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Factors associated with failure to disconnect patients from continuous renal replacement therapy. A single-center observational study.

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Received: June 18, 2024.
Accepted: August 29, 2024.
Published: August 30, 2024.
Editor: Dr. Franklin Mora Bravo.

Cite:
Valderrama D, Sevilla F, Osorio W, Merino M, Guerrero E, Ibarra M, Esquivel J, Molina J, Galindo P. Factors associated with failure to disconnect patients from continuous renal replacement therapy. A single-center observational study. REV SEN 2024;12(2):175-182.

DOI: http://doi.org/10.56867/87
Sociedad Ecuatoriana de Nefrología, Diálisis y Trasplantes.

ISSN-L: 2953-6448

Abstract

Introduction: Critically ill patients who survive a severe episode of acute kidney injury (AKI) recover sufficient renal function to allow withdrawal of renal replacement therapy (RRT). However, the criteria for deciding withdrawal need to be standardized in clinical practice. This study aimed to determine the factors associated with failure to disconnect in patients on continuous renal replacement therapy.

Methods: This observational study was carried out in adult patients hospitalized in the intensive care service of the National Institute of Nutrition "Salvador Zubirán" in Mexico between October and December 2023 who required continuous renal replacement therapy. Retrospective data, including demographic characteristics, comorbidities, type of renal replacement therapy, and clinical outcome, were collected. The SOFA score was used to assess disease severity.

Results: A total of 18 patients were analyzed, 14 with unsuccessful disconnection and 4 with successful disconnection, with an average stay of 14 ± 8 days in the ICU; 72% were men, 44% had a history of diabetes, and 72.2% had a history of high blood pressure. A total of 94.4% of the patients required vasopressors and invasive mechanical ventilation. The primary RRT modality was CVVHDF (88.9%). The main indications for initiation were overload (38.9%) and anuria (44.4%). There were no differences between population characteristics or RRT modality. Differences in mortality were evident, probably explained by the greater severity of the patients, as evidenced by the better SOFA score upon admission ($P = 0.001$).

Conclusion: Patients who were unable to disconnect from the replacement therapy program had increased mortality. The factor that contributed the most to this outcome was a higher SOFA score.

Keywords:

Acute kidney injury, Renal replacement therapy, Continuous renal replacement therapy, Failure to wean.

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Acute kidney injury (AKI) is a common complication in critically ill patients. Approximately 5% to 10% of AKI patients require renal replacement therapy (RRT) during their stay in the ICU, with mortality rates ranging from 30% to 70%. Risk factors for AKI that require RRT include older age, male sex, African American race, greater severity of the disease, sepsis, decompensated heart failure, cardiac surgery, liver failure, and the use of mechanical ventilation [1].

RRT has become essential in the management of patients with severe AKI. Thus, its use is estimated at 23.5% in patients with AKI in the intensive care unit, and its use has increased to 10% per year in the last decade [2]. The general objectives sought when RRT is indicated are to optimize the volume status, correct acid-base and electrolyte alterations early, and avoid distant damage to other organs. However, these benefits must be weighed against the risks and burdens associated with RRT, including vascular access (e.g., bleeding, thrombosis, vascular injury, infection), intradialysis hypotension, resource utilization, and potential concerns that RRT may impair the subsequent recovery of kidney function [1].

Multiple studies in critical nephrology focus on the optimal initiation of RRT, with diverse results among them [3 -5]. However, more needs to be discussed about the withdrawal of the RRT. There are no specific criteria for the interruption of RRT. In the KDIGO clinical guidelines of the working group for AKI (Kidney Diseases Improving Global Outcomes), withdrawal is suggested when RRT is no longer required because renal function has recovered and is adequate to meet the needs of the patient or because the TRR no longer meets the objectives for which it was needed [6].

