

# Prevalence and factors associated with acute kidney injury in patients in intensive care units

*Prevalência e fatores associados à lesão renal aguda em pacientes nas unidades de terapia intensiva*  
*Prevalencia y factores asociados a la lesión renal aguda en pacientes en unidades de cuidados intensivos*

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## ABSTRACT

**Objectives:** to identify the prevalence and factors associated with the development of acute kidney injury in critically ill patients. **Methods:** a cross-sectional study, conducted from June 2018 to August 2019. The Kidney Disease Improving Global Outcomes was used to classify acute kidney injury. A significant value was set at  $p < 0.05$ . **Results:** a total of 212 patients were included, of whom 35.8% evolved into an acute kidney injury. Patients with acute kidney injury had hypertension, higher levels on severity scores and a higher baseline creatinine rate  $> 1.5$  mg/dL, also, when applied logistic regression, were 7 times more likely to develop acute kidney injury, Odds Ratio 7.018. More than half (56.6%) of the patients with acute kidney injury died. Moreover, 26.7% of these patients developed pressure sore. **Conclusions:** the prevalence of kidney injury was high (35.8%). The patients who developed it had a higher severity, mortality, and pressure sore index.

**Descriptors:** Acute Kidney Injury; Intensive Care Unit; Critical Care; Mortality; Prevalence.

## RESUMO

**Objetivos:** identificar a prevalência e fatores associados ao desenvolvimento de lesão renal aguda em pacientes graves. **Métodos:** estudo transversal, realizado entre junho de 2018 e agosto de 2019. Para classificação da lesão renal aguda, utilizou-se o *Kidney Disease Improving Global Outcomes*. O valor  $p < 0,05$  foi considerado significativo. **Resultados:** incluíram-se 212 pacientes, destes 35,8% evoluíram para lesão renal aguda. Os pacientes com lesão renal aguda tinham hipertensão, maior pontuação nos scores de gravidade e maior taxa de creatinina basal  $> 1,5$  mg/dl, além de, quando aplicada a regressão logística, apresentarem sete vezes mais chances de desenvolver lesão renal aguda, *Odds Ratio* 7,018. Mais de metade (56,6%) dos pacientes com lesão renal aguda foram a óbito. Além disso, 26,7% desses pacientes desenvolveram lesão por pressão. **Conclusões:** a prevalência de lesão renal foi elevada (35,8%). Os pacientes que a desenvolveram apresentaram maior índice de gravidade, mortalidade e índice de lesão por pressão.

**Descritores:** Lesão Renal Aguda; Unidade de Terapia Intensiva; Cuidados Críticos; Mortalidade; Prevalência.

## RESUMEN

**Objetivos:** identificar la prevalencia y los factores asociados al desarrollo de lesión renal aguda en pacientes críticos. **Métodos:** estudio transversal, efectuado entre junio de 2018 y agosto de 2019. Para clasificar la lesión renal aguda, se utilizó el *Kidney Disease Improving Global Outcomes*. Se consideró significativo el valor  $p < 0,05$ . **Resultados:** se incluyeron 212 pacientes, de los cuales el 35,8% evolucionó para lesión renal aguda. Los pacientes con lesión renal aguda tenían hipertensión, grados más altos en las puntuaciones de gravedad y una tasa de creatinina basal más alta  $> 1,5$  mg/dL, además de que, cuando se aplica la regresión logística, tenían 7 veces más probabilidades de desarrollar lesión renal aguda, *Odds Ratio* 7,018. Más de la mitad (56,6%) de los pacientes con lesión renal aguda fallecieron. Además, el 26,7% de estos pacientes desarrolló lesiones por presión. **Conclusiones:** la prevalencia de lesión renal fue alta (35,8%). Los pacientes que la desarrollaron tuvieron mayor severidad, mortalidad e índice de lesión por presión.

**Descriptorios:** Lesión Renal Aguda; Unidad de Cuidados Intensivos; Cuidados Críticos; Mortalidad; Prevalencia.

## INTRODUCTION

Acute kidney injury (AKI) has significant representativeness in the morbidity and mortality of patients in the Intensive Care Unit (ICU) and is associated with poorer outcomes even after hospital discharge<sup>(1)</sup>. The prevalence of AKI in critically ill patients highlighted in the study by Benichel and Meneguim (2020) was 7.5%<sup>(2)</sup>, while the incidence can surpass 50%<sup>(3)</sup>, and the mortality for those who needed replacement therapy reaches up to 72.9%<sup>(4)</sup>. For patients who survive this condition, regardless of going through dialysis, it is associated with a higher risk of mortality for at least 90 days after hospital discharge, increasing proportionally with the severity of AKI<sup>(5)</sup>.

