Role of Acute Kidney Injury in High-Risk Surgical Patients. A Multicenter Prospective Cohort Study.

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Research article

Keywords: acute kidney injury, surgeries, high risk, intensive care unit, risk factors, perioperative

Posted Date: November 9th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-103751/v1>

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Abstract

Background: Patients who develop postoperative acute kidney injury (AKI) have a poor prognosis, especially when undergoing high-risk surgery. Therefore, the objective of this study was to evaluate the outcome of patients with AKI acquired after noncardiac surgery and the possible risk factors for this complication.

Methods: A multicenter, prospective cohort study with patients admitted to intensive care units (ICUs) after noncardiac surgery was conducted to assess whether they developed AKI. The outcomes of patients who developed AKI were then compared to those of patients who did not develop it.

Results: A total of 29 ICUs participated, of which 904 involved high-risk surgical patients who were included in the study. The occurrence of AKI in the postoperative period was 15.8%, and the mortality rate of postoperative AKI patients at 28 days was 27.6%. AKI was strongly associated with 28-day mortality (OR = 2.91; 95% CI 1.51-5.62; P= 0.001), and higher length of ICU stay (P< 0.001), length of hospital stay (P<0.001) and length of mechanical ventilator stay (P<0.001). Independent factors for the risk of developing AKI were preoperative anemia (OR=7.0; P= 0.001), SAPS 3 (OR= 1.04, P<0.001), postoperative vasopressor use (OR= 2.47; P<0.001), postoperative infection (OR= 8.8; P<0.001), need for reoperation (OR= 7.1; P<0.001) and elective surgery (OR= 0.4; P<0.001) was protective for AKI. In addition, patients with higher perioperative fluid balance had more chance for AKI.

Conclusions: AKI is associated with risk of death. Patients with anemia prior to surgery, who had a higher SAPS 3, needed a postoperative vasopressor or had postoperative infection or needed reoperation were more likely to develop AKI, as were those with a higher perioperative fluid balance.

Background

Acute kidney injury (AKI) is characterized by a rapid and significant decrease in the glomerular filtration rate (GFR) and is usually of multifactorial origin [1]. Studies that have evaluated perioperative AKI were performed mostly after cardiac and vascular surgery, and there are still major deficiencies in the literature regarding the development of AKI in patients undergoing noncardiac surgery because most recent studies involve retrospective analyses [2, 3].

The development of AKI is commonly associated with sepsis, low cardiac output and the postoperative period of major surgeries [4]. One out of every three cases of AKI occurs during the perioperative period [5]; such cases represent approximately 18 to 47% of the cases of hospital-acquired AKI [6].

The incidence of AKI in surgical patients varies according to the type and severity of surgery, with reported rates of 19% after cardiac surgery and approximately 12–13% after general and thoracic surgery [7]. In a large epidemiological study of patients undergoing major noncardiac surgery in intensive care units (ICUs) in Brazil, 30% of patients had postoperative complications, and AKI was the postoperative

complication with the second-highest occurrence rate. Postoperative complications are common in high-risk patients after major surgery [8].

Therefore, our hypothesis is that perioperative AKI is common and is associated with a worse prognosis. Thus, evaluating the incidence and characteristics of patients underwent major noncardiac surgery and developed postoperative AKI, in addition to determining whether perioperative volemic adjustments correlate with AKI, is relevant for adequately improving the therapeutic management of these patients.

The main objective of this study was to evaluate the incidence, impact on outcomes and main risk factors for developing AKI in patients underwent noncardiac surgery and developed AKI after admission to the ICU. Because of the importance of fluid balance in surgical patients, we also evaluated the association between this variable and the development of AKI.

Methods

A prospective, multicenter cohort study was conducted between May 1 and November 1, 2018, with a 28-day follow-up period. This study was approved by the Research Ethics Committee of the study coordinating center, Hospital Israelita Albert Einstein (CAAE: 55828016.1.1001.0071) and of all participating centers. A signed written informed consent form was obtained from all patients or their respective legal representatives. Two of the participating centers were exempted from providing the form due to the observational nature of the study. This study is a complementary analysis of a multicenter study recently published [8].

Patients aged 18 years or older who were undergoing noncardiac surgery requiring postoperative ICU care were included. Because the criteria for determining the need for postoperative intensive care were not standardized among the centers, all patients with this indication were high-risk.

Patients with terminal cancer, those receiving palliative care and those with severe liver failure (Child C) were excluded because they had lower, or no prospect of cure and their inclusion could lead to inaccurate results. Pregnant women were also excluded. Furthermore, we excluded patients with a length of hospital stay of less than 12 hours because it was not possible to determine whether they had received ICU care or because they were not considered high-risk. Patients who were readmitted to the ICU during the same hospitalization were excluded to avoid including them in the study more than once.

