Original Article

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INCIDENCE, RISK FACTORS AND SURVIVAL OF CRITICALLY-ILL PATIENTS WITH ACUTE KIDNEY INJURY

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ABSTRACT

Objective: to analyze the incidence, risk factors and survival of critically-ill patients with acute kidney injury.
Method: a concurrent cohort study, conducted with 126 participants between May and September 2019 in a public Intensive Care Unit of the state of Acre. The Kaplan-Meier method was used to estimate the probability of death (log-rank 95% test) and the Cox regression model was employed to determine the prognostic factors of death.
Results: the incidence of acute kidney injury was 37.3 per 1,000 individuals admitted to the intensive Care Unit. Disease recovery was the outcome in 36.7% of the patients, and 42.9% evolved to death. The conditional probability of death was higher in the female gender and in those who did not use mechanical ventilation, with glomerular filtration rate at admission < 60 ml/min/1.73 m^2 and sepsis diagnosis. Regardless of the acute kidney injury diagnosis, the risk factors associated with death in the population of critically-ill patients were serum creatinine above 1.2 mg/dl at admission and glomerular filtration rate < 60 ml/min/1.73 m^2 at admission.
Conclusion: in this population, survival is aggravated by gender dimorphism and by the reduction of the glomerular filtration rate.

DESCRIPTORS: Acute kidney injury. Incidence. Survival. Intensive Care Unit. Longitudinal studies. Prognosis.

HOW CITED: Araújo LP, Lopes WF, Prado PR, Amaral TLM. Incidence, risk factors and survival of critically-ill patients with acute kidney injury. Texto Contexto Enferm [Internet]. 2021 [cited YEAR MONTH DAY]; 30:e20200501. Available from: https://doi.org/10.1590/1980-265X-TCE-2020-0501

INCIDÊNCIA, FATORES DE RISCO E SOBREVIDA DE PACIENTES EM ESTADO CRÍTICO COM LESÃO RENAL AGUDA

RESUMO

Objetivo: avaliar a incidência, os fatores de risco e a sobrevida de pacientes críticos com lesão renal aguda.
Método: coorte concorrente, realizada entre maio e setembro de 2019 em uma Unidade de Terapia Intensiva pública do estado do Acre, com 126 pacientes. Utilizaram-se o método Kaplan Meier, para estimar a probabilidade do óbito (teste de log-rank 95%) e o modelo de regressão de Cox, para determinar os fatores prognósticos do óbito.
Resultados: a incidência de lesão renal aguda foi de 37,3 a cada 1.000 indivíduos admitidos na unidade de terapia intensiva. A recuperação da doença ocorreu em 36,7% deles, e 42,9% evoluíram ao óbito. A probabilidade condicional de óbito foi maior no sexo feminino e naqueles que não utilizaram ventilação mecânica, taxa de filtração glomerular admissional < 60 ml/min/1,73 m^2 e diagnóstico de sepse. Os fatores de risco associados ao óbito na população de pacientes críticos, independentemente do diagnóstico de lesão renal aguda, foram creatinina sérica maior que 1,2 mg/dl na admissão e taxa de filtração glomerular < 60 ml/min/1,73 m^2 na admissão.
Conclusão: a sobrevida nessa população é agravada pelo dimorfismo de gênero e pela redução da taxa de filtração glomerular.

DESCRITORES: Lesão renal aguda. Incidência. Sobrevida. Unidade de terapia intensiva. Estudos longitudinais. Prognóstico.

INCIDENCIA, FACTORES DE RIESGO Y SOBREVIDA DE PACIENTES EN ESTADO CRÍTICO CON INSUFICIENCIA RENAL AGUDA

RESUMEN

Objetivo: evaluar la incidencia, los factores de riesgo y la sobrevida de pacientes en estado crítico con insuficiencia renal aguda.
Método: estudio de cohorte concurrente, realizado con 126 pacientes entre mayo y septiembre de 2019 en una Unidad de Cuidados Intensivos pública del estado de Acre. Se utilizó el método Kaplan-Meier para estimar la probabilidad de fallecimiento (prueba de log-rank 95%) y se empleó el modelo de regresión de Cox para determinar los factores que pronostican el fallecimiento.
Resultados: la incidencia de insuficiencia renal aguda fue de 37,3 cada 1000 individuos ingresados en la unidad de cuidados intensivos. El 36,7% de los pacientes se recuperó de la enfermedad y el 42,9% falleció. La probabilidad condicional de fallecimiento fue mayor en el sexo femenino y en las personas que no se encontraban en ventilación mecánica, con tasas de filtración glomerular al momento de la admisión < 60 ml/min/1,73 m^2 y diagnóstico de sepsis. Los factores de riesgo asociados al fallecimiento en la población de pacientes en estado crítico, independientemente del diagnóstico de insuficiencia renal aguda, fueron los siguientes: creatinina sérica superior a 1,2 mg/dl y tasa de filtración glomerular < 60 ml/min/1,73 m^2, ambos al momento de la admisión.
Conclusión: la sobrevida en esta población se ve agravada por el dimorfismo de género y por la disminución en la tasa de filtración glomerular.

DESCRIPTORES: Insuficiencia renal aguda. Incidencia. Sobrevida. Unidad de cuidados intensivos. Estudios longitudinales. Pronóstico.