Clinical factors such as patient characteristics (hemodynamic stability, hydro electrolyte alterations, fluid balance), renal function parameters (diuresis, glomerular filtration, urea clearance), and aspects of logistics (availability of nursing staff, dysfunction of vascular access, or coagulation of the circuit) influence the withdrawal of RRT or a change to another modality. These factors can positively or negatively affect RRT withdrawal [7].

Failure to withdraw RRT may contribute to increased patient mortality, increased volume overload, the persistence of distant organ damage, the requirement for more extended mechanical ventilation, and increased care costs. On the other hand, prolonging the withdrawal of RRT also has harmful effects on patients, ranging from adverse effects such as hypotension, infections associated with vascular access, bleeding, and exposure to inappropriate doses of medications [8].

An initial manifestation of recovery of renal function is increased diuresis, although specific criteria are scarce. In the observational study Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney), a urine output> 400 ml/day without concomitant diuretic treatment predicted successful cessation of CRRT. It has also been proposed that a urine output> 500 ml/d could be used as a criterion for the interruption of RRT in a study on the initiation and interruption of treatment in patients with ARF. However, the usefulness of this criterion is still being determined, as treating physicians continued RRT despite this recommendation approximately two-thirds of the time, citing volume overload as the most common reason for continuing RRT [9].

In the ATN study, a urine collection programmed for six hours was obtained when the urine production was > 750 ml/d. RRT was continued if the measured creatinine clearance was <12 ml/min, suspended if it was > 20 ml/min, and left to the physician's discretion if the measured creatinine clearance was between 12 and 20 ml/min. Although these strategies can inform clinical decision-making, precise criteria for interrupting RRT must still be provided [10].

The transition of patients with better hemodynamic status but persistent ARF to other RRT modalities is also highly variable. PIRRT can be used as transition therapy, or patients can transition directly to IHD, as the clinical status warrants. The transition from CRRT to PIRRT or IHD can facilitate the initiation of physical therapy and mobilization to get out of bed. In general, patients with persistent RRT-dependent ARF should switch to an intermittent hemodialysis modality before being discharged from the ICU [1].

Other factors that have been described in patients who fail to withdraw from RRT include a prolonged stay in the ICU, which is equivalent to greater severity since these patients have a more significant requirement for RRT, a higher SOFA score as a severity scale, a urinary volume less than 300 ml in 24 hours, and an age over 65 [7].

Multiple biomarkers, including NGAL, KIM-1, CISTATIN-C, and Nephro Check (TIMP-2XIGFBP7), have been considered to correlate them with potential predictors of renal recovery. A decrease in these biomarkers throughout an AKI event could predict renal function recovery [11,12].

This study aimed to determine the factors associated with disconnection failure in patients receiving continuous renal replacement therapy in a population with acute kidney injury over three months in a national nephrology referral center in Mexico City.

Materials and methods

Research type

The present study is observational and analytical. The source is retrospective.

Stage

The study was carried out in the intensive care service of the Salvador Zubirán National Institute of Nutrition in Mexico City from October 1, 2023, to December 31, 2023.

Universe and sample
The study's universe corresponds to the anonymized documentary records of the institution's intensive care patients. The sampling was simple and random.

Inclusion criteria
Patients older than 18 years who required the start of continuous renal replacement therapy were included. Two groups were formed for the analysis: Group 1, with successful weaning, and Group 2, with unsuccessful weaning.

Exclusion criteria
Patients with a previous diagnosis of chronic kidney disease in stages 1 to 4 who required the start of renal replacement therapy were excluded.

Variables
The variables studied are presented in Table 1.

Data sources/measurements
The source was retrospective, and the database of hospitalized patients in the intensive care service of the institution was reviewed. For the follow-up data, the intensive care progress notes were reviewed. For the study, successful disconnection was defined as maintaining a urinary volume greater than 500 ml without diuretics. For survival outcomes, nephrology and intensive care services reviewed and evaluated follow-up notes. Similarly, the characteristics of renal function deterioration were described, with all patients meeting the criteria for urinary volume, serum creatinine, or both. Within the established therapy, although two patients started renal replacement therapy with intermittent modality, they later migrated to continuous modality owing to intradialytic hypotension.