The following variables were evaluated: age; type of surgery; American Society of Anesthesiologists (ASA) classification; Simplified Acute Physiology Score III score (SAPS 3); Sequential Organ Failure Assessment score (SOFA); previous comorbidities; presence of infection, sepsis or septic shock during ICU stay; creatinine level (mg/dl) at admission and during ICU stay; daily fluid balance; mean arterial blood pressure at ICU admission; mechanical ventilation; vasoactive drugs; length of hospital stay and complications. Day 1 was considered the day of surgery plus admission to the ICU before 11:59 pm.

AKI was identified by the presence of at least one of the following parameters, Disease Improving Global Outcomes (KDIGO) criteria 2012 diagnostic score: increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 $\mu\text{mol/l}$) within 48 hours; increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; urine volume < 0.5 ml/kg/h for 6 hours or need for renal replacement therapy during ICU stay in patients with no history of chronic kidney failure [9, 10]. Creatinine was measured at the entrance and reassessed in the first 5 days of ICU stay. Oliguria was assessed for 24 hours to classify AKI severity.

The fluid balance was calculated as the difference between the infused fluids (crystalloids, colloids, fluid-diluting drugs, blood derivatives and water via nasogastric tube) and eliminated fluids (via diuresis, bleeding, dialysis, and drains).

The other postoperative complications were defined as follows: cardiovascular, based on the need for vasopressors for more than one hour despite adequate volume resuscitation; respiratory, in the presence of a partial pressure of arterial oxygen to fraction of inspired oxygen ratio ($\text{PaO}_2/\text{FiO}_2$) < 200 in patients without previous lung disease, the need for reintubation or the failure to wean from mechanical ventilation during the postoperative period; neurological, based on a sharply fluctuating and nonzero Richmond Agitation-Sedation Scale (RASS) score [11], within 24 hours and agitation (determined by a RASS score greater than or equal to +2); and gastrointestinal, in the presence of acute abdominal distension, uncontrolled nausea or vomiting, or moderate- to high-output fistulas.

The main outcome was 28-day mortality after surgery, which was evaluated face-to-face or by telephone. A 28-day follow-up period was chosen to standardize the follow-up time specifically related to surgery.

Statistical analysis

Considering data from the literature, we assumed a renal complication rate of 15% in high-risk surgical patients [4, 7, 12]. Therefore, we estimated that at least 1,000 patients would be required to conduct the study with the inclusion of fifteen explanatory variables in a robust logistic regression model, with 28-day mortality as the dependent variable.

Categorical variables are presented as absolute and relative frequencies. Quantitative variables are expressed as the mean and standard deviation (SD) or as the median and interquartile range (IQR), when appropriate. We used the Kolmogorov-Smirnov test to evaluate the distribution pattern of continuous numerical variables.

Proportions were compared using the chi-square test or Fisher's exact test, as appropriate. Quantitative variables with multiple measurements were compared using general linear model (GLM) analysis, the consistency of the model was tested using Mauchly's sphericity test, and a post hoc Bonferroni correction was performed in these analyses. The Bonferroni correction set the significance cutoff P value; it was used to detect the time points at which the differences were significant in multiple comparisons.

The associations between explanatory and response variables were evaluated using fixed logistic regression models. Variables that were statistically significant in the univariate analyses ($p < 0.05$) were selected for inclusion in the multiple logistic regression models. Collinearity was first evaluated by examining the dispersion matrix and the Pearson correlation coefficient for continuous variables or the cross-tabulation for categorical variables. We also evaluated collinearity using the variance inflation factor (VIF). Variables with substantial collinearity ($VIF \geq 10$) were excluded from the final model. The results of the logistic regression analyses are expressed as the odds ratio (OR) and respective 95% confidence interval (95% CI).

All probabilities of significance (p-values) were two-tailed. P-values were considered statistically significant when $p < 0.05$. The Statistical Package for Social Sciences v. 26.0 (SPSS Inc.®; Chicago, IL, USA) and R v. 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) were used to perform the analyses.

Results

A total of 55 ICUs from 55 hospitals were selected for participation in the study (chosen for having accepted to participate in the screening). There were no significant differences in operational characteristics among the ICUs when the regions of the country were compared. Twelve of these ICUs (21.8%) were not eligible for participation for different reasons, i.e., 5 ICUs (9.1%) refused to participate because they did not treat the anticipated number of surgical patients, and 9 ICUs (16.4%) returned questionnaires with incomplete study data. Therefore, 29 ICUs participated in the study. During the study period, 25,500 patients underwent noncardiac surgery. Of these, 904 (3.5%; 95% CI 3.3% – 3.8%) were admitted to the ICUs and involved in analyze of the study.

The median (IQR) patient age was 62 (50–72) years, and 53.8% of the patients were male. The median (IQR) SAPS 3 was 42 (32–53) points. Approximately 80.4% of the patients had at least one comorbidity, and hypertension, cancer and smoking were the most frequently occurring.