INTRODUCTION

Acute Kidney Injury (AKI) is characterized by a sudden decrease in the renal function[1]. It represents a severe health condition worldwide, as it exerts several impacts on survival and increases the risk of progression to Chronic Kidney Disease (CKD)[2].

During the course of a hospitalization, one out of five adults suffer some kind of AKI episode[3]. In a meta-analysis conducted with 24 observational studies on AKI in patients with trauma admitted to the Intensive Care Unit (ICU), a six-day increase in the hospitalization time and three times greater risk of mortality [RR 3.4 (2.1–5.7)] were identified, when compared to the group without AKI[4].

AKI represents an independent factor for mortality. In a multicentric study carried out with 15,132 patients in North America, Europe and Australia, the hospital death rate due to AKI was 27%, with higher percentage values according to injury progression[5].

Thus, assessing the incidence of AKI in patients proves to be an important mechanism to analyze health status; however, these isolated data are insufficient to generate information relevant to the daily clinical practice, as they do not show the contributing factors to death. Consequently, the objective of this study was to assess the incidence, risk factors and survival of patients who evolved to acute kidney injury in an ICU.

METHOD

This is concurrent cohort study conducted with patients aged at least 18 years old admitted to the Intensive Care Unit of a tertiary-level public hospital in the city of Rio Branco, Acre, between May and September 2019, who evolved with and without AKI.

The study population was composed of the total of patients admitted to the ICU within the period established, and the follow-up time was between the patient's hospitalization and discharge, transfer or death. Those with a diagnosis of chronic kidney disease in any stage at admission were excluded, as well as those who had undergone some type of renal replacement therapy in the three previous months, kidney transplant recipients, with hospitalization times less than 24 hours or with imminent death risk within the first 48 hospitalization hours, as pregnant and puerperal women.

For data collection, a specific form with sociodemographic data, data on hospitalization, history of comorbidities, vital signs and use of oxygen therapy was used. Other information included use of nephrotoxic medications (angiotensin-converting enzyme inhibitors [ACEIs], angiotensin receptor blockers [ARBs], vancomycin, aminoglycosides, cephalosporins, quinolones, sulfonamides, antifungals, non-steroidal anti-inflammatory drugs [NSAIDs], acyclovir, mannitol, phenytoin, amphotericin B, diuretics and carbapenems), use of vasoactive drugs and anthropometric data (weight was identified by means of the scale incorporated into the Hospimetal brand 4-motor Fawler bed model HM2002E, with a maximum capacity of 250 kg). The neurological evaluation list was completed with laboratory tests, data on renal replacement therapy and Water Balance (WB), clinical manifestations and outcome (discharge/death date).

All the patients admitted had their glomerular filtration rate (GFR) calculated and, for those with AKI, this rate was measured by day of assessment D1, D3, D7 and exit from hospital (discharge/death). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to assess GFR[6].

In Water Balance (WB), the cumulative amount of 24 hours was used, subtracting entrance from exit.

The acute kidney injury (AKI) dependent variable was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, such as increase of the serum creatinine level above

0.3 mg/dl in 48 hours; or a 1.5-time serum creatinine increase in relation to baseline in seven days; or diuresis below 0.5 ml/kg/h during six hours[7].

The AKI cases were classified according to the KDIGO criteria in stages 1, 2 and 3. Stage 1 is defined by a 1.5-1.9-time creatinine increase in relation to the baseline value in seven days or by an increase of serum creatinine > 0.3 mg/dl in 48 hours or urinary volume < 0.5 ml/kg/h for 6-12 hours. Stage 2 refers to a 2-2.9-time increase in relation to the baseline creatinine value or urinary volume < 0.5 ml/kg/h for > 12 hours. Finally, stage 3 is related to an increase > 3 times in relation to the baseline creatinine value, to a rise to > 4.0 mg/dl, or to initiation of the renal replacement therapy or anuria for > 12 hours[7].

For baseline creatinine, the value obtained at admission to the ICU was considered, for having already been used in other studies on this theme[7–8].

Recovery of the renal function was defined by the absence of creatinine and urinary volume criteria for any stage from 2 to 3 during the hospitalization period, that is, not meeting the AKI criteria at any stage and not requiring Renal Replacement Therapy (RRT)[9].

In the description of the continuous variables, measures of central tendency (mean and standard deviation) were presented, and the categorical variables were expressed by distribution of absolute and relative frequencies. In the comparison of groups, the Student's t and Pearson's Chi-square or Fisher's exact tests were performed, considering the nature of the continuous and categorical variables, respectively.

The admission date to the ICU was used as the cohort's zero-time (T0) and the follow-up time (ΔT) was the time elapsed between T0 and AKI; the outcome was the occurrence of death. The Kaplan-Meier method was employed to estimate the conditional probability of death at the 3rd and 7th days of follow-up in those patients who evolved with AKI, the long-rank 95% test was used to assess the differences between the curves.

The following was considered for the calculation of incidence: the number of new AKI cases and the person-time (PT) total, period in which the individual was at risk of falling ill, using days as time unit. The sum of PT was performed during the entire monitoring period.