Biases
To avoid interviewer, information, and memory biases, the principal investigator protected the data and always protected the data approved in the research protocol. Observation and selection biases were avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the period were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

Study size
The sample was nonprobabilistic. All possible cases were included in the study.

Quantitative variables
The quantitative variables were the results of scale measurements of data such as hemoglobin, phosphorus, and serum ALB. Categorical data, such as sex or the presence or absence of comorbidities, are presented as proportions.

Table 1. Study variables.

Variable	Encoding
Gender	0: Female. 1: Male.
Age	Years
PA from diabetes	0: absent. 1: present.
PA of arterial hypertension	0: absent. 1: present.
PA of kidney disease	0: absent. 1: present.
PC for Heart Failure	0: absent. 1: present.
Days of hospitalization	Days.
Days in ICU	Days.
Weight at admission	Kilograms.
Etiology of exacerbation	0: Acute coronary syndrome. 1: Sepsis. 2: Rhabdomyolysis. 3: Tumor lysis.
Initial kidney replacement therapy	0: HDFVVC. 1: HDi.
Indication of the initiation of CRRT.	0: Overload. 1: Anuria. 2: intradialytic hypotension. 3: Metabolic acidosis.
TRRC modality.	0: HDFVVC. 1: HDVVC.
Anticoagulation.	0: absent. 1: present.
Weight at the start of CRRT	Kilograms.
Use of vasopressor	0: absent. 1: present.
Use of invasive mechanical ventilation	0: absent. 1: present.
Sepsis	0: absent.1: present.
SOFA	Value
Use of diuretics	0: absent.1: present.
Weaning from TRRC.	0: absent.1: present.
Death	0: absent.1: present.
Cause of death.	Described cause.
Hemoglobin at the beginning of CRRT.	g/dL.
Phosphorus at the beginning of the CRRT.	mg/dL.
Albumin at the beginning of CRRT.	g/dL.
Hemoglobin at weaning from CRRT or death	g/dL.
Phosphorus at weaning from CRRT or death	Mg/dL.
Albumin at weaning from CRRT or death	g/dL.
Glucose	Mg/dl.
Creatinine	Mg/dL.
Hemoglobin	g/dL.

AP: Personal history. CRRT: continuous renal replacement therapy.

Statistical analysis
Descriptive statistics are used for numerical variables, including central tendency and dispersion measures, means or medians, and standard deviations or interquartile ranges (IQRs). Categorical variables are presented as absolute and relative frequencies. Differences between the groups with successful weaning and those with unsuccessful weaning from CRRT were analyzed via the 2-sample Student's t-test and the Mann–Whitney U test. Correlations between variables were explored via Pearson and Spearman tests. A 95% confidence interval was used, with a value of $P \leq 0.05$ considered statistically significant. The Statistical Package for the Social Sciences (SPSS) version 25

(IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used.

Results

Study participants

Eighteen patients with continuous renal function replacement therapy were included in the study. Of these, 14 had unsuccessful disconnection (77.8%, 95% CI 58.6%, 97%), and 4 had successful disconnection.

Characteristics of the study groups

Table 2 presents the characteristics of the study groups. There were no differences in age between the two groups. There were also no differences due to the distributions of type 2 diabetes mellitus, hypertension, chronic kidney disease, heart failure, weight at admission, the use of vasopressors, or mechanical ventilation. The SOFA score was higher in the unsuccessful disconnection group (Table 2).

Baseline characteristics of acute kidney injury patients

There were no differences in the etiology of acute kidney injury between the groups. There was also no difference between the modalities and indications for initiating renal replacement therapy (Table 3).

Table 2. Characteristics of the study groups.