The median (IQR) length of ICU stay was 2 days (1–4). The median (IQR) length of hospital stay was 9.5 days (5.4–18.6).

The postoperative 28-day mortality rate for the entire cohort was 9.6%, and half of these patients (5.2%) presented with AKI. The total incidence of postoperative complications was 29.9%, with 15.8% of renal complications.

In the logistic regression model, the independent factors associated with 28-day mortality were age (OR = 1.034; 95% CI 1.013–1.054), SAPS 3 (OR = 1.036; 95% CI 1.012–1.061), SOFA at ICU admission (OR = 1.159; 95% CI 1.053–1.275), emergency surgery (OR = 2.7441; 95% CI, 1.197–6.273) and postoperative development of AKI (OR = 2.911; 95% CI 1.507–5.623) (Table 1).

When comparing patients with and without AKI, it was identified that higher SAPS 3 scores, physical status other than ASA 2, diabetes and anemia, i.e., hemoglobin level prior surgery ≥ 10 g/dl, had a significant association with AKI (Table 2).

During the intraoperative period, the variables that were significantly associated with AKI were type of surgery, intraoperative hypotension without the need for reversal with vasopressors, need for vasopressors and blood transfusion and abdominal and oncological surgery (Table 2).

In addition, during the postoperative period, AKI was more strongly correlated with a lower hemoglobin level, higher arterial lactate level and mechanical ventilation at ICU admission, in addition to the need for vasopressors during this period, the presence of postoperative infection and the need for unplanned reoperation (Table 2).

However, when logistic regression was applied to the perioperative variables that were identified as statistically significant in the univariate analysis comparing patients with and without AKI during the postoperative period, only preoperative anemia (OR = 7.01; 95% CI 1.69–29.07), elective surgery (OR = 0.45; 95% CI 0.21–0.97), SAPS 3 (OR = 1.04; 95% CI 1.02–1.06), postoperative vasopressor use (OR = 2.47; 95% CI 1.34–4.55), postoperative infection (OR = 8.82; 95% CI 2.43–32.05) and the need for reoperation (OR = 7.15; 95% CI 2.58–19.79) were independent factors associated with AKI.

Specifically, regarding daily fluid adjustment during the perioperative period, AKI exhibited an association in the univariate analysis with the median total volume, median fluid balance and 0.9% saline volume received every 24 hours. However, when these variables were adjusted for the identified risk factors for developing AKI, only a high fluid balance was strongly correlated with AKI (Table 3 and Fig. 2).

Regarding the evolution of the daily fluid balance in patients with AKI, the GLM showed significant differences ($P = 0.007$) in fluid balance from the day of surgery to the fifth day between patients with and without AKI. The difference was most evident on the second ($P = 0.05$) and fifth ($P = 0.005$) postoperative days (Fig. 3).

Discussion

The main findings of this study were a high incidence of AKI (15.8%) with high mortality in noncardiac surgery patients admitted to the ICU and the association of AKI with infection, reoperation, circulatory shock, preoperative anemia, and positive fluid balance.

Major surgeries account can reach 40% of cases of hospital-acquired AKI [13]. Patients with AKI admitted to the ICU during the postoperative period in cardiovascular surgery accounted for 7.7–40% of cases [14], and gastrointestinal tract surgery patients accounted for almost 22% [15].

The presence of AKI during the perioperative period in this subgroup of patients undergoing major surgery was associated with unfavorable outcomes, with a hospital mortality rate of 27.6%. In addition, the length of hospital stay of patients with AKI was higher than that of patients without AKI; patients with AKI spent

approximately one extra week in the hospital. Similarly, a large multicenter observational study in European countries reported that mortality among patients with AKI was more than twice that observed in other patients [16]. In a recent study, the occurrence and severity of AKI were strongly associated with risk of death after surgery. However, the relationship between preoperative renal function, as assessed by serum creatinine-based estimated GFR, and the risk of death depended on patient age and whether AKI developed postoperatively [17]. In our study, we identified a high mean age (over 60 years), but we did not analyze small existing changes in renal function that could indicate a low physiological reserve and thus predispose the patient to a higher risk of AKI.

In our study, patients who developed AKI were more severe (higher SAPS 3), had a greater need for advanced support with catecholamines and frequently had infections. The systemic inflammatory response that occurs in patients with infection is correlated with the induction of AKI. Although the pathophysiology of sepsis-induced renal disorders is still poorly understood, experimental models suggest that, at least in the initial phase of the disease, functional changes associated with microvascular shunting and tubular cell injury are part of the picture [18]. In addition, the intensity of the inflammatory response to surgical trauma determines both tissue hypoperfusion and the ischemia-reperfusion response, which intensifies the inflammatory response. Furthermore, mechanical ventilation, intra-abdominal hypertension, pain and surgical stress are factors that increase the release of antidiuretic hormones and contribute to the development of AKI. Prospective studies have reported a relationship between AKI and sepsis and the need for mechanical ventilation [6, 19, 20].

