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Perioperative risk factors for acute kidney ınjury in major abdominal surgeries: a retrospective observatioal study

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ABSTRACT

Aims: Acute kidney injury (AKI), particularly as a postoperative complication related to surgery, has been independently associated with morbidity and mortality. AKI also develops at a significant rate after major abdominal surgery. In this study, it was aimed to identify the risk factors contributing to the development of AKI following major abdominal surgery.

Methods: The study was retrospectively planned. Patients who underwent major abdominal surgery were included in the study. Patients' demographic data, preoperative laboratory data, intraoperative data, and postoperative data were recorded from patient files. The diagnosis and severity of postoperative acute kidney injury (PO-AKI) were assessed using serum creatinine and/or urine output criteria in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The patients were divided into two groups: AKI and non-AKI.

Results: A total of 64 patients with complete data were included in the study. Among these patients, 6 developed AKI (9.3%). The mean age in the AKI group was found to be statistically significantly higher (p: 0.043). The Frailty index was significantly higher in the AKI group (p: 0.020). Additionally, it was observed that the use of aspirin and angiotensin-converting enzyme inhibitor (ACEI) / angiotensin receptor blocker (ARB) was statistically significantly higher in the AKI group (p: 0.022, p: 0.044, respectively). When patients were evaluated in terms of intraoperative parameters, the amount of colloid used, the amount of ES used, and vasopressor usage were found to be statistically significantly higher in the AKI group ($p<0.001$, p: 0.036, p: 0.022, respectively). Lastly, vasopressor usage and diuretic usage were found to be statistically significantly higher in the AKI group for postoperative period (p: 0.002, p: 0.044, respectively)

Conclusion: Many parameters covering the perioperative period can cause PO-AKI. Especially in elderly patients, frailty and age are significant factors that must be kept in mind.

Keywords: Abdominal surgery, acute kidney injury, perioperative, postoperative, risk factors

INTRODUCTION

Recent studies have shown that major noncardiac surgery is associated with significanst morbidity and mortality. The development of acute kidney injury (AKI), particularly as a postoperative complication related to surgery, has been independently associated with morbidity and mortality. Even if a patient's kidney function improves, AKI has been associated with long-term adverse events, including the development of chronic kidney disease (CKD) and late mortality.[1,2]

AKI is a common condition among hospitalized patients and has various adverse effects on patient outcomes.[3,4] These effects can be listed as increased in-hospital mortality, prolonged length of hospital stay, increased healthcare costs, progression of CKD, and increased cardiovascular events.[5,6] The relationship between postoperative AKI and cardiovascular surgery has been extensively researched (11% to 31%). Factors such as the type of surgery (coronary artery bypass grafting, valve repair or replacement), advanced age, congestive heart failure, chronic obstructive pulmonary disease (COPD), longer cardiopulmonary bypass duration, and pre-existing CKD have been identified as risk factors for AKI.[7] There are fewer studies related to AKI following abdominal surgery. The incidence of AKI in major abdominal surgery has been reported to vary between 0.8% and 22.4%. This variability may be attributed to differences in case populations across studies and variations in diagnostic criteria for AKI. Additionally, changes in intraabdominal pressure and renal perfusion pressure during and after abdominal surgery lead to various pathophysiological mechanisms. Considering this, it can

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be said that the risk factors for AKI after major noncardiac surgery may not be similar to those after cardiovascular surgery.[5,7]

In recent years, the definition of AKI has evolved from the old term acute renal failure to a set of uniform criteria that combine small changes in creatinine and urine output, ultimately defining AKI. Initially, the risk, injury, failure, loss, and end-stage kidney disease (RIFLE) classification was used for AKI, followed by the Acute Kidney Injury Network (AKIN) classification. In recent years, the RIFLE and AKIN classifications have been integrated into the Kidney Disease: Improving Global Outcomes (KDIGO) classification. This consolidation aims to provide simpler and more cohesive criteria that can be applied in clinical practice, research, and public health surveillance. As a result, AKI is defined as an increase in serum creatinine (SCr) of ≥0.3 mg/dl (≥26.5 µmol/l) within 48 hours; or an increase in SCr≥1.5 times the baseline value known or presumed to have occurred within the previous 7 days; or a urine volume 0.5 ml/kg/hour for 6 hours.[3,8-10]

The hypothesis of this study is that if the risk factors for postoperative AKI (PO-AKI) can be identified more specifically, necessary measures can be taken to reduce the incidence of PO-AKI. As a result of all these, this study aimed to identify the risk factors contributing to the development of PO-AKI following major abdominal surgery.