Critically ill patients are more susceptible to developing it mainly because of clinical instability and previous risk factors, such as advanced age, sepsis, hypovolemia, surgery, use of nephrotoxic drugs, among others<sup>(6-7)</sup>. Furthermore, AKI is related to different comorbidities that include the deficiency to self-regulate organs, such as hypertension and diabetes<sup>(8)</sup>.

AKI is one of the most common complications observed in ICU; however, it is sometimes underdiagnosed and is associated with a greater need for vasoactive drugs, mechanical ventilation (MV), sedation, as well as longer hospital stay and increased hospital costs, which can even evolve into chronic kidney disease and even death<sup>(1,9)</sup>.

In this scenario, the health team is required to hold a schedule of safe and quality care, capable of recognizing the clinical profile and severity of these patients. Moreover, patients with this illness require additional care from the team, when compared to individuals without this condition<sup>(10)</sup>. Accordingly, the Kidney Disease Improving Global Outcomes (KDIGO)<sup>(11)</sup> proposes a classification aiming at standardizing the definition of AKI and allow the daily assessment of patients at risk of developing it, increasing the sensitivity and early diagnosis.

Studies that address the clinical characteristics of a given population are essential so that renal protection and early diagnosis measures can be taken to minimize the prevalence of this illness<sup>(8)</sup>. Thus, it is understood that knowledge about these characteristics works as a marker for the most vulnerable patients or high-risk groups, intending to obtain a standardized approach and better definition of long-term results<sup>(5,12)</sup>.

## OBJECTIVES

To identify the prevalence and factors associated with the development of acute kidney injury in critically ill patients.

## METHODS

### Ethical aspects

The present study complied with national and international standards of ethics in research involving human beings, according to Resolution 466/12. And was approved by the Research Ethics Committee of the *Universidade Federal de Sergipe*.

### Study design, period, and setting

A cross-sectional study guided by the STROBE tool, carried out in the only two Intensive Care Units in the State of Sergipe,

in the *agreste* region, located in the cities of Itabaiana (HRI) and Lagarto (HUL), both with 10 beds. In both hospitals studied, ICUs are classified as general ICUs that serve clinical and surgical patients, without separation by specialty. Data collection took place from August 2018 to July 2019.

### Sample, inclusion, and exclusion criteria

The sample was outlined in a non-probabilistic way and individuals were selected by convenience. A sample of 212 patients was obtained, who met the following inclusion criteria: minimum stay of 24 hours in ICU, age greater than or equal to 18 years, and without a previous diagnosis of AKI upon admission to ICU. Those who did not follow up on creatinine and urine output were excluded, as well as those diagnosed with chronic kidney disease undergoing dialysis.

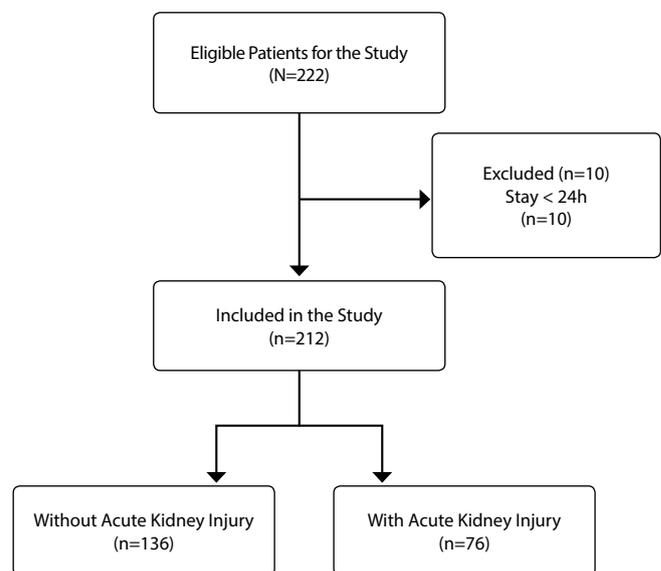


Figure 1 – Flowchart of eligibility and inclusion in the study

### Study protocol

The patients included in the study were followed up from admission to discharge, death, or transfer from ICU. Data collection took place by filling out the research instrument itself. The instrument comprised sociodemographic data, clinical history, support for admission to ICU, and devices in use.