There is a close correlation between hypotension and the development of AKI. A recent meta-analysis showed that goal-directed hemodynamic adjustments reduce the likelihood of AKI in orthopedic and abdominal surgery patients [21]. We observed the most frequent use of vasopressors in this group of patients. The duration of intraoperative hypotension (particularly relative to the patient's normal arterial blood pressure), including brief episodes of mean arterial pressure lower than 55 mmHg, has been associated with kidney injury [5]. Careful maintenance of cardiovascular stability, including fluid infusion, throughout this period is vital for protecting renal perfusion while avoiding volume overload. A study of high-risk surgical patients showed that the customized maintenance of blood pressure according to the patient's previous levels during surgery was able to reduce organ dysfunction [22]. Moreover, the association between the use of vasoactive drugs and mortality is consistent with the results of other studies [23–25].

Interestingly, a correlation was noted between preoperative anemia (such as hemoglobin concentration less than 10 g/dl) and impaired renal function. This pathophysiology is multifactorial, but mainly involves a decrease in the oxygen transport capacity and subsequent tissue hypoxia [26].

Besides, patients who developed AKI had a more positive mean daily fluid balance. In fact, reduced ultrafiltration is rarely the only cause of AKI; inflammation, direct vascular injury or tubular obstruction usually accompany kidney injury during the perioperative period. The subsequent rupture of intercellular junctions leads to the release of cells into the tubular lumen and to polarity loss of the transmembrane

ion channel. It is expected that, in many cases, simply restoring the circulating volume does not improve the results and may be counterproductive [4, 5]. Elevated intratubular pressure decreases glomerular filtration and activation of tubuloglomerular feedback, with consequent preglomerular vasoconstriction, which leads to an additional reduction in glomerular filtration. Studies have shown that excess fluid is an independent factor for the development of AKI and that in patients with AKI, a more positive fluid balance was correlated with higher mortality [27]. In general, a positive fluid balance, if necessary, can be applied with caution within the first 36 hours. After this, a more conservative approach to volume is the most appropriate and safe method. Regarding the type of solution used, epidemiologic data suggest that 0.9% saline solution, when compared with balanced salt solutions such as balanced solutions, may increase the risk of AKI, the need for renal replacement therapy and mortality in ICU patients. In addition, there is evidence of harm (increased rates of AKI) with the use of hetastarch solutions, which should generally be avoided [28]. In our study, we did not detect a negative influence of any type of colloid on the development of AKI.

Major advances associated with a decrease in postoperative mortality have been observed worldwide in recent years, but the complication rates remain high [29]. AKI is associated with significant morbidity and mortality after major surgery. Patients should be stratified according to their risk of developing AKI based on their exposure and susceptibility, including such factors as severity, the presence of sepsis, mechanical ventilation use and vasoactive drug use, among others [30, 31], and preemptive measures should be taken [5]. We must remember that there are well-established interventions in the KDIGO guidelines that, when used, can reduce the impact of AKI in high-risk surgical patients [32].

Study limitations

The main strengths of our study are associated with its multicenter nature, as it included ICUs located in several regions of Brazil. However, there was a reasonable rate of refusal to participate in the study that affected external validity to some degree. In addition, the adjusted regression model could be performed with a priori defined AKI prediction variables, and not based on statistically important findings from the unadjusted analysis.

There were failures in capturing some relevant data that could have been included in the analyses. Additionally, the need to obtain informed consent in epidemiological studies such as this tends to skew the sample due to the nonconsent of more critical patients, whose families may be psychologically fragile. Another aspect to be considered is the lack of standardization among the centers regarding indications for postoperative intensive care. In addition, this study was not able to assess long-term complications and mortality, and some complications may have occurred after the study period.

Conclusion

AKI is a major complication in high-risk surgical patients and is associated with risk of death. Patients with anemia prior to surgery, those with a higher SAPS 3, those requiring vasopressors during the postoperative period and those with postoperative infection or the need for reoperation are the most likely

to develop AKI, as are patients with a higher perioperative fluid balance. Fluid type did not influence AKI development.

Abbreviations

Acute kidney injury (AKI); glomerular filtration rate (GFR); American Society of Anesthesiologists (ASA); Simplified Acute Physiology Score III (SAPS 3); intensive therapy unit (ICU); Richmond Agitation-Sedation Scale score (RASS); Kidney Disease Improving Global Outcomes criteria (KDIGO criteria); Sequential Organ Failure Assessment (SOFA).

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the study's coordinating center, the Hospital Israelita Albert Einstein (CAAE: 55828016.1.1001.0071). And written informed consent was obtained from all patients.

