



Factors associated with acute kidney injury in surgical patients at the intensive care unit

Fatores associados à lesão renal aguda em pacientes cirúrgicos na unidade de terapia intensiva

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Objective: to analyze factors associated with acute kidney injury in surgical patients at the intensive care unit. **Methods:** case-control study including survey of patient history records and a sample of 246 patients. For the differences of proportions and means, the chi-squared and Student's t-test were used, respectively. The association between variables was verified by means of univariate and later multivariate analyses with logistic regression. The odds ratio was used as an effect measure and significance was set at 5%. **Results:** the main associated factors were: period of hospitalization, gastrointestinal etiology, mechanical ventilation, sepsis, hypovolemia, arrhythmia, furosemide, vasopressors, simultaneous antibiotics and concomitant occurrence of more than three factors. **Conclusion:** acute kidney injury represented a systemic event, affected patients of advanced age who were hospitalized longer and predisposed to death. It was associated with gastrointestinal etiologies, problems, nephrotoxic drugs and concomitant factors that contribute to increase the risk of its development.

Descriptors: Acute Kidney Injury; Risk Factors; Critical Care; Case-Control Studies.

Objetivo: analisar fatores associados à lesão renal aguda em pacientes cirúrgicos na unidade de terapia intensiva. **Métodos:** estudo caso-controle com levantamento dos registros de prontuário e amostra de 246 pacientes. Para as diferenças entre proporções e médias, foram utilizados os testes qui quadrado e *t* de *Student*, respectivamente. A associação entre variáveis foi verificada por meio de análises univariadas e, posteriormente, multivariadas, com regressão logística. Foi empregada *odds ratio*, como medida de efeito, e considerado nível de significância de 5%. **Resultados:** os principais fatores associados foram: tempo de internação, etiologia gastrointestinal, ventilação mecânica, sepse, hipovolemia, arritmia, furosemida, vasopressores, antibióticos simultâneos e concomitância de mais de três fatores. **Conclusão:** a lesão renal aguda representou evento sistêmico, acometeu pacientes com idade avançada e maior tempo de internação, e predispôs ao óbito. Foi associada a etiologias gastrintestinais, intercorrências, drogas nefrotóxicas e concomitância de fatores que contribuiu para aumentar o risco do seu desenvolvimento.

Descritores: Lesão Renal Aguda; Fatores de Risco; Cuidados Críticos; Estudos de Casos e Controles.

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Introduction

Acute kidney injury results in the decrease of the glomerular filtration rate and urinary volume, triggering hydroelectrolytic disorders and in the acid-base system⁽¹⁾. Considered a challenge in the hospital context, it varies according to the patients' severity and complexity, accounting for about 1.0% of all hospitalizations, and complicating up to 7.0% of the cases admitted for other diagnoses⁽²⁾.

In an intensive care unit, acute kidney injury raises mortality by up to 80.0%⁽¹⁾. It is associated with pre-existing clinical conditions, exposures during hospitalization and patients' increased susceptibility, as well as other synergistic conditions, such as higher age range, chronic-degenerative diseases and vulnerability in view of the therapies employed, including postoperative periods⁽¹⁾.

Evidence suggests that acute renal injury has significant repercussions in the evolution of surgical cases in an intensive care setting, mainly associated with large procedures, hemodynamic instability, comorbidities, severity and mechanical ventilation⁽³⁻⁴⁾.

Detecting these factors early and outlining the profile of patients admitted postoperatively in intensive care units are essential for the prevention and care of patients potentially at risk of developing acute kidney injury. This confirms the importance of high-quality health care, especially in nursing, with a systematic and evidence-based practice.

In this sense, the purpose of this research was to answer the following questions: What is the profile of critical surgical patients who developed acute kidney injury in a medium-complexity hospital? What are the factors associated with this dysfunction? Is there a difference between the factors associated with surgical patients when compared to their controls? Is the concomitant occurrence of risk factors a predictor of acute kidney injury in intensive care?

Thus, the objective in this study was to analyze factors associated with acute renal injury in surgical patients in the intensive care unit.

Methods

An exploratory case-control study with a quantitative approach was carried out in an adult intensive care unit of a private hospital in the interior of São Paulo, offering 20 beds. Non-probabilistic sample of patients who developed acute kidney injury and were hospitalized in this unit in the years 2014 and 2015. The data were collected from January to November 2016 by consulting the electronic medical records.

To test the research hypothesis, the participants were divided into two groups: Group I (case), consisting of surgical patients who developed acute kidney injury in the postoperative period; and Group II (control), composed of patients hospitalized in the same period who did not develop acute renal injury.