Cox regression models, gross and adjusted, with the respective 95% confidence intervals, were used to estimate the risk factors of death for patients admitted to the ICU. The independent variables that showed statistical significance in the univariate analysis were included in Cox multivariate regression model adjusted by age and reason for hospitalization. In all the analyses, a significance level of $\alpha = 5\%$ was adopted. The data were analyzed with the SPSS® program, version 20.0.

This study was approved by the Research Ethics Committee and observed Resolution No. 466/2012.

RESULTS

Of the 161 patients hospitalized in the ICU during the collection period, 35 were excluded for not meeting the research criteria. Thus, the population consisted of 126 patients, the majority aged less than 50 years old, with predominance of the male gender, and surgical hospitalization as the main reason, presenting some type of comorbidity reported at admission. Most of them needed mechanical ventilation support and vasoactive drugs at admission and the mean hospitalization time was approximately 17 days. The serum creatinine at admission, glomerular filtration rate at admission, age, weight at admission, platelets, glycaemia, urea, PAO_2/FIO_2, HCO_3, outcome, and hospitalization time variables presented statistically significant differences in the individuals who had AKI when compared to those who did not develop the injury, as shown in Table 1.

Throughout the monitoring period, 38.9% of the critically-ill patients met the AKI criteria. Incidence was 37.3 per 1,000 individuals admitted to the ICU.

When monitoring the individuals with AKI, it was observed that a large percentage evolved with stages II and III of the injury at the first monitoring day (D1). The glomerular filtration rate was below 60 ml/min/1.73m^2 on the days analyzed. Oliguria, partial and total anuria were present in the group throughout the period, mainly at D1 and D3. Water Balance (WB) proved to be more positive at D1, with a discrete reduction throughout the other days; however, the WB mean remained above 1.1 liter in 24 hours. Important laboratory changes were noticed in the patients, such as hyperglycemia, hyperlactatemia, uremia and high creatinine, as shown in Table 2.

Table 1 – Clinical and epidemiological characteristics of the patients with and without acute kidney injury in an Intensive Care Unit in Rio Branco, Acre, Brazil, 2019. (n=126)

Variables	Total	Without AKI* N (%)	With AKI* N (%)	p-value **
Age (Mean±SD)	46.8±18.0	44.0±17.1	51.4±18.7	0.024
Age group (years old)				0.460
< 50	72 (57.1)	46 (59.7)	26 (53.1)	
≥ 50	54 (42.9)	31 (40.3)	23 (46.9)	
Gender				0.043
Male	90 (71.4)	50 (64.9)	40 (81.6)	
Female	36 (28.6)	27 (35.1)	9 (18.4)	
Reason for admission				1.000
Surgical	90 (71.4)	55 (71.4)	35 (71.4)	
Clinical	36 (28.6)	22 (28.6)	14 (28.6)	
Comorbidities				0.842
No	58 (46.0)	37 (48.1)	21 (42.9)	
Yes	68 (54.0)	40 (51.9)	28 (57.1)	
Mechanical ventilation				0.736
No	46 (36.5)	29 (37.7)	17 (34.17)	
Yes	80 (63.5)	48 (62.3)	32 (65.3)	
PEEP†	8.66±1.50	8.75±1.67	8.53±1.24	0.529
Vasoactive drugs				0.130
No	59 (47.2)	40 (52.6)	19 (38.8)	
Yes	66 (52.8)	36 (47.4)	30 (61.2)	
Sepsis				0.409
No	95 (75.4)	60 (77.9)	35 (71.4)	
Yes	31 (24.6)	17 (22.1)	14 (28.6)	
Nephrotoxic medications				0.553
No	71 (56.3)	45 (58.4)	26 (53.1)	
Yes	55 (43.7)	32 (41.6)	23 (46.9)	
Serum creatinine at admission (mg/dl) (Mean±SD‡)	1.2±0.9	0.8±0.2	1.8±1.1	<0.001
Glomerular filtration rate (ml/min/1.73 m^2) at admission (Mean±SD)	87.6±35.35	104.8±22.9	60.6±34.7	<0.001
Weight at admission (kg) (Mean±SD)	73.3±15.6	70.9±15.0	77.1±16.0	0.028
Laboratory tests at admission				
Platelets (Mean±SD)	206,229.4± 117,314.6	224,942.7± 129,880.3	176,822.4± 87,674.1	0.024

Table 1 – Cont.

Variables	Total	Without AKI* N (%)	With AKI* N (%)	p-value **
Glycaemia (Mean±SD)	161.2±77.1	150.3±56.5	178.3±99.7	0.047
Urea (Mean±SD)	50.2±29.2	40.6±20.1	65.3±34.5	<0.001
Potassium (Mean±SD)	4.2±0.9	4.1±0.7	4.9±5.5	0.192
Lactate (Mean±SD)	38.7±40.7	33.5±40.6	47.0±40.1	0.095
Blood gas test (n=82)				
HP§ (Mean±SD)	7.4±0.2	7.0±0.1	7.4±0.4	0.770
PAO_2/FIO_2‖ (Mean±SD)	313.2±149.1	344.9±169.7	266.2±96.5	0.018
HCO_3¶ (Mean±SD)	19.8±5.7	20.9±6.2	18.2±4.6	0.032
Vital signs at admission				
Mean blood pressure (Mean±SD)	90.4±19.4	89.5±19.2	91.9±19.9	0.500
Heart rate (Mean±SD)	93.2±24.8	92.1±21.2	94.9±29.6	0.528
Outcome				<0.001
Discharge	72 (57.1)	57 (74.0)	15 (30.6)	
Death	54 (42.9)	20 (26.0)	34 (69.7)	
Hospitalization time (Mean±SD)	16.5±13.8	14.3±12.4	20.1±15.1	0.019
Total	126 (100.0)	77 (61.1)	49 (38.9)	

*AKI: Acute Kidney Injury; **p-value: Chi-square test; †PEEP: Positive End-Expiratory Pressure; ‡SD: Standard Deviation; §HP: Hydrogen Potential; ‖PAO_2/FIO_2: Relation between partial oxygen pressure in arterial blood and fraction of inspired oxygen; ¶HCO_3: Bicarbonate.