Consent for publication

Written informed consent was obtained from all patients or their legal representatives.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

Conceived and designed the study: JMSJr, HTK. Performed the study: JMSJr, BCG, RCFC, TDC, SMAL, MSCA, LMSM. Analyzed the data: JMSJr, HTK, BCG, ASN. Contributed to data collection: BRASIS study group. Wrote the paper: JMSJr, HTK, BCG, SMAL, LMSM.

All authors have read and approved the manuscript

Acknowledgments

The following have made substantial contributions to the study- Brasis study group: Cristina Prata Amendola, Neymar Elias de Oliveira, Viviane Cordeiro Veiga, Salomón Soriano Ordinola Rojas, Bruno Melo Nobrega de Lucena, Raphael Augusto Gomes de Oliveira, Luciana Coelho Sanches, Antonio Paulo Nassar Junior, Álvaro Réa-Neto, Alexandre Amaral, Flávio Geraldo Rezende de Freitas, Antônio Tonete Bafi, Fernando José Ramos, Maria Augusta Santos Rahe Pereira, Danielle Dourado Magalhães, Diogo Oliveira Toledo, Fernando Suparregui Dias, Marciano de Sousa Nobrega, Claudio Piras, Paulo Lisboa Bittencourt, Mirella Cristine de Oliveira, Jarbas da Silva Motta Júnior, Paula Geraldine David, Luana Alves Tannous, Lorena Macedo Araújo Miranda, José Arthur dos Santos Brasil, Rafael Alexandre de Oliveira Deucher, Marcos Henrique Borges Ferreira, Wagner Luis Nedel, Wilson de Oliveira Filho, Gilberto Friedman, Afonso José Celente Soares.

The present study was endorsed by the Brazilian Research in Intensive Care Network (AMIBnet).

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Tables

TABLE 1.
FACTORS RELATED TO POSTOPERATIVE 28-DAY MORTALITY (UNIVARIATE AND MULTIVARIABLE ANALYSIS).

	Univariate			Multivariate		
	OR	95% CI	P-value	OR	95% CI	P-value
Male sex	1.105	0.658–1.855	0.707			
Caucasian ethnicity	0.926	0.115–7.492	0.943			
Age (per year)	1.019	1.003–1.035	0.017	1.034	1.013–1.054	0.001
BMI (per kg/cm ²)	0.971	0.918–1.027	0.301			
SAPS 3 (per unit)	1.076	1.057–1.096	0.000	1.036	1.012–1.061	0.003
SOFA score at admission (per unit)	1.281	1.198–1.369	0.000	1.159	1.053–1.275	0.002
ASA (per unit)	2.326	1.684–3.213	0.000	1.280	0.884–1.853	0.192
Duration of surgery (per minute)	0.998	0.996–1.000	0.065			
Type of surgery						
Elective	Reference					
Urgent	3.577	1.880–6.806	0.000	1.515	0.677–3.392	0.312
Emergency	6.739	3.659–12.411	0.000	2.741	1.197–6.273	0.017
Surgery						
Head and neck	4.247	1.077–16.754	0.039	3.039	0.901–10.248	0.073
Abdominal	3.988	1.613–9.856	0.003	1.376	0.654–2.894	0.401
Oncological	0.39	0.434–1.622	0.602			

OR - odds ratio; 95% CI - 95% confidence interval; BMI - body mass index; SAPS 3 - Simplified Acute Physiology Score III; SOFA - Sequential Organ Failure Assessment score; ASA - American Society of Anesthesiologists; Hb - hemoglobin level. Area under the curve: 0.843; 95% confidence interval 0.813–0.870.

Neurological	3.754	1.331–10.593	0.012	1.340	0.604–2.972	0.472
Orthopedic	2.186	0.774–6.75	0.140			
Vascular	2.124	0.604–7.463	0.240			
Thoracic	1.176	0.195–7.101	0.854			
Urological	2.374	0.680–8.293	0.175			
Gynecological	1.325	0.151–11.596	0.799			
Chronic diseases						
Hypertension	1.083	0.775–1.514	0.639			
Cancer	1.089	0.597–1.920	0.774			
Diabetes	1.199	0.639–2.164	0.557			
Smoking	1.165	0.576–2.221	0.654			
Coronary insufficiency	1.010	0.365–2.393	0.983			
Stroke	2.689	0.689–9.162	0.123			
Chronic obstructive pulmonary disease	1.325	0.471–3.227	0.560			
Chronic kidney failure	2.039	0.786–5.289	0.143			
Alcohol use disorder	1.361	0.435–3.579	0.558			
Arrhythmia	3.007	1.181–7.656	0.021	0.653	0.174–2.453	0.528
Anemia prior to surgery (Hb < 10 g/dL)	1.211	0.246–5.954	0.814			

OR - odds ratio; 95% CI - 95% confidence interval; BMI - body mass index; SAPS 3 - Simplified Acute Physiology Score III; SOFA - Sequential Organ Failure Assessment score; ASA - American Society of Anesthesiologists; Hb - hemoglobin level. Area under the curve: 0.843; 95% confidence interval 0.813–0.870.

