic and diastolic blood pressure, central venous pressure, urine output, use of diuretics, fluid balance, type of ventilation, use of amines, creatinine, urea, potassium, pH, and lactate were recorded from the initiation of renal replacement therapy to two days after its discontinuation. Records concerning the prescription of renal replacement therapy, including the type, dose and anticoagulant used were also performed.

The two major reasons justifying the discontinuation of renal replacement therapy were selected from a predefined multiple-choice table that included increased diuresis, improved metabolic/electrolyte status, improved hypervolemia, lowered urea/creatinine, hemodynamic stability, and other. The date of renal replacement therapy discontinuation was recorded, and its duration was calculated. The patient was allowed to receive continuous or intermittent therapy prior to discontinuation. The follow-up assessment of the patient was recorded at the ICU as well as another hospital department in the event that the patient had been transferred. We classified AKI non-recovery as: death during renal support therapy; death on RIFLE-F after discontinuation of renal replacement therapy; survivor continuing on renal replacement therapy; and survivor without renal replacement therapy but persistent RIFLE-F on hospital discharge. Acute kidney injury recovery was defined as a survivor without need for renal replacement therapy and without persistent RIFLE-F at hospital discharge. Non-survivors who died after renal replacement therapy and without RIFLE-F were also recorded as AKI recovery.

The continuous variables are expressed as percentages, medians, and interquartile ranges (IQR). Inter-group analyses were performed using the chi-square test and the Mann-Whitney U test, where appropriate IBM Statistical Package for Social Science, version 20, was used for all analyses, and a 0.05 significance threshold was applied.

**RESULTS**

The sample characteristics are outlined in table 1. Over two-thirds of the 41 patients had at least one comorbidity (i.e., high blood pressure, diabetes mellitus, heart failure, or cirrhosis). Eighteen patients (43.9%) had septic shock, and most of cases were related to medical disorders (73.2%). The median Simplified Acute Physiology Score II (SAPS II) was 56 (50 - 77), with a predicted mortality of 59.8%. Baseline creatinine was 1.0mg/dL (0.8 - 1.4), and the glomerular filtration rate estimated using the Modification of Diet in Renal Disease (MDRD) was 71mL/min (44 - 93), with 36.6% of patients showing glomerular filtration rates less than 60mL/min. The cumulative fluid balance during renal replacement therapy was 7,910mL.
Table 1 - General data

| General data                  | General data |
|-------------------------------|--------------|
| Number of patients           | 41           |
| Age (years)                  | 67 [54 - 77] |
| Men                           | 28 [68.3]    |
| SAPS II                      | 56 [50 - 77] |
| Comorbidities                |              |
| High blood pressure          | 19 [46.3]    |
| Heart failure                | 9 [22]       |
| Diabetes mellitus            | 16 [39]      |
| Cirrhosis                    | 5 [12.2]     |
| Absent                       | 12 [29.3]    |
| Type of admission            |              |
| Medical                      | 30 [73.2]    |
| Unscheduled surgery          | 11 [26.8]    |
| Baseline creatinine (mg/dL)  | 1.0 [0.8 - 1.4] |
| Glomerular filtration rate, MDRD (mL/min) | 71 [44 - 93] |
| Etiology of AKI              |              |
| Sepsis                       | 18 [43.9]    |
| Cardiorenal type I           | 9 [22]       |
| Hypovolemia                  | 9 [22]       |
| Pharmaceutical drugs         | 6 [14.6]     |
| Major surgery                | 7 [17.1]     |
| Contrast                     | 10 [24.4]    |
| Urinary obstruction          | 1 [2.4]      |
| Other                        | 10 [24.4]    |
| Mechanical ventilation       | 37 [90.2]    |
| Amine therapy                | 41 [100]     |
| T0 creatinine (mg/dL)        | 2.8 (1.9 - 3.7) |
| T0 urea (mg/dL)              | 135 (88 - 159) |
| T0 lactate (mmol/L)          | 3.1 (1.6 - 4.75) |
| T0 pH                        | 7.3 (7.24 - 7.38) |
| T0 hemoglobin (g/dL)         | 11.1 (9.4 - 12.1) |
| T0 PaO2/FiO2                 | 203 (140 - 235) |
| T0 albumin (g/L)             | 24 (19 - 26)  |
| T0 central venous pressure (mmHg) | 12 (10 - 14) |
| Reason for initiating renal replacement therapy | 17 [41.5] |
| Reason for discontinuing renal replacement therapy (among survivors) | 19 [46.3] |