Variable	Successful Disconnection N=4	Unsuccessful disconnection N = 14	*P*
Age (x± DS)	64 ± 20	65 ± 17	0.78
Gender male (%)	3 (75%)	10 (71.4%)	0.88
Type 2 diabetes (%)	1 (25%)	7 (50%)	0.37
Hypertension (%)	3 (75%)	10 (71.4%)	0.88
Chronic kidney disease	2 (50%)	4 (30.8%)	0.48
Heart failure.	1 (25%)	4 (28.6%)	0.88
Weight at admission (kg)	84.2 ± 9.2	76.8 ± 7.2	0.19
Days of hospitalization	18 ± 6	13 ± 8	0.12
Days in ICU	8 ± 7	11 ± 8	0.62
Use of vasopressor	4 (100%)	13 (92.3%)	0.58
Mechanical ventilation	4 (100%)	13 (92.3%)	0.58
SOFA upon admission	12 ± 1	14 ± 1	0.007
Basal Creatinine (mg/dl)	2.2 ± 0	1.9 ± 0.4	0.75
Initial hemoglobin (g/dL)	10 ± 1.6	11.5 ± 2.8	0.44
Initial phosphorus (mg/dl)	5.8 ± 0.9	6 ± 1.5	0.87
Initial albumin (g/dL)	2.9 ± 0.4	2.8 ± 0.6	0.87
Weaning hemoglobin (g/dL)	10.8 ± 0.5	10.8 ± 2.4	0.38
Weaning phosphorus (mg/dL)	4.8 ± 2.2	3.9 ± 1.2	0.72
Albumin at weaning (g/dL)	2.3 ± 0.5	2.3 ± 0.6	0.57

CKD: chronic kidney disease. HF: heart failure. ICU: intensive care unit.

Main objective

The primary outcome studied was the mortality of the patients, and a statistically significant difference was found between the two groups, not only because of general mortality but also because of specific causes of mortality (Table 4). Once these data were obtained, a chi-square comparison was performed, grouping the patients according to mortality, revealing a statistically significant difference ($P = 0.045$) between the patients who had sepsis and those who did not, without finding a difference in other quantitative variables.

The previously mentioned findings revealed correlations between age and initial hemoglobin ($R = 0.551$, $P = 0.018$), days of stay in the intensive care unit, and phosphorus at weaning ($R = -0.571$, $P = 0.028$) and between days of hospital stay and initial hemoglobin ($R = -0.585$, $P = 0.011$), as shown in graphs 1, 2 and 3, respectively.

Table 3. Characteristics of the study groups.

Variable	Successful Disconnection N=4	Unsuccessful disconnection N = 14	*P*
Etiology of acute kidney injury			
ACS	1 (25%)	5 (35.7%)	0.733
Sepsis	2 (50%)	9 (50%)	
Tumor lysis	1 (25%)	1 (7.1%)	
Rhabdomyolysis	0 (0%)	1 (7.1%)	
RRT initiation mode			
CVVHDF	3 (75%)	13 (92.9%)	0.88
IHD	2 (11.1%)	1 (7.1%)	
RRT start indication			
Overload	2 (50%)	5 (35.7%)	0.59
Anuria	2 (50%)	6 (42.9%)	
Intradialytic hypotension	0 (0%)	3 (21.4%)	
Weight gain (kg)	6.5 ± 1.91	5.29 ± 2.93	0.505
Use of anticoagulants	4 (100%)	11 (78.6%)	0.31

IHD: intermittent hemodialysis. CVVHDF: continuous veno-venous hemodiafiltration. ACS: Acute coronary syndrome. RRT: renal replacement therapy.

Table 4. Mortality study.

Variable	Successful Disconnection N=4	Unsuccessful disconnection N = 14	*P*
Mortality	0 (0%)	12 (85.7%)	0.001
	Cause of mortality		0.016
Sepsis	0 (0%)	5 (35.7%)	
Multiorgan failure	0 (0%)	6 (42.9%)	
Acute myocardial infarction	0 (0%)	1 (7.1%)	

Figure 1. Hemoglobin was correlated with days of hospital stay.