Table 2 – Stratification of the acute kidney injury cases and clinical characteristics per days of assessment in an Intensive Care Unit in Rio Branco, Acre, Brazil, 2010. (n=249)

Variables	Day 1 N (%)	Day 3 N (%)	Day 7 N (%)	Exit N (%)
KDIGO* classification				
Stage I	03 (6.1)	06 (12.2)	06 (12.2)	06 (4.8)
Stage II	21 (42.8)	12 (24.5)	05 (10.2)	01 (0.8)
Stage III	25 (51.0)	21 (42.9)	17 (34.7)	32 (25.4)
Glomerular filtration rate (ml/min/1.73m²) (Mean±SD†)	44.4±19.5	45.3±29.8	48.2±35.4	84.3±46.9
Urinary output 24h (Mean±SD) (Min-Max)	1,932.7±1,494.3 (0;5,800)	1,756.8±1,324.0 (0; 4750)	1,290.5±1,047.2 (60;3,800)	--
Water balance (Mean±SD) (Min-Max)	2,221.6±1,831.5 (-1,041; +8,796)	1,116.2±1,725.9 (-3,023; +4,226)	1,631.8±1,465.8 (-1,875; +5,579)	--
Laboratory tests				
Platelets (Mean±SD)	205,136.7± 159,104.6	178,354.2± 131,316.4	199,085.7± 96,722.7	296,768.3± 166,031.4
Leukocytes (Mean±SD)	15,248.9± 7,700.4	16,650.0± 14,730.3	16,297.4± 7,743.5	16,234.9± 28,471.7
Glycaemia (Mean±SD)	179.6±109.6	193.5±120.9	211.8±132.9	139.6±99.8
Urea (Mean±SD)	79.0±35.9	92.7±51.7	126.9±76.7	72.0±62.6
Creatinine (Mean±SD)	2.0±1.0	2.4±1.5	2.4±1.8	1.5±1.4
Sodium (Mean±SD)	138.7±7.4	138.5±7.9	139.8±9.4	136.5±8.5

Table 2 – Cont.

Variables	Day 1 N (%)	Day 3 N (%)	Day 7 N (%)	Exit N (%)
Potassium (Mean±SD)	4.3±0.9	4.0±0.8	3.8±0.8	4.1±1.1
Lactate (Mean±SD)	31.2±19.2	25.9±9.0	32.3±37.5	30.2±34.0
Blood gas test (n=82)				
HP‡ (Mean±SD)	7.3±0.1	7.4±0.1	7.4±0.1	7.3±0.2
PAO_2/FIO_2§ (Mean±SD)	295.9±151.1	314.1±110.8	352.3±106.7	235.0±132.0
HCO_3‖ (Mean±SD)	18.2±4.9	19.7±3.9	20.8±6.2	17.8±8.6
Vital signs				
Mean blood pressure (Mean±SD)	92.7±19.0	98.7±14.8	96.4±12.5	85.6±16.5
Heart rate (Mean±SD)	107.9±25.9	102.4±22.1	99.2±18.1	92.6±25.6

KDIGO: Kidney Disease Improving Global Outcomes; †SD: Standard Deviation; ‡HP: Hydrogen Potential; §PAO_2/FIO_2: Relation between partial oxygen pressure in arterial blood and fraction of inspired oxygen; ‖HCO_3: Bicarbonate.

The mean time elapsed between admission and AKI diagnosis was 4.57 days±9.10 days, and 50.0% of the cases received disease confirmation on the first hospitalization day; the mean time for the onset of AKI was of 6.63 days (SD: ±7.97; Median: 2.50).

When assessing recovery, 36.7% of the patients had their AKI condition reverted throughout the period. Only the severe AKI at some point, renal replacement therapy (RRT), creatinine and outcome variables presented statistically significant differences ($p<0.05$).

According to the survival analyses, female individuals presented higher conditional probability of death, reaching 25.0% in seven days after the identification of AKI. Those who did not require mechanical ventilation also had this increase in the probability of evolving to death, as well as in GFR at admission (< 60) and in individuals diagnosed with sepsis during their stay in the ICU, as shown in Table 3.

Table 3 – Conditional probability of death according to the clinical and epidemiological characteristics of patients who evolved with acute kidney injury in an Intensive Care Unit in Rio Branco, Acre, Brazil, 2019. (n=126)

Variable	Survival (%)*		p-value†
	3 days	7 days	
Age			
< 50	3.8	15.7	0.349
≥ 50	4.3	13.3	
Gender			
Male	5.0	15.2	0.020
Female	12.5	25.0	
Reason for hospitalization			
Surgical	5.7	8.8	0.505
Clinical	7.1	37.1	
Comorbidity			
No	4.8	15.1	0.627
Yes	3.6	18.2	
Mechanical ventilation			

Table 3 – Cont.