To assess the severity, the Simplified Acute Physiology Score III (SAPS 3) scores were used on admission and discharge, and the Sequential Organ Failure Assessment (SOFA) was used daily after 24h of admission. The primary outcome was the AKI in ICU and secondary outcomes were: length of stay in ICU and hospital, the occurrence of pressure sore, and mortality.

The results of laboratory tests were collected daily according to the availability of these values in the medical chart. The serum creatinine value on admission was considered as baseline creatinine and this served for comparisons with the other results collected daily to then define the occurrence or not of AKI, according to

KDIGO: Stage 1: serum creatinine at values  $\geq 0.3\text{mg/dl}$  or urinary volume less than  $0.5\text{ml/kg/h}$  for 6 to 12 hours; Stage 2: 2 to 2.9 times increase in serum creatinine concerning baseline or urinary volume  $< 0.5\text{ ml/kg/h}$  for a period greater than or equal to 12 hours; Stage 3: a 3-fold increase in serum creatinine compared to baseline, creatinine values  $\geq 4\text{mg/dl}$  or beginning of renal replacement therapy<sup>(11)</sup>.

### Analysis of results and statistics

The data obtained were inputted in Excel 2010 program tables and subsequently to statistical analysis with the Statistical Package for the Social Sciences (SPSS), version 25.0. The categorical variables were presented in absolute and relative frequencies, while the continuous variables were presented as average and standard deviation or median and interquartile range. Kolmogorov-Smirnov tested the normality of the collected data, while the Chi-square and Fisher's exact tests, when appropriate, were used to test the associations between categorical variables. To test the associations between continuous variables, Student's t and Mann Whitney tests were used, when appropriate, as well as binary logistic regression analysis to test the influence of variables on the primary outcome. A significant value was set at  $p < 0.05$ .

### RESULTS

Of the total number of patients evaluated in the study period, 76 (35.8%) developed AKI. There was no significant difference between groups for most clinical characteristics. Nevertheless, the number of patients with systemic arterial hypertension (SAH) and with creatinine greater than  $1.5\text{ mg/dl}$  on admission to ICU was higher in the group of patients who developed AKI during hospitalization. Regarding the profile of patients on admission, there was a higher frequency of patients using a central venous catheter (37.3% vs. 55.3%,  $p=0.012$ ) in the group of AKI patients. Moreover, the values of the prognosis score (SAPS 3) and the organ failure assessment (SOFA) were higher in patients in the AKI group (Table 1).

In the analysis of secondary outcomes, there was a significant difference in the number of deaths (29.6% vs. 56.6%,  $p < 0.001$ ) and pressure sore (8.1% vs. 26.7%,  $p < 0.001$ ) between groups without and with AKI respectively (Table 2).

When considering the prevalence of AKI by stages separately, it was observed that 36.8% were in KDIGO 1, 19.7% were in KDIGO 2, and 43.4% in KDIGO 3. Table 3 shows the distribution of outcomes according to each KDIGO stage. It should be underlined that there was no significant association between the outcomes in any of the stages (1, 2, or 3).

In the analysis of factors associated with the prevalence of AKI in the evaluated patients, the factors that influenced the development of AKI were identified as the SOFA score value in the first 24 hours of admission and had a baseline creatinine greater than  $1.5\text{ mg/dl}$  on admission to ICU. Patients with changed creatinine had seven times more risk for the outcome; and for each additional point in the SOFA values, there is a 17.6% increase in the risk for the outcome (Table 4).