SAPS II - Simplified Acute Physiology Score II; MDRD - Modification of Diet in Renal Disease; T0 - initiation of renal replacement therapy; PaO2/FiO2 - partial pressure of oxygen/fraction of inspired oxygen ratio; RIFLE - Risk, Injury, Failure, Loss, End Stage. Results are expressed as medians (IQR) or rates (%).

The etiology of AKI was often multifactorial (56.1%), although sepsis was the predominant cause. All patients received amine therapy, and most received invasive mechanical ventilation at the initiation of renal replacement therapy (90.2%).

Approximately 61% of patients were admitted directly to the ICU, and the days of hospitalizations before ICU admission was 0 (0.0 - 4.0). The time between hospital admission and the initiation of renal replacement therapy was 2 days (0.5 - 7.5), and the time between admission to the ICU and the initiation of renal replacement therapy was 1 day (0 - 2). Continuous veno-venous hemofiltration was chosen to initiate renal replacement therapy for 87.8% of all cases, and continuous veno-venous hemodiafiltration was chose for 12.2% of all cases. In most cases, the prescription sought to ensure an effective dose of 20 - 25mL/kg/hour, except in cases of continuous veno-venous hemodiafiltration, given the temporary need for a high renal replacement therapy dose in the context of significant metabolic or electrolyte alterations, usually switching to continuous veno-venous hemofiltration during treatment. Twenty patients (48.8%) initiated renal replacement therapy without anticoagulation because of coagulation disorder, 15 (36.6%) were anticoagulated with heparin, and six (14.6%) received regional citrate anticoagulation. The solution buffer bicarbonate was exclusively used when regional citrate anticoagulation was not used. Seventeen patients (41.5%) died during renal replacement therapy. The median number of days on renal replacement therapy was 4.5 (1.2 - 7.8).

The length of hospital stay at the ICU was nine days (4 - 17.5). The ICU and hospital mortality rates were 48.8% and 53.7%, respectively.

No significant differences were observed between patients who survived and those who died in the ICU with regard to age, urea, creatinine at initiation of renal replacement therapy, SAPS II, and baseline variables.
Table 2 - Comparison between survivors and non-survivors in the intensive care unit