Other	1.271	0.738– 2.189	0.388			
Type of anesthesia						
General anesthesia	Reference					
Neuraxial anesthesia	0.522	0.183– 1.489	0.224			
Combined anesthesia (general + neuraxial)	0.544	0.252– 1.172	0.120			
Postoperative acute kidney injury	6.718	3.978– 11.343	0.000	2.911	1.507– 5.623	0.001
OR - odds ratio; 95% CI – 95% confidence interval; BMI - body mass index; SAPS 3 - Simplified Acute Physiology Score III; SOFA - Sequential Organ Failure Assessment score; ASA - American Society of Anesthesiologists; Hb - hemoglobin level. Area under the curve: 0.843; 95% confidence interval 0.813–0.870.						

TABLE 2.
CHARACTERISTICS OF PATIENTS PRESENTING WITH AND WITHOUT ACUTE KIDNEY INJURY (AKI)

Variable	All patients	No AKI	AKI	P-value
Age (years), mean $\pm$ SD Median (IQR)	60.1 $\pm$ 17.7 62.0 (50.0–72.0)	59.9 $\pm$ 17.5 62.0 (50.0–72.0)	61.0 $\pm$ 18.5 63.0 (53.0–76.0)	0.489
Male sex	444 (53.8)	358 (51.9)	86 (63.7)	0.012
BMI, mean $\pm$ SD Median (IQR)	25.3 $\pm$ 4.7 25.0 (22.0–28.0)	25.3 $\pm$ 4.7 25.0 (22.0–28.0)	25.1 $\pm$ 4.8 25.0 (22.0–27.0)	0.628
SAPS 3, mean $\pm$ SD Median (IQR)	43.4 $\pm$ 15.5 42.0 (32.0–53.0)	40.8 $\pm$ 13.9 39.5 (31.0–49.0)	56.4 $\pm$ 16.6 56.0 (45.0–66.7)	< 0.001
ASA 1	78 (9.2)	58 (8.2)	20 (14.2)	0.438
ASA 2	405 (47.8)	365 (51.6)	40 (28.4)	0.005
ASA 3	296 (34.9)	243 (34.4)	53 (37.6)	0.659
ASA 4	61 (7.2)	38 (5.4)	23 (16.3)	0.163
Chronic diseases				
None	172 (19.6)	140 (19.0)	32 (22.5)	0.330
Hypertension	396 (44.2)	325 (43.1)	71 (50.0)	0.129
Cancer	191 (21.3)	165 (21.9)	26 (18.3)	0.340
Diabetes	188 (21.0)	149 (19.8)	39 (27.5)	0.039
Smoking	134 (15.0)	108 (14.3)	26 (18.3)	0.222
Coronary insufficiency	67 (7.5)	51 (6.8)	16 (11.3)	0.061
Chronic obstructive pulmonary disease	54 (6.0)	43 (5.7)	11 (7.7)	0.348
Alcohol use disorder	46 (5.1)	34 (4.5)	12 (8.5)	0.051
Arrhythmia	44 (4.9)	34 (4.5)	10 (7.0)	0.200
Stroke	27 (3.0)	21 (2.8)	6 (4.2)	0.357
Anemia prior to surgery (Hb < 10 g/dL)	15 (1.7)	8 (1.1)	7 (4.9)	0.001
INTRAOPERATIVE CHARACTERISTICS OF PATIENTS				
Time of surgery (min), mean $\pm$ SD Median (IQR)	282.9 $\pm$ 165.0 240 (180–360)	285.7 $\pm$ 164.7 240 (180–360)	268.5 $\pm$ 166.8 240 (180–360)	0.275