METHODS

The study was retrospectively planned at Ankara Bilkent City Hospital. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. After obtaining approval from Ankara Bilkent City Hospital Clinical Researches Ethics Committee (Date: 17.03.2021, Decision No: E1/1605/2021), patients who underwent major abdominal surgery between 2020 and 2021 were included in the study. Patients aged between 18 and 80 years, classified as American Society of Anesthesiologists (ASA) I-III, with normal preoperative serum creatinine levels (Normal value: 1.2 mg/dl) and preoperative glomerular filtration rate (GFR) values, without a history of kidney failure - liver failure - heart failure, scheduled for elective surgery, under general anesthesia with inhalation, and with complete data available in the patient files, were included in the study.

Patients' demographic data (*age, gender, body mass index (BMI), comorbidities, medication history*), Geriatric Nutritional Risk Index (GNRI) score,[11] Prognostic Nutritional Index (PNI) score,[12,13] Frailty Index,[14] Model for End-Stage Liver Disease (MELD) score,[15] preoperative laboratory data (serum creatinine, hematocrit, albumin, lymphocyte count, bilirubin, international normalized ratio (INR), sodium), intraoperative data (anesthesia duration, amount of crystalloid, colloid volume, Erythrocyte Suspension (ES) volume, Fresh frozen plasma (FFP) volume, amount of bleeding, urine output, vasopressor usage, nephrotoxic agent usage, diuretic usage), and postoperative data (Acute Physiology and Chronic Health Evaluation (APACHE)-II score, vasopressor usage, diuretic usage, presence of complications, length of stay in intensive care unit (ICU), creatinine at ICU discharge, length of hospital stay, creatinine at hospital discharge, hospital mortality, and three-month mortality) were recorded from patient files.

Patients underwent anesthesia induction with 0.3 mg/kg midazolam, 0.25-0.50 µg/kg remifentanil, 1.5-2 mg/kg 2% propofol, and 0.6 mg/kg rocuronium intravenous (iv) bolus. They were then intubated with an appropriate endotracheal tube (7-8.0 cuffed). Anesthesia maintenance was achieved with Desflurane at 1.0-1.2 MAC, a continuous infusion of 0.5 µg/kg/h remifentanil, and additional doses of rocuronium as needed.

The diagnosis and severity of PO-AKI were assessed using serum creatinine and/or urine output criteria in accordance with the KDIGO guidelines.[8,16] The most recent serum creatinine level before surgery was considered as the baseline value. Serum creatinine levels were monitored at least once daily during the initial 3 days post-surgery.Patients were staged with KDIGO according to Serum creatinine and Urine output status[16,17](Table 1).

Table 1. Staging of acute kidney injury

Stage	Serum creatinine	Urine output
1	1.5 to 1.9 times baseline or ≥0.3 mg/dl (≥26.5 µmol/l) increase	<0.5 ml/kg/hour for 6 to 12 hours
2	2.0 to 2.9 times baseline	<0.5 ml/kg/hour for ≥12 hours
3	3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dl (≥353.6 µmol/l) or initiation of renal replacement therapy	<0.3 ml/kg/hour for ≥24 hours or anuria for ≥12 hours

Statistical Analysis

Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables was normal or not was determined by the Kolmogorov-Smirnov test. The Levene test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as mean±standard deviation (SD) for normal distributions, and median (Q_1; 25^{th} percentile - Q_3; 75^{th} percentile) for skewed distributions. Categorical data were described as several cases (%). Statistical analysis differences in normally distributed variables between two independent groups were compared by Student's t-test, Mann-Whitney U test was applied for comparisons of the not normally distributed data. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test was accepted p-value <0.05 as a significant level on all statistical analysis.

RESULTS

Between 2020 and 2021, a total of 64 patients with complete data were included in the study. Among these patients, 6 developed AKI (9.3%). Four of these patients were classified as KDIGO Stage I, and 2 as KDIGO Stage II. The demographic data of the patients are presented in Table 2. The mean age in the AKI group was found to be statistically significantly higher (p: 0.043). ASA score was statistically significantly higher in patients in the AKI group (p: 0.002). Additionally, The Frailty Index was significantly higher in the AKI group (p: 0.020). Lastly, it was observed that the use of aspirin and aniotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) was statistically significantly higher in the AKI group (p: 0.022, p: 0.044, respectively) Table 2.