For the cases, patients were considered eligible if 18 years of age or older, male and female, with an increase of 0.3 mg/dL over baseline serum creatinine in the first 48 hours of admission to the intensive care unit, according to the definition of the Acute Kidney Injury Network (AKIN), by the creatinine criterion. Baseline creatinine was determined by the last value established by the institution's laboratory measure, taken at least 30 days and no more than six months before the date of admission to the intensive care unit. For those patients who did not have previous creatinine test, the first value collected upon the patient's admission to the hospital was considered and, also, when not available, the first value taken during the hospitalization in the research scenario. Only the creatinine criterion was adopted to stratify the patients, considering urinary flow as a dynamic variable and influenced by clinical and hemodynamic factors.

As controls, surgical patients who were 18 years of age or older were eligible; male and female; and who did not show an increase of 0.3 mg/dL over baseline serum creatinine in the first 48 hours of admission to the intensive care unit. They were matched according to the criterion of the patients' mean age in Group I, in a ratio of 1:1, due to the influence of this characteristic on the development of acute kidney in-

jury in intensive care units^(1,3-4).

For both groups, patients with chronic kidney failure documented in the medical records and rehospitalizations were excluded.

Initially, data were collected from the patients in Group I and, after their matching by age, the data were collected for Group II. We selected 123 patients who developed acute kidney injury in the study period and the same number of controls.

For both groups, a six-part form was used: identification data (gender, age, color and marital status), hospitalization variables (days of hospitalization, hospitalization development, mechanical ventilation and diagnosis upon admission), antecedents and/or clinical conditions (cardiovascular and nephrological risk factors and comorbidities), procedures performed (vascular, contrast, cardiac and extracorporeal surgery), nephrotoxic drugs and laboratory tests.

Cardiovascular risk factors and associated comorbidities were: diabetes mellitus, arterial hypertension, dyslipidemia, obesity, thromboembolic diseases, sepsis, chronic obstructive pulmonary disease, stroke, rhabdomyolysis, congestive heart failure, myocardio-pathy (ischemic and/or dilated), cardiac arrhythmia (atrioventricular block, fibrillation and/or arrhythmia), hypovolemia (hemorrhage and/or dehydration) and cardiorespiratory arrest event.

Use of furosemide, non-steroidal or hormonal anti-inflammatory drugs, angiotensinogen-converting enzyme inhibitors, chemotherapeutic agents, antibiotics and vasoactive drugs were included as nephrotoxic drugs⁽⁵⁻⁸⁾. Simultaneous antibiotic corresponded to the concomitant use of two or more drugs.

Initially, a descriptive analysis was performed for all variables. For the differences between proportions and means, chi-square and Student's t tests were used, respectively. The association between variables was verified through univariate and, later, multivariate analyses with logistic regression. Odds ratio was used as an effect measure with a 95% confidence interval. In all analyses, a 5% significance level was considered. The analyses were carried out in the software Statistical Package for the Social Sciences, version 21.

The study complied with the formal requirements contained in the national and international regulatory standards for research involving human beings.

Results

The prevalence of acute kidney injury corresponded to 4.5% and, of all participants, practically half was classified in stage I according to the AKIN criteria (data not presented in table).

In Table 1, the study participants' sociodemographic and clinical characteristics are described.

Table 1 – Sociodemographic and clinical variables of study participants

Variable	Group I		Group II		P
	Yes n (%)	No n (%)	Yes n (%)	No n (%)	
Male sex	64 (52.0)	59 (48.0)	61 (49.6)	62 (50.4)	0.702
With partner	67 (54.5)	56 (45.5)	87 (70.7)	36 (29.3)	0.008*
Caucasian	109 (88.6)	14 (11.4)	102 (82.9)	21 (17.1)	0.202
Diabetes	37 (30.1)	86 (69.9)	29 (23.6)	94 (76.4)	0.250
Hypertension	71 (57.7)	52 (42.3)	64 (52.0)	59 (48.0)	0.370
Diagnoses upon admission					
Cardiovascular	37 (30.1)	86 (69.9)	30 (24.4)	93 (75.6)	0.317
Gastrointestinal	36 (29.3)	87 (70.7)	19 (15.5)	104 (84.5)	0.009*
Neurologic	10 (8.1)	113 (91.9)	21 (17.1)	102 (82.9)	0.034*
Respiratory	3 (2.4)	120 (97.6)	5 (4.1)	118 (95.9)	0.473
Trauma/ orthopedics	24 (19.5)	99 (80.5)	34 (27.6)	89 (72.4)	0.133
Urinary	9 (7.3)	114 (92.7)	9 (7.3)	114 (92.7)	1.000
Others	4 (3.3)	119 (96.7)	5 (4.1)	118 (95.9)	0.734
Mechanical ventilation	73 (59.3)	50 (40.7)	24 (19.5)	99 (80.5)	<0.000*
Death	38 (30.9)	85 (69.1)	3 (2.4)	120 (97.6)	<0.000*
Age (years) mean (±standard deviation)	72.3 (16.2)		70.6 (9.7)		0.168
Mean days hospitalized (±standard deviation)	8.3 (11.2)		3.1 (3.0)		<0.001*

*p<0.05

The participants' mean age was approximately 70 years. The majority lived with a partner (54.5%) and was Caucasian (88.6%). As for the diagnoses upon admission, gastrointestinal (29.3%) and neurological (8.1%) diagnoses stood out. Among the associated comorbidities, although arterial hypertension (57.7%) and diabetes (30.1%) were the most prevalent in Group I, they were not statistically significant when compared with Group II.