|                        | ICU survivors (N = 21) | ICU deceased (N = 20) | p-value |
|------------------------|------------------------|-----------------------|---------|
| Age (years)            | 64.0 (54.0 - 82.0)     | 67.5 (53.7 - 74.5)    | 0.651   |
| Creatinine at admission (mg/dL) | 1.0 (0.8 - 1.5)     | 1.0 (0.9 - 1.3)       | 0.860   |
| Glomerular filtration rate, MDRD (mL/min) | 68.0 (44.0 - 99.0) | 71.5 (46.5 - 89.8) | 0.938   |
| T0 urea (mg/dL)        | 133 (82 - 149)        | 137 (89 - 168)        | 0.885   |
| T0 creatinine (mg/dL)  | 2.9 (2.3 - 4.7)       | 2.1 (1.9 - 3.4)       | 0.420   |
| T0 systolic blood pressure (mmHg) | 93 (91 - 102)      | 95 (88 - 100)         | 0.885   |
| T0 diastolic blood pressure (mmHg) | 47 (41 - 51)       | 47 (43 - 53)          | 0.885   |
| T0 central venous pressure (mmHg) | 13 (10 - 14)       | 11.5 (9.3 - 14.8)     | 0.630   |
| T0 albumin (g/L)       | 24 (21 - 27)          | 22 (17.3 - 25.8)      | 0.403   |
| T0 lactate (mmol/L)    | 2.2 (1.5 - 4.8)       | 3.7 (2.0 - 4.8)       | 0.086   |
| T0 Hb (g/dL)           | 11.1 (9.2 - 12.6)     | 10.7 (9.4 - 11.9)     | 0.885   |
| T0 pH                   | 7.31 (7.2 - 7.4)      | 7.29 (7.23 - 7.37)    | 0.873   |
| RIFLE                  |                        |                       |         |
| R                      | 3 (14.3)               | 2 (10.0)              | 0.890   |
| I                      | 8 (38.1)               | 9 (45.0)              |         |
| F                      | 10 (47.6)              | 9 (45.0)              |         |
| T0 PaO2/FiO2 ratio     | 210 (160 - 280)        | 192 (95 - 225)        | 0.425   |
| Pre-ICU days           | 0 (0.0 - 1.0)          | 2.5 (0.0 - 9.75)      | 0.084   |
| ICU stay (days)        | 14 (7.5 - 20.0)        | 5.5 (2.3 - 13.0)      | 0.158   |
| Cumulative fluid balance (mL) | 3600 (1175 - 8025)    | 12000 (6625 - 17875)  | 0.004   |
| ICU/Initiation of renal replacement therapy | 1 (0.0 - 2.0)       | 1.0 (0.0 - 1.0)       | 0.541   |
| Hospital admission/Initiation of renal replacement therapy | 1 (0.0 - 4.5)       | 3.5 (1.0 - 13.3)      | 0.276   |
| SAPS II                | 51 (46 - 57)           | 77 (58 - 84)          | 0.005   |
| Congestive heart failure | 6                      | 3                     | 0.454   |
| Cirrhosis              | 0                      | 5                     | 0.014   |

ICU - intensive care unit; MDRD - modification of diet in renal disease; T0 - initiation of renal replacement therapy; Hb - hemoglobin; RIFLE - Risk, Injury, Failure, Loss, End Stage; PaO2/FiO2 - partial pressure of oxygen/fraction of inspired oxygen ratio; SAPS II - Simplified Acute Physiology Score II. Results are expressed as medians (IQR) or rates (%).

replacement therapy, creatinine at admission, glomerular filtration rate, serum albumin, hemoglobin, pH, PaO2/FiO2 ratio, need for amine therapy, number of days between hospital admission and initiation of renal replacement therapy, and number of days between ICU admission and initiation of renal replacement therapy (Table 2).

Although survivors showed a lower level of lactacidemia (2.2mmol/L [1.5 - 4.8] versus 3.7mmol/L [2.0 - 4.8]) and briefer hospital stays prior to admission to the ICU (zero days [0 - 1] versus 2.5 days [0 - 9.75]) than non-survivors, these results were not significant (p = 0.086 and p = 0.084, respectively).

Survivors showed lower SAPS II (51 [46 - 57] versus 77 [58-84]; p = 0.005) and lower cumulative fluid balance (3,600mL [1,175 - 8,025] versus 12,000mL [6,625 - 17,875]; p = 0.004) than the deceased. These differences were significant.

No differences were observed in age, creatinine at hospital admission, urea, creatinine, glomerular filtration rate, serum albumin, hemoglobin, pH, PaO2/FiO2 ratio at initiation of renal replacement therapy, need for amine therapy, and number of days between ICU admission and initiation of renal replacement therapy (Table 3).

Although patients with recovered renal function had fewer days between hospital admission and renal replacement therapy initiation as well as between hospital admission and ICU admission, these results were not significant (p = 0.158 and p = 0.14, respectively; Table 3).