Variable	Survival (%)*		p-value†
	3 days	7 days	
No	10.0	20.0	0.002
Yes	5.1	15.9	
Use of vasoactive drug			
No	5.3	15.8	0.955
Yes	6.7	13.7	
Nephrotoxic exposure			
No	4.5	14.1	0.135
Yes	7.4	15.0	
Serum creatinine at admission (mg/dl)			
< 1.2	13.3	13.3	0.186
≥ 1.2	6.1	21.3	
Glomerular filtration rate at admission (ml/min/1.73 m^2)			
< 60	6.7	20.7	0.019
≥ 60	5.3	5.3	
Bicarbonate (HCO_3)			
< 22	7.1	10.9	0.831
≥ 22	33.3	33.3	
PAO_2/FIO_2‡			
≤ 200	22.2	33.3	0.108
> 200	4.5	4.5	
Potassium (mEq/l)			
< 3.6	5.9	23.5	0.760
≥ 3.6	3.1	9.7	
Sodium (mEq/l)			
≤ 145	4.3	13.4	0.629
> 145	50.0	50.0	
Glycaemia (mg/dl)			
< 180	3.1	15.9	0.951
≥ 180	5.9	18.4	
Platelets (mm^3)			
< 350,000	4.2	14.9	0.230
≥ 350,000	100	100	
Hematocrit (%)			
< 35	3.6	10.9	0.570
≥ 35	4.8	24.9	
Sepsis			
No	2.9	12.0	0.051
Yes	14.3	28.6	
Severe acute kidney injury at some moment			
No	10.0	10.0	0.260
Yes	5.1	15.8	

*SBV (%): Survival, Kaplan-Meier method; †log-rank; ‡PAO_2/FIO_2: Relation between partial oxygen pressure in arterial blood and fraction of inspired oxygen.

Of the patients hospitalized in the ICU during the period, 42.9% evolved to death. When assessing the dynamics of this outcome, it was observed that the highest proportion of deaths was in patients who were not on mechanical ventilation (MV) (37.0%), diagnosed with sepsis (33.3%), with serum creatinine at admission > 1.2 (42.6%), GFR at admission < 60 (38.9%), diagnosed with AKI (63.0%), severe AKI (94.1%), subjected to RRT (27.8%), leukocytes > 12,000 (76.6%), potassium < 3.6 (37.7%) and PAO_2/FIO_2 ratio < 200 (36.1%), all statistically significant, as shown in Table 4.

Table 4 – Clinical and epidemiological characteristics of the survivors and non-survivors in an Intensive Care Unit in Rio Branco, Acre, Brazil, 2019. (n=126)

Variables	Total	Survivors N (%)	Non-survivors N (%)	p-value*
Age				0.161
< 50	72 (57.1)	45 (62.5)	27 (50.0)	
≥ 50	54 (42.9)	27 (37.5)	27 (50.0)	
Gender				0.820
Male	90 (71.4)	52 (72.2)	38 (70.4)	
Female	36 (28.6)	20 (27.8)	16 (29.6)	
Reason for admission				0.155
Surgical	90 (71.4)	55 (76.4)	35 (64.8)	
Clinical	36 (28.6)	17 (23.6)	19 (35.2)	
Comorbidities				0.302
No	58 (46.0)	36 (50.0)	22 (40.7)	
Yes	68 (54.0)	36 (50.0)	32 (59.3)	
Mechanical ventilation				< 0.001
No	24 (19.0)	04 (5.6)	20 (37.0)	
Yes	102 (81.0)	68 (94.4)	34 (63.0)	
Vasoactive drugs				0.105
No	59 (47.2)	38 (53.5)	21 (38.9)	
Yes	66 (52.8)	33 (46.5)	33 (61.1)	
Nephrotoxic medications				0.111
No	64 (50.8)	41 (56.9)	23 (42.6)	
Yes	62 (49.2)	31 (43.1)	31 (57.4)	
Sepsis				0.049
No	95 (75.4)	59 (81.9)	36 (66.7)	
Yes	31 (24.6)	13 (18.1)	18 (33.3)	
Serum creatinine at admission				0.001
> 1.2	35 (27.8)	12 (16.7)	23 (42.6)	
≤ 1.2	91 (72.2)	60 (83.3)	31 (57.4)	
Glomerular filtration rate at admission (ml/min/1.73 m^2)				0.003
≥ 60	94 (74.6)	61 (84.7)	33 (61.1)	
< 60	32 (25.4)	11 (15.3)	21 (38.9)	
Acute Kidney Injury (AKI)				< 0.001
No	77 (61.1)	57 (79.2)	20 (37.0)	
Yes	49 (38.9)	15 (20.8)	34 (63.0)	

Table 4 – Cont.