Type of surgery	< 0.001			
Elective	613 (69.2)	553 (74.3)	60 (42.3)	
Urgent	147 (16.6)	112 (15.1)	35 (24.6)	
Emergency	126 (14.2)	79 (10.6)	47 (33.1)	
Type of anesthesia	0.111			
General	642 (73.6)	529 (72.4)	113 (80.1)	
Neuraxial	80 (9.2)	68 (9.3)	12 (8.5)	
General and neuraxial	150 (17.2)	134 (18.3)	16 (11.3)	
Diuresis (ml), mean $\pm$ SD Median (IQR)	816.4 $\pm$ 830.8 500 (300-1007.5)	836.6 $\pm$ 813.7 600 (300-1100)	722.2 $\pm$ 905.3 400 (200-825)	0.221
Fluid balance (mL), mean $\pm$ SD Median (IQR)	2151.8 $\pm$ 1730.4 1850 (1000-2925)	2113.8 $\pm$ 1701.7 600 (300-1100)	2326.6 $\pm$ 1853.5 400 (200-825)	0.208
Hypotension not requiring vasopressors	92 (10.5)	55 (7.5)	37 (26.2)	< 0.001
Use of vasopressors	130 (14.9)	83 (11.3)	47 (33.3)	< 0.001
Need for blood transfusion	146 (16.9)	105 (14.5)	41 (29.1)	< 0.001
Surgery				
Oncological	250 (27.9)	222 (29.4)	28 (19.7)	0.018
Neurological	186 (20.8)	160 (21.2)	26 (18.3)	0.433
Head and neck	39 (4.4)	36 (4.8)	3 (2.1)	0.154
Thoracic	53 (5.9)	8 (5.6)	45 (6.0)	0.877
Abdominal	252 (28.1)	193 (25.6)	59 (41.5)	< 0.001
Vascular	74 (8.3)	60 (8.0)	14 (9.9)	0.450
Orthopedic	143 (16.0)	121 (16.0)	22 (15.5)	0.868
Urological	48 (5.4)	40 (5.3)	8 (5.6)	0.873
Gynecological	19 (2.1)	18 (2.4)	1 (0.7)	0.202
Other surgeries	56 (6.2)	45 (6.0)	11 (7.1)	0.625
POSTOPERATIVE CHARACTERISTICS				
MAP (mmHg) at ICU admission, mean $\pm$ SD	90.5 $\pm$ 18.3	91.0 $\pm$ 18.1	87.9 $\pm$ 18.8	0.070

Median (IQR)	90.0 (78.7-101.3)	90.3 (79.3-101.8)	88.5 (77.0-100.3)	
Hemoglobin (g/dl) at ICU admission, mean $\pm$ SD Median (IQR)	11.4 $\pm$ 2.2 11.5 (10.0-12.9)	11.5 $\pm$ 2.2 11.6 (10.1-13.0)	10.8 $\pm$ 2.4 10.8 (9.4-12.4)	0.001
Hematocrit (%) at ICU admission, mean $\pm$ SD Median (IQR)	33.9 $\pm$ 6.9 34.1 (30.2-38.6)	34.3 $\pm$ 6.6 34.6 (30.8-38.7)	32.1 $\pm$ 8.2 32.9 (27.9-37.0)	0.001
Lactate (mmol/L) at ICU admission, mean $\pm$ SD Median (IQR)	2.1 $\pm$ 1.6 1.7 (1.1-2.7)	2.0 $\pm$ 1.5 1.7 (1.1-2.6)	2.5 $\pm$ 1.9 1.8 (1.3-3.0)	0.002
Creatinine (mg/dl)				
Day 1, mean $\pm$ SD Median (IQR)	1.1 $\pm$ 1.3 0.8 (0.6-1.1)	1.0 $\pm$ 1.0 0.8 (0.6-1.0)	1.7 $\pm$ 2.0 1.0 (0.7-1.6)	< 0.001
Day 2, mean $\pm$ SD Median (IQR)	1.1 $\pm$ 1.2 0.8 (0.6-1.1)	0.9 $\pm$ 0.9 0.8 (0.6-1.0)	1.8 $\pm$ 2.1 1.1 (0.7-2.1)	< 0.001
Day 3, mean $\pm$ SD Median (IQR)	1.1 $\pm$ 1.2 0.8 (0.5-1.2)	0.9 $\pm$ 0.9 0.7 (0.5-1.0)	1.7 $\pm$ 1.7 1.0 (0.6-2.2)	< 0.001
Diuresis (mL)				
Day 1, mean $\pm$ SD Median (IQR)	1104.9 $\pm$ 1118.5 900 (500-1400)	1152.5 $\pm$ 1164.6 1150 (700-2000)	853.1 $\pm$ 789.6 1200 (575-1900)	0.006
Day 2, mean $\pm$ SD Median (IQR)	1246.3 $\pm$ 1066.6 1000 (550-1657)	1298.4 $\pm$ 1105.0 1050 (600-1700)	1000.3 $\pm$ 821.8 812 (350-1500)	0.002
Day 3, mean $\pm$ SD Median (IQR)	1466.9 $\pm$ 1274.2 1150 (700-2000)	1444.8 $\pm$ 1144.2 1150 (700-2000)	1539.7 $\pm$ 1634.2 1200 (575-1900)	0.468
Invasive MV at ICU admission	148 (17.7)	81 (11.7)	67 (46.9)	< 0.001
Vasopressor use				
Day 1	157 (18.0)	101 (13.8)	56 (39.4)	< 0.001
Day 2	202 (24.0)	123 (17.6)	79 (55.2)	< 0.001
Day 3	142 (25.4)	77 (17.8)	65 (51.6)	< 0.001
Need for hemodialysis	18 (2.0)	0 (0.0)	18 (13.4)	< 0.001