It was also verified that the highest percentage of mechanical ventilation use was found for Group I participants ($p < 0.000$). Length of hospital stay and death were significant factors for patients who developed acute renal injury ($p < 0.000$).

In Table 2, data are presented on the univariate and multivariate logistic regression analysis of the statistically significant variables in the comparison between the groups, associated with the development of acute kidney injury.

Table 2 – Logistic regression of study participants' significant variables

Variables	Odds ratio	95%CI	p
Days of hospitalization	1.126	1.058-1.198	0.000*
With partner	0.495	0.292-0.837	0.008*
Mechanical ventilation	6.022	3.365-10.681	<0.001*
Diagnoses upon admission			
Gastrointestinal	2.265	1.213-4.229	0.010*
Neurological	0.429	0.193-0.955	0.038*
Sepsis	14.666	3.383-63.583	0.000*
Arrhythmia	4.727	1.312-17.032	0.017*
Hypovolemia	3.277	1.152-9.322	0.019*
Furosemide	3.001	1.418-6.347	0.004*
Vasoactive drug (noradrenalin)	8.901	4.663-16.993	<0.000*
Simultaneous antibiotics (glycopeptides and/or lipopeptides)	32.701	4.359-24.295	<0.000*
Concomitant factors (>3)	4.598	2.672-7.912	<0.000*
Multivariate analysis			
Hypovolemia	3.154	1.148-8.981	0.026*
Furosemide	2.370	0.979-5.736	0.003*
Vasoactive drugs (noradrenalin)	4.885	2.224-10.731	<0.000*
Simultaneous antibiotics (glycopeptides and/or lipopeptides)	22.928	2.875-182.849	0.003*
Concomitant factors (> 3)	1.268	1.074-1.498	0.005*

* $p < 0.05$. 95%CI: 95% confidence interval

The variable days of hospitalization in the intensive care unit emerged as a risk factor, with a 12.6% increase in the chance of renal dysfunction with each additional day of hospitalization. The diagnosis of hospitalization associated with gastrointestinal causes increased the chances of developing the problem twofold, while the neurological factors represented a protective factor. For patients who used mechanical ventilation, the risk increased sixfold.

Sepsis was one of the factors associated with a higher odds ratio for renal dysfunction, that is, 14.6 times. Arrhythmia also increased the odds for the development of acute kidney injury by approximately five times, and hypovolemia three times.

As for the participants' use of drugs with nephrotoxic potential, furosemide and the vasoactive drug increased the risk for acute renal injury three and eightfold, respectively. The use of antibiotics only showed significance when using glycopeptides and/or polypeptides concomitant with antibiotics of other classes during the therapies, with a considerable increase in the participants' risk of acute renal injury. It should be noted that up to three antibiotics were used simultaneously.

More than three concomitant risk factors increased the odds for renal problems among Group I participants by about four times ($p < 0.000$).

According to the multivariate analysis, the main effects of each exposure that maintained their predictive value for acute kidney injury were simultaneous antibiotics, vasoactive drug, hypovolemia and furosemide, with an increased chance of renal impairment by 22.9, four, three and two times, respectively.

The concomitant occurrence of more than three associated factors also represented a predictor for renal dysfunction, doubling the chances for its development ($p < 0.000$).

Although significant, the odds ratio for thromboembolic disease ($p = 0.044$), renal obstructive disease ($p = 0.024$), renal tumor and cardiorespiratory arrest ($p = 0.044$) could not be estimated, as their frequency among the control participants was equal to zero (data not shown in the table).

Discussion

The limitations were related to the development of the study at a single private hospital, lack of records in electronic medical files, absence of patients' severity index and non-use of scales standardized in the literature to identify acute kidney injury.

Nevertheless, based on the results, the profile of the patients affected by acute kidney injury and the main associated factors were shown, also contributing to reflections about the importance of the care health and especially nursing professionals provide in the prevention and minimization of damages in patients admitted to an intensive care unit⁽⁹⁾. In this environment, the expectation is to guarantee the best outcome within the patients' clinical conditions and severity, with the lowest possible complication rates due to the necessary procedures and interventions⁽¹⁰⁾.