**Table 1** – Univariate analysis of the clinical and demographic admission-related characteristics of the surveyed patients

Variable	Without Acute Kidney Injury (n=136)	With Acute Kidney Injury (n=76)	p value
Age in years, n(%)	59 ± 19	60 ± 19	0.935
Male gender, n(%)	80 (58.8)	37 (48.7)	0.155
White race, n(%)	78 (57.8)	46 (62.2)	0.537
Previous surgery, n(%)	25 (18.7)	18 (24.3)	0.334
Heart failure, n(%)	15 (11.3)	11 (15.1)	0.433
SAH, n(%)	48 (36.1)	39 (52.7)	0.002
DM, n(%)	35 (26.3)	25 (33.8)	0.256
Current smoker, n(%)	19 (14.3)	8 (10.8)	0.477
Previous smoker, n(%)	21 (15.8)	15 (20.3)	0.415
Atrial Fibrillation, n(%)	9 (6.9)	4 (5.4)	0.699
Previous AMI, n(%)	14 (10.5)	7 (9.5)	0.808
Previous CVA, n(%)	18 (13.5)	13 (17.6)	0.436
Creatinine $> 1,5\text{ mg/dL}$ , n(%)	15 (11.3)	37 (50.0)	<b>&lt;0.001</b>
Admission Support			
Dobutamine, n(%)	5 (3.7)	3 (4.0)	0.914
Noradrenaline, n(%)	34 (25.0)	24 (32.0)	0.257
Fentanyl, n(%)	85 (62.5)	43 (57.3)	0.462
Midazolam, n(%)	43 (31.6)	32 (42.1)	0.126
NT, n(%)	77 (57.5)	46 (64.5)	0.319
NG, n(%)	22 (16.4)	11 (14.5)	0.710
BC, n(%)	117 (88.0)	62 (81.6)	0.205
CVC, n(%)	50 (37.3)	42 (55.3)	0.012
OTT, n(%)	70 (52.2)	50 (65.8)	0.057
SOFA on the 1st day of ICU, average ± SD	3.8 ± 4.4	5.1 ± 2.5	0.010
SAPS 3 on admission to ICU, average ± SD	29.9 ± 12.4	37.6 ± 15.8	<b>&lt;0.001</b>
Charlson's score, average ± SD	2.9 ± 2.3	2.9 ± 2.2	0.970

Note: data were expressed in absolute number and percentage (%). Where: n – absolute frequency; % – relative frequency; HF – heart failure; AMI – acute myocardial infarction; SAH – systemic arterial hypertension; DM – Diabetes Mellitus; CVC – cerebrovascular accident; NT – nasogastric tube; NG – nasogastric tube; BC – bladder catheter; CVC – central venous catheter; OTT – orotracheal tube; SOFA – Sequential Organ Failure Assessment; SAPS 3 – Simplified Acute Physiology Score 3; Charlson score – Charlson's Comorbidity Index; SD – standard deviation.

**Table 2** – Clinical outcomes of patients evaluated in the study

Variable	Without Acute Kidney Injury (n=136)	With Acute Kidney Injury (n=76)	p value
Deaths, n(%)	40 (29.6)	43 (56.6)	<b>&lt;0.001</b>
Pressure sore, n(%)	11 (8.1)	20 (26.7)	<b>&lt;0.001</b>
Acute myocardial infarction, n(%)	6 (4.5)	4 (5.3)	0.797
Cerebrovascular accident, n(%)	10 (7.5)	7 (9.2)	0.655
MV $> 48$ horas, n(%)	68 (50.4)	45 (59.2)	0.216
Infection, n(%)	56 (42.1)	37 (48.7)	0.357
Readmission, n(%)	5 (3.9)	2 (2.9)	0.709
LIS, average ± SD	15.3 ± 15.9	13.5 ± 11.3	0.639
LHS, average ± SD	22.6 ± 15.6	17.7 ± 13.7	0.682
SAPS 3 discharge/death, average ± SD	38.1 ± 14.3	46.4 ± 19.8	0.246
SOFA discharge/death, average ± SD	14.9 ± 14.0	19.5 ± 16.6	0.177

Note: data were expressed as average, standard deviation, absolute number, and percentage (%). Where: n – absolute frequency; % – relative frequency; SD – standard deviation; PI – pressure sore; MV – mechanical ventilation; LIS – length of ICU stay; LHS – length of hospital stay; SOFA – Sequential Organ Failure Assessment; SAPS 3 – Simplified Acute Physiology Score 3.