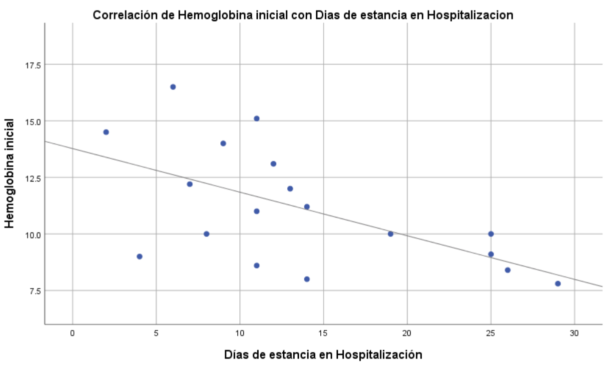


Figure 2. Correlation of hemoglobin with age.

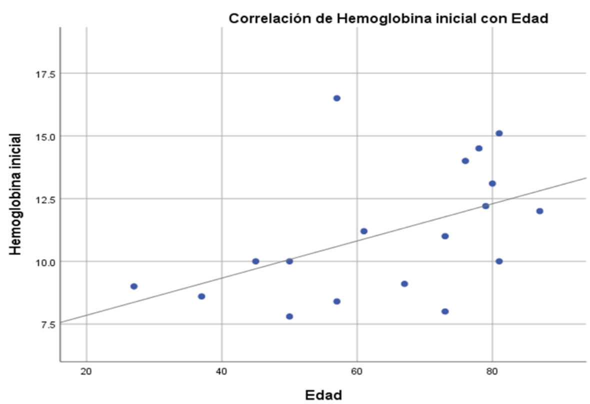
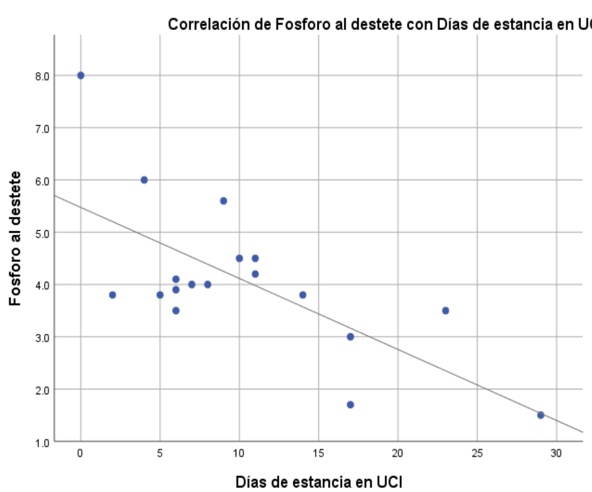


Figure 3. Correlation between phosphorus and days of stay in the ICU.



Discussion

The main finding of the present study is that the percentage of patients who cannot successfully suspend renal replacement therapy in acute kidney injury was 14/18 (77.8%), with a confidence interval of 95%, ranging from 58.6% to 97%. There were no demographic or population differences between patients who successfully discontinued renal replacement therapy, in contrast to the results in the previously published literature [7]. The SOFA score at admission in patients who could not be weaned from renal replacement therapy was higher than in patients who could be successfully separated (14 versus 12). The SOFA (Sequential Organ Failure Assessment) scale is a scoring system used to assess the severity of the disease in critically ill patients and their risk of death. In the context of acute renal failure, specific components of this scale are particularly relevant, such as serum creatinine, with a significant increase in creatinine levels being a direct indicator of deterioration of renal function. Another component is the presence of diuresis: a marked decrease in urinary volume is another clear sign of kidney failure. These two markers directly reflect kidney function: creatinine and diuresis are specific biological markers of kidney function. They are affected early in the early stages of acute kidney failure, allowing early disease detection. Additionally, these parameters correlate with severity: an increase in the SOFA score related to renal function indicates a greater severity of acute renal failure and a worse prognosis.