In this study, the prevalence of acute kidney injury was lower than that described in the literature, as evidenced in two retrospective studies conducted in a regional American database, with approximately 25,000 critical patient records and analysis of 114 patient records, in which the indices corresponded to 44.0% and 60.0%, respectively^(4,11). This data can be attributed to the inclusion of exacerbated patients only with no history of other renal diseases, as well as to the use of the creatinine criterion of the AKIN classification.

The sample consisted mainly of Caucasian men with a mean age of 70 years. Age is a risk predictor⁽¹⁾ but, in this study, it was not statistically significant, probably due to the pairing of this variable with the control group.

As for the diagnosis upon admission, gastrointestinal etiologies (29.0%) prevailed. In surgical patients, this is not the main etiology that favors renal dysfunction, commonly associated with hemodynamic and postoperative cardiovascular complications⁽¹¹⁻¹³⁾ which, related to comorbidities, influence the prognoses

and length of hospital stay^(1,11,14).

Patients who developed acute kidney injury had a longer hospital stay, approximately eight days. Recent prospective studies, developed in an intensive care unit with 100 and 41 patients, hospitalized for 10⁽⁴⁾ and 9⁽¹⁵⁾ days, respectively, corroborate these data. This study showed that, with each additional day of hospitalization, the risk for acute kidney injury increased by 12.6%. Hospitalization time is presumed to be associated with severity, comorbidities and dependence on ventilation, favoring the exposure to the risk factors that may contribute to acute kidney injury and death.

In this study, 30.9% of patients in Group I died, similar to a prospective study of 152 patients, whose mortality rate was 35.0%⁽¹²⁾. It is worth mentioning the variation in mortality described in the literature, between 12.0% and 60.0%^(3-4,12). These results are possibly related to the severity and renal problem, often associated with mortality, synergy of factors, multiple interventions, poor clinical outcome and prognosis⁽¹⁾. Among these, the occurrence of mainly hemodynamic complications increased the chances of renal problems. These conditions alter the circulatory dynamics, interfering with cardiac output and renal blood flow^(12,14).

In this sense, sepsis and hypovolemia were the causes of hemodynamic instability that increased the chances for the development of acute kidney injury. Sepsis and hypovolemia represent risk factors that affect the renal function, as they require the use of drug therapies that may be harmful⁽²⁾, depending on dosage and time of use, as is the case with vasopressors.

A multicenter study carried out in six French intensive care units showed that the use of vasopressor drugs was also considered a risk factor for the development of acute kidney injury in critical patients⁽¹⁶⁾. This fact was also corroborated in another investigation conducted at 97 centers with 1,032 pa-

tients during the first week of hospitalization⁽¹⁷⁾. As vasoconstriction mechanisms, vasopressors are one of the possible causes of renal injury, predisposing to acute kidney injury⁽⁶⁾. When used for prolonged periods associated with other nephrotoxic drugs, they are a predictive factor for nephrotoxicity⁽⁷⁾.

Among the potentially nephrotoxic drugs investigated in this study, furosemide represented a risk factor, doubling the chances for renal impairment. A retrospective study of 109 patients who progressed with acute kidney injury in the intensive care unit showed that furosemide use was significant among the investigated cases, especially those requiring dialysis therapy⁽⁶⁾. This association indicates that the drug is one of the potential risk factors for renal injury^(6,12).

In addition to furosemide, other drugs and substances with some nephrotoxic potential are commonly used in an intensive setting, such as antibiotics and contrasts, which contribute significantly to the development of renal dysfunction^(13,14,18).

It is important to consider that antibiotics therapy is usually used postoperatively but, if performed with several simultaneous antibiotics, it enhances the risk for renal dysfunction⁽¹⁶⁾, as observed in this study, in which the concomitant use of glycopeptide and polypeptide antibiotics significantly increased the chances for acute kidney injury.

The occurrence of associated factors represented a predictor for renal dysfunction, doubling the chances of its development ($p < 0.000$). It should be noted that, when concomitant, they generate a greater impact for the development of kidney injuries⁽⁴⁾.

The results can contribute to support the care practice at the institution where the research was carried out, through the elaboration of care protocols for the early detection and prevention of acute kidney injury among surgical patients hospitalized in an intensive care unit, in addition to the development of future multicenter studies.

Conclusion

Acute kidney injury represented a systemic event, affected patients of advanced age who were hospitalized longer and predisposed to death. It was associated with gastrointestinal etiologies, problems, nephrotoxic drugs and the concomitant occurrence of factors that contributed to increase the risk of its development.

Collaborations

Benichel CR collaborated with the conception and project, analysis and interpretation of the data, writing of the article and relevant critical review of the intellectual content. Meneguim S collaborated with the data analysis and interpretation, writing of the article, relevant critical review of the intellectual content and final approval of the version for publication.

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