**Table 3** – Distribution of clinical outcomes of patients evaluated according to the Kidney Disease Improving Global Outcomes classification stage

Outcome	KDIGO 1 (n=28)	KDIGO 2 (n=15)	KDIGO 3 (n=33)	p value
Deaths, n(%)	13 (46.4)	5 (33.3)	14 (46.7)	0.523
PI, n(%)	11 (40.7)	4 (26.7)	7 (22.6)	0.094
AMI, n(%)	1 (3.7)	0 (0.0)	0 (0.0)	NS
CVC, n(%)	3 (11.1)	1 (6.7)	1 (3.2)	0.179
MV > 48 hours, n(%)	16 (57.1)	8 (53.3)	19 (61.3)	0.419
Infection, n(%)	14 (51.9)	8 (53.3)	14 (46.7)	0.400
LIS, average ± SD	14.1 ± 11.3	18.0 ± 13.5	13.7 ± 14.8	NS
LHS, average ± SD	18.6 ± 13.2	23.1 ± 20.1	18.5 ± 18.6	NS

Note: Data were expressed as average, standard deviation, absolute number, and percentage (%). Where: n – absolute frequency; % – relative frequency; KDIGO – Kidney Disease Improving Global Outcomes; SD – standard deviation; NS – not significant; PI – pressure sore; AMI – acute myocardial infarction; CVC – cerebrovascular accident; MV – mechanical ventilation; LIS – length of ICU stay; LHS – length of hospital stay; SOFA – Sequential Organ Failure Assessment; SAPS 3 – Simplified Acute Physiology Score 3.

**Table 4** – Factors associated with the development of Acute Kidney Injury in the evaluated patients

Variable	OR	CI 95%	p value
Use of a central venous catheter	1.710	0.847 – 3.454	0.135
Baseline creatinine > 1,5mg/dL	7.018	3.216 – 15.316	<0.001
Male gender	1.891	0.939 – 3.808	0.075
Use of orotracheal tube	0.909	0.432 – 1.913	0.801
NAS in the first 24 hours	1.011	0.977 – 1.047	0.257
SAPS 3 on admission	1.011	0.981 – 1.043	0.469
SOFA in the first 24h	1.176	1.032 – 1.340	0.015

Note: OR – odds ratio; CI – confidence interval; NAS – Nursing Activities Score; SOFA – Sequential Organ Failure Assessment; SAPS 3 – Simplified Acute Physiology Score 3.

## DISCUSSION

The results found in this study show the real situation of the only ICUs that are located outside the capital of the State of Sergipe and are considered as of medium complexity. From the data of this work, we could observe that the clinical outcomes of the evaluated patients are directly related to the prevalence of development of AKI. These patients also had a higher prevalence of systemic arterial hypertension and baseline creatinine above 1.5 mg/dl, as well as the use of a central venous catheter. Such findings confirm the characteristic clinical profile found in studies that also analyzed variables associated with the development of AKI<sup>(8,13)</sup>.

The main evidence about this condition and prognosis points out that these patients are at higher risk for developing chronic kidney disease or a new episode of AKI<sup>(14)</sup>. It is also associated with the risk of hospital readmission, besides a higher risk of hypertension and the occurrence of cardiovascular events and, consequently, increased morbidity and mortality<sup>(13)</sup>.

The prevalence of AKI found in this study was 35.8%, which is in line with data presented by other national studies (25.5% and 44.2%)<sup>(15-16)</sup>. When analyzing the stage according to the KDIGO criterion, there is a predominance of stage 3, which represents greater severity. This fact may be associated with the late diagnosis of AKI due to significant clinical deterioration since patients who developed AKI had poorer indexes in the severity scores at

the time of admission<sup>(8)</sup>. Nevertheless, no statistically significant difference was observed regarding the different stages of AKI according to the KDIGO criterion and the outcomes.

In this study, the gender variable was not statistically different between groups with and without AKI. However, in the national and international literature, the male population is predominant<sup>(2,17-18)</sup>. Although age did not show a significant difference between groups, there is a consensus that high age is a risk factor for AKI<sup>(15-16)</sup>.

Comorbidities such as diabetes mellitus and systemic arterial hypertension are predisposing factors for the development of AKI<sup>(14)</sup>. In this study, it was observed that more than half had SAH, thus requiring a more rigorous follow up because they are more susceptible to poorer prognosis<sup>(19)</sup>. Furthermore, other previous comorbidities such as heart failure, acute myocardial infarction, and stroke showed a significant difference in the study.