Variables	Total	Survivors N (%)	Non-survivors N (%)	p-value*
Severe AKI at some moment				< 0.001
No	10 (20.4)	08 (53.3)	02 (5.9)	
Yes	39 (19.6)	07 (46.7)	32 (94.1)	
AKI Stage II or III at admission (n=49)*				0.235
Stage II	20 (45.5)	09 (60.0)	11 (37.9)	
Stage III	24 (54.5)	06 (40.0)	18 (62.1)	
Renal Replacement Therapy (n=49)*				0.018
No	110 (87.3)	71 (98.6)	39 (72.2)	
Yes	16 (12.7)	01 (1.4)	15 (27.8)	
Red blood cells (millions/mm^3)				0.498
> 3.9	57 (59.6)	35 (52.2)	22 (45.8)	
≤ 3.9	58 (40.4)	32 (47.8)	26 (54.2)	
Hematocrit (%)				0.703
> 35	42 (33.3)	23 (31.9)	19 (35.2)	
≤ 35	84 (66.7)	49 (68.1)	35 (64.8)	
Hemoglobin (g/dl)				0.493
> 12	29 (25.9)	15 (23.4)	14 (29.2)	
≤ 12	83 (74.1)	49 (76.6)	34 (70.8)	
Platelets (mil/mm^3)				0.757
> 350,000	11 (8.7)	07 (9.7)	04 (7.4)	
≤ 350,000	115 (91.3)	65 (90.3)	50 (92.6)	
Leukocytes (mm^3)				0.029
> 12,000	74 (64.9)	38 (56.7)	36 (76.6)	
≤ 12,000	40 (35.1)	29 (43.3)	11 (23.4)	
Glycaemia (mg/dl)				0.108
> 180	35 (27.8)	16 (22.2)	19 (35.2)	
≤ 180	91 (72.2)	56 (77.8)	35 (64.8)	
Urea (mg/dl)				0.050
> 40	57 (45.2)	38 (52.8)	19 (35.2)	
≤ 40	69 (54.8)	34 (47.2)	35 (64.8)	
Potassium (mEq/l)				0.014
> 3.6	92 (73.6)	59 (81.9)	33 (62.3)	
≤ 3.6	33 (26.4)	13 (18.1)	20 (37.7)	
Sodium (mEq/l)				0.493
> 145	09 (7.2)	04 (5.6)	05 (9.4)	
≤ 145	116 (92.8)	68 (94.4)	48 (90.6)	
PAO_2/FIO_2				0.006
> 200	64 (78.0)	41 (89.1)	23 (63.9)	
≤ 200	18 (22.0)	5 (10.9)	13 (36.1)	
HCO_3 (mEq/l)				0.696
> 22	22 (27.2)	13 (28.9)	09 (25.0)	
≤ 22	59 (72.8)	32 (71.1)	27 (75.0)	
Total	126 (100)	72 (57.1)	54 (42.9)	

*p-value: Chi-square test; †PAO_2/FIO_2: Relation between partial oxygen pressure in arterial blood and fraction of inspired oxygen; ‡HCO_3: Bicarbonate.

The individuals with creatinine higher than or equal to 1.2 mg/dl at admission had their risk of evolution to death increased by 77.0% when compared to those with creatinine below 1.2 mg/dl at admission. The risk of death was 2 times higher among the patients with GFR below 60 ml/min/1.73 m^2 and mechanical ventilation proved to be a protective factor against mortality in these individuals, as indicated in Table 5.

Table 5 – Gross and adjusted Hazard Ratio (HR) of the risk factors for death in an Intensive Care Unit in Rio Branco, Acre, Brazil, 2019. (n=126)

Variable	Gross Hazard Ratio (95% CI*)	Adjusted Hazard Ratio (95% CI)†
Mechanical ventilation		
No	1	1
Yes	0.40 (0.23-0.70)	0.41 (0.23-0.72)
Renal replacement therapy		
No	1	1
Yes	1.04 (0.56-1.95)	0.64 (0.30-1.34)
Acute kidney injury		
No	1	1
Yes	1.68 (0.96-2.96)	1.68 (0.95-2.95)
Serum creatinine at admission (mg/dL)		
≤ 1.2	1	1
> 1.2	1.82 (1.06-3.13)	1.77 (1.02-3.07)
Glomerular filtration rate at admission (ml/min/1.73 m^2)		
≥ 60	1	1
< 60	2.23 (1.26-3.93)	2.15 (1.21-3.82)
PAO_2/FIO_2‡		
> 200	1	1
≤ 200	1.94 (0.96-3.90)	2.09 (0.97-4.50)
Potassium (mEq/l)		
< 3.6	1	1
≥ 3.6	1.14 (0.65-2.00)	0.97 (0.53-1.77)
Leukocytes (mm^3)		
< 12,000	1	1
≥ 12,000	1.67 (0.83-3.37)	1.65 (0.81-3.35)
Sepsis		
No	1	1
Yes	1.79 (1.00-3.19)	1.69 (0.93-3.07)
Urea (mg/dl)		
< 40	1	1
≥ 40	1.49 (0.84-2.66)	1.40 (0.74-2.64)
Vasoactive drugs		
No	1	1
Yes	1.00 (0.58-1.75)	0.91 (0.50-1.65)
Glycaemia (mg/dl)		
< 180	1	1
≥ 180	1.26 (0.71-2.24)	1.21 (0.68-2.17)

Table 5 – Cont.