The presence of cirrhosis was a risk factor for renal function non-recovery (p = 0.02). Patients with recovered renal function had lower SAPS II (51.0 [45.8 - 56.2] versus 73 [54 - 85]; p = 0.005) and lower cumulative fluid balance (3,850mL [1,425 - 8,025] versus 11,500mL [6,625 - 16,275]; p = 0.004) than those without recovered renal function (Table 3).
Table 3 - Comparison between patients with recovered renal function and those without recovered renal function

|                        | Recovered (N = 20) | Non-recovered (N = 21) | p-value |
|------------------------|--------------------|------------------------|---------|
| Age (years)            | 62.0 (51.8 - 79.8) | 67 (56.4 - 75.5)       | 0.860   |
| Creatinine at admission (mg/dL) | 1.0 (0.8 - 1.4)   | 1.0 (0.8 - 1.4)        | 0.860   |
| Glomerular filtration rate, MDRD (mL/min) | 69.5 (46.0 - 99.5) | 72.0 (42.5 - 89.5)     | 0.835   |
| T0 urea (mg/dL)        | 134 (78.5 - 146.0) | 140 (90 - 166)         | 0.630   |
| T0 creatinine (mg/dL)  | 2.8 (2.2 - 5.0)    | 2.1 (1.8 - 3.4)        | 0.650   |
| T0 Systolic blood pressure (mmHg) | 93 (91.5 - 103.2) | 97 (89 - 100)          | 0.630   |
| T0 Diastolic blood pressure (mmHg) | 48.5 (42 - 54.2)  | 45 (42 - 50.0)         | 0.162   |
| T0 Central venous pressure (mmHg) | 12.5 (10.2 - 14.0) | 12 (9.0 - 14.5)       | 0.885   |
| T0 albumin (g/L)       | 24.5 (20.0 - 27.0) | 24 (18.5 - 25.5)       | 0.278   |
| T0 lactate (mmol/L)    | 2.5 (1.6 - 5.6)    | 3.5 (1.7 - 4.8)        | 0.873   |
| T0 Hb (g/dL)           | 11.3 (10.2 - 12.4) | 10.2 (8.6 - 12.0)      | 0.440   |
| T0 pH                  | 7.32 (7.18 - 7.38) | 7.29 (7.24 - 7.38)     | 0.642   |
| RIFLE                  |                    |                        |         |
| R                     | 3 (15.0)           | 2 (9.5)                | 0.406   |
| I                     | 9 (45.0)           | 8 (38.1)               |         |
| F                     | 8 (40.0)           | 11 (52.4)              |         |
| T0 PaO2/FiO2 ratio     | 210 (160 - 280)    | 200 (95 - 225)         | 0.425   |
| Pre-ICU days           | 0 (0 - 1.5)        | 2 (0.0 - 9.5)          | 0.140   |
| ICU stay days          | 15 (8 - 25)        | 5 (2.5 - 12.5)         | 0.086   |
| Cumulative fluid balance (mL) | 3850 (1425 - 8025) | 11500 (6625 - 16275)   | 0.004   |
| ICU/initiation of renal replacement therapy | 1.0 (0.0 - 2.0)   | 1.0 (0.0 - 1.5)        | 0.925   |
| Hospital admission/initiation of renal replacement therapy | 1.0 (0.0 - 4.0)   | 4.0 (1.0 - 15.0)       | 0.158   |
| SAPS II                | 51 (45.8 - 56.2)   | 73 (54 - 84)           | 0.005   |
| Congestive heart failure | 4                   | 5                      | 0.77    |
| Cirrhosis              | 0                   | 5                      | 0.020   |

MDRD - modification of diet in renal disease; T0 - initiation of renal replacement therapy; Hb - hemoglobin; RIFLE - Risk, Injury, Failure, Loss, End Stage; PaO2/FiO2 - partial pressure of oxygen/fraction of inspired oxygen ratio; ICU - intensive care unit; SAPS II - Simplified Acute Physiology Score II. Results are expressed as medians (IQR) or rates (%).

**DISCUSSION**

SAPS II at admission, liver cirrhosis, and cumulative fluid balance during renal replacement therapy are risk factors for mortality and renal function non-recovery among critically ill patients with AKI needing renal replacement therapy.