Duration of MV (days), mean $\pm$ SD Median (IQR)	5.7 $\pm$ 6.3 3.0 (1.0–8.0)	4.2 $\pm$ 5.2 2.0 (1.0–5.0)	8.3 $\pm$ 7.1 7.0 (3.0–12.0)	< 0.001
Length of ICU stay (days), mean $\pm$ SD Median (IQR)	3.8 $\pm$ 5.4 2.0 (1.0–4.0)	3.1 $\pm$ 4.4 2.0 (1.0–3.0)	8.2 $\pm$ 7.9 5.9 (2.8–11.0)	< 0.001
Length of hospital stay (days), mean $\pm$ SD Median (IQR)	14.4 $\pm$ 14.9 9.5 (5.3–18.6)	13.1 $\pm$ 14.2 8.5 (4.7–16.6)	21.3 $\pm$ 17.1 16.7 (9.5–29.6)	< 0.001
Infection	16 (1.8)	5 (0.7)	11 (7.7)	< 0.001
Reoperation	30 (3.3)	11 (1.4)	19 (13.3)	< 0.001
ICU mortality	41 (4.9)	14 (2.0)	27 (20.3)	< 0.001
Hospital mortality	74 (8.9)	31 (4.5)	43 (31.6)	< 0.001
28-day mortality	68 (9.6)	31 (5.4)	37 (27.6)	< 0.001
BMI: body mass index; SAPS 3: Simplified Acute Physiology Score III; ICU: intensive care unit; Urgent: surgery required 24 to 48 hours after diagnosis of the problem; Emergency: surgery required immediately after diagnosis of the problem; Other surgeries: ophthalmological and plastic surgeries and transplants; MAP: mean arterial pressure; MV: mechanical ventilation; ICU: intensive care unit. Values are expressed as the mean $\pm$ standard deviation, median (IQR-interquartile range) or absolute value (%).				

TABLE 3.
COMPARISON OF PATIENTS WITH OR WITHOUT ACUTE KIDNEY INJURY (AKI) ACCORDING TO FLUIDS
RECEIVED DURING THE PERIOPERATIVE PERIOD, UNIVARIATE AND MULTIVARIATE ANALYSIS
(ADJUSTED FOR SAPS 3, PREOPERATIVE ANEMIA, ELECTIVE SURGERY, POSTOPERATIVE
VASOPRESSOR USE, POSTOPERATIVE INFECTION AND REOPERATION).

Variable (daily median)	Univariate				Multivariate	
	All patients	No AKI	AKI	P-value	OR (95% CI)	P-value
Total volume (mL)	1900 (1253-2502)	1820 (1250-2500)	2000 (1500-2927)	0.007	1.001 (0.998-1.003)	0.186
Fluid balance (mL)	800 (183-1500)	786 (126-1459)	840 (300-1506)	0.04	1.001(1.001-1.002)	0.048
0.9% saline solution (mL)	1044(720-2000)	1000 (642-1750)	1500 (1000-2527)	0.000	1.000 (0.999-1.001)	0.840
Lactated Ringer's solution (mL)	1500(1000-2500)	1500 (1000-2500)	1500(1000-2500)	0.337	1.000 (0.998-1.002)	0.800
Plasma-Lyte (mL)	1500 (1000-2164)	1500 (1000-2500)	1150 (500-2000)	0.121	0.999 (0.998-1.007)	0.544
Hydroxyethylamide 130/0.4 (mL)	500 (500-1000)	500 (500-500)	1000 (750-1000)	0.137	——	
OR: odds ratio; 95% CI: 95% confidence interval. Values are expressed as the median (interquartile range); adjusted OR in the multivariate analysis.						

Figures

Figure 1

Risk factors related to AKI during the postoperative period (multivariate analysis). SAPS 3: Simplified Acute Physiology Score III; Hb: hemoglobin; ASA: American Society of Anesthesiologists. Area under the curve: 0.844; 95% confidence interval 0.814-0.871.

Figure 1

Risk factors related to AKI during the postoperative period (multivariate analysis). SAPS 3: Simplified Acute Physiology Score III; Hb: hemoglobin; ASA: American Society of Anesthesiologists. Area under the curve: 0.844; 95% confidence interval 0.814-0.871.

Figure 2

Plot of AKI probability in relation to fluid balance adjusted to SAPS 3 (first) and Youden diagram (second) showing more patients with AKI when SAPS 3 and fluid balance were higher.

Figure 2

Plot of AKI probability in relation to fluid balance adjusted to SAPS 3 (first) and Youden diagram (second) showing more patients with AKI when SAPS 3 and fluid balance were higher.

Figure 3

Multiple analysis model (GLM) for variables repeated over time in relation to fluid balance in patients with and without AKI. P-values were corrected by the Bonferroni method.

Figure 3

Multiple analysis model (GLM) for variables repeated over time in relation to fluid balance in patients with and without AKI. P-values were corrected by the Bonferroni method.

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