Variable	Gross Hazard Ratio (95% CI*)	Adjusted Hazard Ratio (95% CI)†
Nephrotoxic medications		
No	1	1
Yes	1.58 (0.90-2.75)	1.65 (0.94-2.90)
Reason for hospitalization§		
Surgical	1	1
Clinical	1.35 (0.77-2.37)	1.35 (0.77-2.36)
Age‖		
< 50	1	1
≥ 50	1.24 (0.72-2.12)	1.23 (0.72-2.11)

*95% CI: 95% Confidence Interval; †Adjustment variables: Age and reason for hospitalization; ‡PAO_2/FIO_2: Relation between partial oxygen pressure in arterial blood and fraction of inspired oxygen; §Adjustment variable: Age; ‖Adjustment variable: Reason for hospitalization.

DISCUSSION

In this study, the incidence of AKI in individuals admitted to the ICU was high. There was recovery in more than one third of those who evolved with the disease, and the survival of this group was more compromised for the following variables: female gender, not using mechanical ventilation, GFR at admission < 60 ml/min/1.73 m^2 and sepsis diagnosis. The risk factors associated with death in the population of critically-ill patients, regardless of the AKI diagnosis, were serum creatinine above 1.2 mg/dl and GFR < 60 ml/min/1.73 m^2 at admission.

The high incidence is considered expected according to the data found in literature and in some databases; however, the large variation of AKI values in ICU due to the ambiguous use of criteria to define the disease must be taken into account[10–11]. In addition, renal dysfunction is one of the main complications in critically-ill individuals. In the study that traced the clinical characteristics and severity of the patients admitted to public and private ICUs in the municipality of São Paulo, it was identified that almost 70% presented some level of this dysfunction, evidencing the assertion regarding its protagonism in the field of organic dysfunctions in severe patients[12].

In a meta-analysis carried out between 2005 and 2015 using three different databases and comparing incidence in the ICUs of developed and developing countries, the AKI incidence values were between 39.3 and 35.1, respectively. This corroborates the findings of the public ICU of a state in northern Brazil portrayed in this research[13].

During the analysis of the AKI group, it was observed that 67.3% were already admitted with some stage of the injury, mainly II and III, values which are higher than those found in countries like Spain and Japan, where the incidence values of stage III of the injury were 8.7% and 15.7%, respectively[14,15]. These data show the need for better interventions in the assistance before hospitalization in the ICU, from the diagnosis to the course of action, as well as they evidence the high incidence of AKI in the pre-ICU hospital setting that is possibly underdiagnosed.

The mean time elapsed between admission and the AKI diagnosis was similar to that verified in a multicentric trial conducted in 2012 with 30 ICUs in Beijing, China: most of the individuals developed AKI up to the fourth hospitalization day[1].

The high percentage of individuals who arrived with severe AKI led to a more positive WB mean and to a more reduced urinary behavior, even with the employment of clinical resources. Oliguria and anuria are bad predictors for the patient with AKI, despite being one of the phases of disease progression. They must be avoided and managed in a way so as to seek euvolemia, given

the already recognized unfavorable outcomes such as increased risk of mortality, non-recovery of the renal function, and greater dependence on mechanical ventilation[16–17].

Fluid management is an extremely necessary care measure in these patients; therefore, management with fluid replacement must be cautious. In septic patients, there is volume replacement therapy guided by institutionalized goals;[18] however, for the AKI group, the most recent guidelines do not stipulate specific parameters for this therapy[7].

This gap somehow contributes to the non-standardization of courses of action directed to the patient with AKI regarding fluid use. Their accumulation must be managed, offering the individual a more neutral or slightly negative balance. Diuretics must be used with caution both to reduce overload and to avoid it. However, the clinical observation regarding the patient's response to the therapy is essential for a better outcome. At the end, those who do not respond to the diuretics must be considered as candidates for early RRT[19].

RRT is an indispensable support factor for patients with severe AKI; however, it exposes them to risks already known and described in the literature, such as bloodstream infection associated with catheters. In a study carried out with 129 dialysis patients in Maringá, Brazil, the occurrence of infection associated with dialysis catheters was approximately 50%[20].

Continuous Renal Therapy (CRT) is an excellent dialysis treatment option for critically-ill patients; through it, slow removal of volume and slag is performed, offering more safety to critically-ill patients with hemodynamic instability and cerebral edema. There appears to be an improvement in survival, renal recovery and less dependence on dialysis in the long-term[21].

It is worth highlighting that severe AKI represents a high risk for mortality, increase in the hospitalization days, and risk of developing CKD in the long-term. Advanced age and male gender are proven risk factors for this evolution[22].

In a multinational study on the epidemiology of AKI in critically-ill patients, it was evidenced that hospital mortality was associated with disease progression, in which the chance for stage 3 was seven times higher. That is, progression to severe AKI represents higher chances of hospital mortality and worse renal function at hospital discharge[8]. In this study, the individuals of the group who did not recover from AKI met the severe AKI criteria, which shows that this condition must be early and adequately managed since, in addition to the increased risk of mortality, there is a high percentage of individuals who do not revert the renal condition.

Analyzing the study survivors, the most intriguing finding was about the use of mechanical ventilation: the group of patients who used it at some moment survived more than those who did not. This refutes results already found in other research studies which, despite not recognizing its indispensability in the treatment of critically-ill patients, associate it with deleterious effects to the individual[23–24].