The creatinine levels of our sample at ICU admission was 1.0mg/dL, which was slightly lower than that of other published studies. However, when the estimated glomerular filtration rate is included, the distribution of our results are identical to previous studies, such that 36.6% of our sample showed a glomerular filtration rate less than 60mL/min.

The creatinine and serum urea levels prior to renal replacement therapy were 2.8mg/dL and 135mg/dL, respectively, which are similar to those of other studies. However, the early renal replacement therapy initiation differs because more than 50% of the patients were in the R or I stages of the RIFLE criteria. Likewise, the number of days between hospital admission and the initiation of renal replacement therapy (2.0 [0.5 - 7.5]) was lower than that reported in the literature. Several reasons might explain this early renal replacement therapy. First, analytical alterations (urea/creatinine) were chosen as a criterion for initiation in only two cases (4.9%). Second, metabolic alterations (58.5%) and oliguria/anuria (53.7%), but not hypervolemia (19.5%), were the reasons given for initiating renal replacement therapy. Lastly, local factors explain why renal replacement therapy is initiated early at our unit.

Continuous veno-venous hemofiltration was the most common technique performed (87.8%). The other patients initially received continuous veno-venous hemodiafiltration, given the temporary need for a high renal replacement therapy dose in the context of significant
metabolic or electrolyte alterations, usually switching to continuous veno-venous hemofiltration during treatment. Greater recovery of renal function after AKI has been observed among patients receiving continuous in place of intermittent renal replacement therapy; however, our study did not examine the use of the intermittent technique as an initial choice for renal replacement therapy.

Patients with AKI who discontinued renal replacement therapy but needed to resume it within seven days showed a higher mortality rate than those who successfully discontinued (seven consecutive days without requiring renal replacement therapy). Thus, accurate criteria of renal support discontinuation are crucial. However, few data exist concerning renal replacement discontinuation methods. Creatinine is clearly limited as an indicator for discontinuing of renal replacement therapy, being urine output the best predictor for it discontinuing, despite having a predictive value that is seriously affected by the use of diuretics. Our efficacy regarding discontinuing renal replacement therapy (i.e., only one patient required restarting the therapy because of a new renal insult resulting from hemorrhagic shock on the fifth day after discontinuing) might be explained by the fact that diuresis recovery was used as a stimulus to discontinue renal replacement therapy in most cases (81%), which is well above the 51% reported in a recently published survey conducted in the United States.

In line with other studies, the hospital mortality rate of our population was high, reaching 53.7%. However, given that sepsis-induced AKI predicts high mortality rates, our populations had sepsis in 43.9% of cases, all received amine therapy and had a high need for mechanical ventilation (90.2%), the mortality was inferior to that predicted by SAPS-II.

Some differences were identified when comparing patients who died with those who survived. A higher level of lactacidemia as well as a longer period between hospital admission and ICU admission was noted among the deceased, matching previous reports. One possible explanation is that some patients might have been under-triaged to a hospital department other than the ICU or expressed refractoriness to a treatment already performed. In our study, however, neither outcome showed a significant difference. As expected, surviving patients had a lower SAPSII, with a lower mortality rate predicted from beginning. Several literature sources indicate that fluid accumulation in critically ill patients increases mortality, whereas only one study reported this finding with regard in renal replacement therapy.

Our study confirmed this result, finding an association between positive fluid balance during renal replacement therapy and mortality among critically ill patients with AKI (p = 0.004).

Some studies have indicated that age, AKI intensity (urea, creatinine, or RIFLE classification), AKI etiology, or severity score are related factors in the context of AKI with regard to renal function recovery. However, those findings are not unanimous, and no strong relationship currently exists between those parameters and renal function recovery. Patients with recovered renal function in our sample had fewer days between hospital admission and renal replacement therapy initiation, although this result was not significant (p = 0.158), possibly because the sample was small. A recent meta-analysis clearly demonstrated this association, characterizing the early initiation of renal replacement therapy as a factor for improved renal function recovery.