Another component of the SOFA score and its relevance in acute renal failure is arterial hypotension, which can contribute to the deterioration of renal function. Oxygenation in ARF patients can affect other organs, such as cerebral and pulmonary perfusion, which can affect oxygenation. Another factor is the level of consciousness: encephalopathy can be a complication of ARF. The SOFA scale makes it possible to assess the disease's severity and predict the risk of death. A high SOFA score is associated with a higher risk of mortality and can be used to guide therapeutic decisions and monitor the evolution of the patient.

Although the test of difference in proportions between both groups is striking when comparing mortality and causes of death, this result is explained both by the difference in the proportion of subjects in both groups and by the absence of a successful outcome in the disconnection group.

Although the study's design allowed preliminary results to be obtained, its main limitation is the impossibility of performing a more exhaustive statistical analysis. The small sample size constitutes an additional obstacle to delving into the findings. Given these limitations, new data collection, monitoring, and statistical analysis methodologies should be explored, taking advantage of the knowledge acquired during the performance of this work. The results of the correlation analyses, although statistically significant, revealed a moderate to weak association between the variables studied. An increased sample size and a more exhaustive follow-up of the subjects would allow us to explore these relationships further.

Given that the data did not meet the normality assumptions and the sample size was small, the Spearman correlation coefficient was used. The expected association between the decrease in phosphorus and hemoglobin levels with the days of stay in the ICU could be explained by the tendency to lose muscle mass in a critical patient and the impossibility of bone marrow reconversion in the context of renal failure [13]. New studies should address these topics of interest.

Conclusions

Patients who were unable to disconnect from the replacement therapy program had higher mortality. The factor that contributed the most to this outcome was a higher SOFA score.

Abbreviations

CKD: chronic kidney disease.
IHD: intermittent hemodialysis.
CVVHDF: continuous veno-venous hemodiafiltration.
HF: heart failure.
AKI: Acute kidney injury.
ACS: Acute coronary syndrome.
CRRT: Continuous renal replacement therapy.
ICU: intensive care unit.

Supplementary information

The supplementary materials have not been declared.

Acknowledgments

Does not apply.

Authors' contributions

Diana Valderrama Ávila: Conceptualization, methodology, research, Writing - Original draft.
Francisco Jesús Sevilla Jimenéz: Conceptualization, Project management, Supervision, validation, visualization, Writing - review and edition.
Washington Xavier Osorio: conceptualization, data curation, formal analysis: Acquisition of funds, Research, and Methodology.
Maribel Merino López: Acquisition of funds:
Research, Methodology, Project Management, Resources.
Eduardo Guerrero Hinzpeter: Formal analysis, Acquisition of funds:
Research, Methodology, Project Management, Resources.
Mariela Ibarra Salce: Research, Methodology, Project Administration, Resources, Software, Monitoring, Validation.
Jennifer Esquivel Amaza: Research, Methodology, Project Management, Resources, Software, Supervision, Validation, Visualization, Writing - original draft.
Juan José Molina García: Research, Methodology, Project Management, Resources, Software, Supervision, Validation, Visualization, Writing - original draft.
Pablo Enrique Galindo Vallejo: Research Methodology, Project Management, Resources, Software, Supervision, Validation, Visualization, Writing - original draft.
All the authors read and approved the final version of the manuscript.

Financing

The study was self-financed by the authors.

Availability of data or materials

Does not apply.

Declarations

Ethics committee approval and consent to participate

The Ethics Committee of the "Salvador Zubirán" National Institute of Nutrition approved the research protocol.

Consent for publication

It does not apply when specific images, radiographs, or photographs of patients are not published.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Authors' information

Not declared.

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DOI: Digital Object Identifier. **PMID**: PubMed Identifier.

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