Observing the behavior related to gender in the outcomes, evolution to AKI and the occurrence of death were higher among the men, even though this analysis was not significant. Gender difference or dimorphism has already been tested in other cohort studies, clinical trials and meta-analyses, and the existence of this behavioral difference of the disease in the genders is undeniable. Many mechanisms were not yet totally clarified, but it is known that this dimorphism is mediated by sex steroids[1].

Individuals with glomerular filtration rates at admission below 60 ml/min/1.73 m^2 had a worse performance in the survival assessment of the AKI group. In this study, the GFR < 60 ml/min/1.73 m^2 and creatinine > 1.2 mg/dl variables, both at admission, were independent factors for mortality. They act together, and isolated creatinine is not a reliable measure of the renal function due to the factors that underestimate or mask its values[25]. However, the GFR estimate is considered more accurate and adequate for patient management[6].

This research showed that AKI conditions the individual to an independent risk of evolving to death when hospitalized in the ICU. It is worth highlighting that the AKI variable did not entirely enter into the final model, but that those which determine the individual's renal function did. Therefore, it is noticeable that changes, even if discrete, in the renal function impose an increased risk of death.

Discrete changes in the renal function and risk of death had already been analyzed in other papers. It was observed that, even small additions to the serum creatinine levels and more discrete reductions in the renal function predispose the individual to a significant risk of death. The meta-analysis in question monitored 78,855 patients, who were distributed among eight studies in a way that the risk of death of those with discrete reductions in the renal function was 1.8 (95%CI 1.3-2.5)[26].

Currently, the care provided to those who recovered from AKI is still neglected; however, a number of studies reinforce the importance of interventions and assessments in this group, given the high risk of complications, such as cardiovascular conditions, CKD and mortality[27]. In view of that, there is a discussion about the need to implement post-AKI care, with monitoring during the 90 days after discharge or recovery of these individuals[28], due to the high incidence of recurrent AKI and to the risk of the aforementioned outcomes.

In a research study that assessed AKI survivors in the long-term with a follow-up time of 2.4 years, it was evidenced that 356 (8.0%) patients evolved to the need of chronic dialysis and that 1,475 (34.0%) died; when the risk for evolution to chronic dialysis was estimated, it was above 10.0% in two different statistical methods[29]. This post-AKI care is already a reality in some centers and presented good results, such as improvement in survival[30].

The use of KDIGO to define AKI can be considered a strength, since data on the incidence of AKI are not uniform due to the previously adopted criteria, such as RIFLE (Risk, Injury, Failure, Loss, End-Stage) and AKIN (Acute Kidney Injury Network). In addition, the death estimate in the AKI condition, the AKI assessment on specific days (D1, D3 and D7), and the determination of prognostic factors for death in patients admitted to the ICU contribute to the robustness of the paper. The relevance of the study for the health area also stands out, especially for Nursing, as it emphasizes the importance of early recognizing AKI, adequately managing fluids (through water balance) and identifying the need for RRT in the ICU.

However, some limitations must be pointed out, such as the absence of detailed data on mechanical ventilation therapy and RRT, in addition to the fact that the progression of those who reverted the AKI condition was not assessed. Even though it was not proposed in the objectives of this paper, this assessment elucidates many questions regarding the behavioral dynamics of AKI in the short- and long-term. Another possible limitation refers to the patients' differences regarding their reason for hospitalization (clinical or surgical) or even their severity, given that this information can distort the results found. It is noted that the reason for hospitalization was included in the adjustment model of the potentially confounding variables.

CONCLUSION

It was verified that the incidence of acute kidney injury is high and that a considerable percentage of cases arrive at the unit in a severe condition. Non-recovery was verified in 63.3% of the patients who evolved to AKI. Survival of the AKI group is aggravated by gender dimorphism and by GFR < 60 ml/min/1.73 m^2. The risk factors for death in the population of critically-ill patients were creatinine > 1.2 mg/dl and GFR < 60 ml/min/1.73 m^2, both at admission.

Therefore, screening actions of individuals at risk of developing AKI must be employed in the pre-ICU setting. The institutionalization of clinical protocols adjusted to the reality is an important strategy to reduce the number of neglected AKI cases. Fluid management, a responsibility of the

Nursing and Medical teams, must be rigorously performed. The assessment of the patient's response to the diuretics is another important aspect, as well as non-hesitation to perform early RRT.

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NOTES

ORIGIN OF THE ARTICLE

Extracted from the Course Competition Paper - Incidence, risk factors and survival of critically-ill patients with acute kidney injury, presented to the Hospital Multiprofessional Residency Program with an emphasis on intensive care of *Universidade Federal do Acre,* in 2020.

CONTRIBUTION OF AUTHORITY

Study design: Lopes WF, Amaral TLM, Prado PR.
Data collection: Araújo LP, Lopes WF.
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APPROVAL OF ETHICS COMMITTEE IN RESEARCH

Approved in the Research Ethics Committee of *Universidad Federal do Acre*, opinion No.3,294,722; Certificate of Presentation for Ethical Appreciation 47577215.2.0000.5009.

CONFLICT OF INTERESTS

There is no conflict of interests.

EDITORS

HISTORICAL

Received: December 01, 2020.
Approved: May 28, 2021.

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