Patients with higher cumulative fluid balance during renal replacement therapy showed lower renal function recovery in a sub-analysis of the Randomized Evaluation of Normal versus Augmented Level Replacement Therapy (RENAI trial) that compared the doses of renal replacement therapy. Conversely, Silversides et al. did not find a relationship between fluid balance during renal replacement therapy and renal function recovery. However, this study only evaluated fluid balance over the first seven days after the initiation of renal replacement therapy and not throughout the entire period of renal replacement therapy. Our study was the first to addresses this topic as a primary outcome; in fact, our sample revealed that excess fluids accumulation during renal replacement therapy were associated with renal function non-recovery among patients with AKI requiring renal replacement therapy. This finding might be explained by increased venous pressure, intrarenal engorgement, and the subsequent decrease in the renal arteriovenous gradient, creating a sort of “renal compartment syndrome”, as well as by the increased intra-abdominal pressure and consequent decrease of renal perfusion that leads to decreased renal function recovery capacity.

The present study has four major caveats. First, this study was observational and conducted at a single center; thus, the results are highly dependent on the standard of care of one department. Second, the sample size was small, which precludes the analysis of the results using a multivariate model. Third, a detailed description of the amines dosage was not performed throughout the renal replacement therapy; thus, we cannot exclude the
possibility that the fluid balance resulted from greater hemodynamic instability. Fourth, only one patient had to resume renal replacement therapy after discontinuing.

Conversely, although some studies have identified risk factors for mortality in patients with AKI receiving renal replacement therapy, few studies thus far have researched the prognostic criteria for renal function recovery as a primary outcome.

**CONCLUSION**

Critically ill patients with acute kidney injury who require renal replacement therapy have a high mortality rate, and the severity score at admission and the cumulative fluid balance during renal replacement therapy are poor prognostic factors. Some survivors are left with permanent kidney damage, which accounts for an elevated morbidity and mortality at medium and long-term. An association was found between excessive fluid balance during renal replacement therapy and renal function non-recovery.

In fact, our study reported that critically ill patients with acute kidney injury receiving renal replacement therapy had one eventual modifiable risk factor to decrease their mortality rate and increase their renal function recovery, suggesting that volume management during renal replacement therapy could affects these variables.

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**REFERENCES**

1. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA, Paganini EP, Chertow GM; Program to Improve Care in Acute Renal Disease. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney Int. 2004;66(4):1613-21.

2. Hsu RK, McCulloch CE, Dudley RA, Lo LJ, Hsu CY. Temporal changes in incidence of dialysis-requiring AKI. J Am Soc Nephrol. 2013;24(1):37-42.

3. Waikar SS, Curhan GC, Waid R, McCarthy EP, Chertow GM. Declining mortality in patients with acute renal failure, 1988 to 2002. J Am Soc Nephrol. 2006;17(4):1143-50.

4. Thakar CV, Christianson A, Freyberg R, Almenoff P, Render ML. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. Crit Care. 2009;13(9):2552-8.

5. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C. Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T Kidney) Investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA. 2005;294(7):813-8.

6. VA/NIH Acute Renal Failure Trial Network, Palevsky PM, Zhang JH, O’Connor TZ, Chertow GM, Crowley ST, Choudhry D, et al. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med. 2008;359(1):7-20. Erratum in N Engl J Med. 2009;361(24):2391.

7. Manns B, Doig CJ, Lee H, Dean S, Tonelli M, Johnson D, et al. Cost of acute renal failure requiring dialysis in the intensive care unit: clinical and resource implications of renal recovery. Crit Care Med. 2003;31(2):449-55.

8. RENAL Replacement Therapy Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lo S, et al. Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med. 2009;361(17):1627-37.

9. Bellomo R, Ronco R, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative (ADQI) Group. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8(4):R204-12.