Another important point is that just as SAH leads to a higher probability of developing AKI, on the other hand, the occurrence of this condition also increases the chance of high blood pressure. Accordingly, a study conducted in an integrated health care system in California found that AKI was independently associated with a 22% increase (95% CI, 12% - 33%) in the chance of increasing blood pressure in individuals without previous SAH, where this chance increases progressively with the severity of AKI<sup>(14)</sup>.

As for intensive support at the time of ICU admission, understood here as the use of vasoactive and sedative drugs, as well as the use of invasive devices, they did not show a correlation with the development of AKI, although these procedures are necessary for patients with greater clinical impairment and contribute significantly to the occurrence of infection and, consequently, with the increased severity and mortality of individuals<sup>(20)</sup>. Moreover, one can understand that the intensive support used has contributed to the more adequate follow up of various parameters (including urine output) of patients, which allows for earlier interventions.

Some factors are known as risky for unfavorable outcomes, which include lengthy hospital stay, old age, comorbidities, as well as the use of vasoactive drugs. Besides contributing to a higher incidence of complications and increased patient weakness, as well as hospital costs<sup>(4)</sup>.

The early detection of patients with risks associated with the development of AKI can lead to a diagnosis in the early stages and help in the development of strategies to prevent and treat it, which are crucial measures to reduce the poor prognosis. In the care process, the act of incorporating uniform measures to define AKI, such as the use of the KDIGO classification, can be an important mechanism for systematic and preventive care<sup>(12)</sup>.

Creatinine is described as a non-specific biomarker for renal function because it overestimates the glomerular filtration rate and is subject to the muscle mass; however, it remains the only biomarker available in clinical practice. Although it is not a satisfactory marker for early diagnosis, since the serum creatinine value above normal happens only after the decrease of around 50%-60% in the glomerular filtration rate<sup>(21)</sup>. In this study, most patients who developed AKI had serum creatinine greater than 1.5 mg/dl on ICU admission. Additionally, the fact of having high creatinine levels increased the chance of developing this outcome seven times during ICU stay. This suggests that, even though it is not the most appropriate biomarker, its importance

on admission points to the possibility of its use in following up and identifying decreased renal function<sup>(22)</sup>.

Among the assessed outcomes, the development of pressure sore and death were associated with AKI. Mortality among these patients was high and is in line with other national studies that showed mortality from 50% to 90% in AKI patients<sup>(4,22)</sup>. The presence of this illness implies a longer ICU stay, more chances of complications, and systemic decline that may influence mechanisms involved in preserving the skin integrity, besides the fact that the patient remains exposed for a longer time restricted to the bed and subject to the development of pressure sore, thus impacting on morbidity and mortality<sup>(8)</sup>.

In our study, the SOFA presented itself as an independent risk factor and each additional point in this score represented a 17.6% increase in the chances for the development of AKI. Nevertheless, the development of acute kidney injury is associated with a substantially greater risk of negative outcomes. Accordingly, a multicenter study observed that the presence of AKI causes a gradual increase in mortality over 28 days according to the worsening of the injury ( $p < 0.001$ )<sup>(23)</sup>, besides an association with rapid progression to chronic kidney disease ( $p = 0.001$ ) and increased mortality within 1 year<sup>(24)</sup>.

### Study limitations

The limitations of this study concern the lack of records in the medical charts, as well as more in-depth assessments in the

scope of renal function. Moreover, one of the study settings did not have hemodialysis treatment available, and the sample size was relatively small.

### Contributions to the health area

The contribution of this research is related to the findings concerning the clinical characterization and the aspects that were associated with the development of AKI, highlighting the relevance of early identification, given its impact on short and long-term morbidity and mortality, and hospital costs. Moreover, the high injury rates in advanced stages emphasize the deficit of hospitals for preventive measures and early diagnosis. In this perspective, the characteristics presented here can assist ICU nurses in the identification of patients at risk for AKI and based on this, make use of strategies to identify early clinical manifestations and preventive measures.

### CONCLUSIONS

The prevalence of acute kidney injury was high in the studied sample (35.8%). Creatinine values greater than 1.5 mg/dl on admission to ICU and elevation of the SOFA score in the first 24 hours of hospitalization were factors associated with the development of AKI. Patients who developed AKI had high severity, mortality, and pressure sore index.

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