10. Bell M; SWING, Granath F, Schön S, Ekborn A, Martling CR. Continuous renal replacement therapy is associated with less chronic renal failure than intermittent haemodialysis after acute renal failure. Intensive Care Med. 2007;33(5):773-80.
11. Mehta RL, McDonald B, Gabbai FB, Pahl M, Pascual MT, Farkas A, Kaplan RM; Collaborative Group for Treatment of ARF in the ICU. A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int. 2001;60(3):1154-63.
12. Wald R, Shariff SZ, Adhikari NK, Bagshaw SM, Burns KE, Friedrich JO, et al. The association between renal replacement therapy modality and long-term outcomes among critically ill adults with acute kidney injury: a retrospective cohort study. Crit Care Med. 2014;42(4):868-77.
13. Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, et al. Discontinuation of continuous renal replacement therapy: a post hoc analysis of a prospective multicenter observational study. Crit Care Med. 2009;37(9):2576-82.
14. Wu VC, Ko, WJ, Chang HW, Chen YY, Lin YF, Shiao CC, Chen YM, Chen YS, Tsai PR, Hu FC, Wang JY, Lin YH, Wu KD; National Taiwan University Surgical ICU Acute Renal Failure Study Group (NSARF). Risk factors of early readialysis after weaning from postoperative acute renal replacement therapy. Intensive Care Med. 2008;34(1):101-8.
15. Mallappallil MC, Mehta R, Yoshiuchi E, Briefel G, Lerma E, Saifü M. Parameters used to discontinue dialysis in acute kidney injury recovery: a survey of United States nephrologists. Nephron. 2015;130(1):41-7.
16. Levi TM, de Souza SP, de Magalhães JG, de Carvalho MS, Cunha AL, Dantas JG, et al. Comparison of the RIFLE, AKIN and KDIGO criteria to predict mortality in critically ill patients. Rev Bras Ter Intensiva. 2013;25(4):290-6.
17. Cruz MG, Dantas JG, Levi TM, Rocha Mde S, de Souza SP, Boa-Sorte N, et al. Septic versus non-septic acute kidney injury in critically ill patients: characteristics and clinical outcomes. Rev Bras Ter Intensiva. 2014;26(4):384-91.
18. Goldhill DR, McNarry AF, Hadjanastassiou VG, Tekkis PP. The longer patients are in hospital before Intensive Care admission the higher their mortality. Intensive Care Med. 2004;30(10):1908-13.
19. RENAL Replacement Therapy Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lee J, et al. An observational study fluid balance and patient outcomes in the Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy trial. Crit Care Med. 2012;40(6):1753-60.
20. Macedo E, Zanetta DM, Abdulkader RC. Long-term follow-up of patients after acute kidney injury: patterns of renal functional recovery. PLoS One 2012;7(5):e36388.
21. Srisawat N, Wen X, Lee M, Kong L, Elder M, Carter M, et al. Urinary biomarkers and renal recovery in critically ill patients with renal support. Clin J Am Soc Nephrol. 2011;6(8):1815-23.
22. Moon SJ, Park HB, Yoon SY, Lee SC. Urinary biomarkers for early detection of recovery in patients with acute kidney injury. J Korean Med Sci. 2013;28(8):1181-6.
23. Alsultan MA. The renal recovery of critically ill patients with acute renal failure requiring dialysis. Saudi J Kidney Dis Transpl. 2013;24(6):1175-9.
24. Karvellas CJ, Farhat MR, Sajjad I, Mogensen SS, Leung AA, Wald R, et al. A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis. Crit Care. 2011;15(1):R72.
25. Silversides JA, Pinto R, Kuint R, Wald R, Hladunewich MA, Lapinsky SE, et al. Fluid balance, intradialytic hypotension, and outcomes in critically ill patients undergoing renal replacement therapy: a cohort study. Crit Care. 2014;18(6):624.
26. Doty JM, Saggi BH, Sugerman HJ, Blocher CR, Pin R, Fakhry I, et al. Effect of increased renal venous pressure on renal function. J Trauma. 1999;47(6):1000-3.