Table 2. Demographic data of the patients

Parameter		Non-AKI n=58	AKI n=6	p
Age, year		57 (43-62)	67 (58-70)	0.043
Gender	Female	36 (62.1)	4 (66.7)	1.000
	Male	22 (37.9)	2 (33.3)	
BMI (kg/m²)		26.3 (22.3-29)	25.0 (24.4-29)	0.927
Frailty index	Yes	18 (31.0)	5 (83.3)	0.020
	No	40 (69.0)	1 (16.7)	
GNRI score		114 (104-122)	108 (107-116)	0.557
PNI score		42.5 (38.3-46)	41 (41-41)	0.225
MELD score		21.7 (20.2-24.4)	20 (19.3-21.5)	0.264
HT	Yes	17 (29.3)	3 (50.0)	0.366
	No	41 (70.7)	3 (50.0)	
CAD	Yes	4 (6.9)	0	1.000
	No	54 (93.1)	6 (100.0)	
CHF	Yes	3 (5.2)	0	1.000
	No	55 (94.8)	6 (100.0)	
DM	Yes	13 (22.4)	3 (50.0)	0.159
	No	45 (77.6)	3 (50.0)	
COPD	Yes	4 (6.9)	0	1.000
	No	54 (93.1)	6 (100.0)	
ASA	II	48 (82.7)	1 (16.7)	0.002
	III	10 (17.3)	5 (83.3)	
Aspirin usage	Yes	5 (8.6)	3 (50.0)	0.022
	No	53 (91.4)	3 (50.0)	
ACEI/ARB usage	Yes	7 (12.1 %)	3 (50.0)	0.044
	No	51 (87.9 %)	3 (50.0)	
Beta-blocker usage	Yes	8 (13.8)	2 (33.3)	0.234
	No	50 (86.2)	4 (66.7)	
Diuretic usage	Yes	3 (5.2)	0	1.000
	No	55 (94.8)	6 (100.0)	
Statin usage	Yes	2 (3.4)	0	1.000
	No	56 (96.6)	6 (100.0)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitney U test, and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant p-values are in bold. AKI: Acute kidney injury; ASA: American Society of Anesthesiologists ; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BMI: Body mass index; GNRI: Geriatric Nutritional Risk Index; PNI: Prognostic Nutritional Index; MELD: Model for End-Stage Liver Disease; MELD-NA: Model for End-stage Liver Disease sodium; HT: Hypertension; CHF: Congestive heart failure; DM: Diabetes mellitus; COPD: chronic obstructive pulmonary disease

There was no significant difference between the groups in terms of patients' preoperative laboratory values Table 3. When patients were evaluated in terms of intraoperative parameters, the amount of colloid used, the amount of ES used, and vasopressor usage were found to be statistically significantly higher in the AKI group (p<.001, p: 0.036, p: 0.022, respectively) (Table 4).

When patients were evaluated in terms of postoperative parameters, vasopressor usage and diuretic usage were found to be statistically significantly higher in the AKI group (p: 0.002, p: 0.044, respectively) Table 5.

Table 3. Patients' preoperative laboratory values

Parameter	Non-AKIn=58	AKIn=6	p
Serum creatinine (mg/dl)	0.77 (0.66-0.92)	0.65 (0.62-0.80)	0.433
Hematocrit (%)	41 (35-44)	38 (32.5-42)	0.374
Serum albumin (g/L)	42.5 (38.3-46)	41 (41-41)	0.248
Lymphocyte (10^9/L))	1.58 (1.12-1.98)	1.66 (1.45-1.97)	0.917
Bilirubin (mg/dl)	0.58 (0.4-0.94)	0.6 (0.45-0.60)	0.945
(INR)	1 (1-1.1)	1 (1-1)	0.902
Sodium (mEq/L)	139 (137-141)	139 (136-141)	0.954

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile). Continuous variables were compared with the Mann-Whitney U test. Statistically significant p-values are in bold. AKI: Acute kidney injury, INR: International normalized ratio

Table 4. Intraoperative parameters

Parameter		Non-AKI n=58	AKIn=6	p
Surgical operation				
Colorectal resection		18 (31.0)	2 (33.3)	0.105
Operation whipple		17 (29.3)	1 (16.7)	
Liver resection		14 (24.1)	0	
Gastric resection		6 (10.3)	1 (16.7)	
Intestinal resection		3 (5.3)	2 (33.3)	
Anesthesia duration, min		420 (288-493)	450 (259-495)	0.991
Crystalloid amount, ml		2950 (2000-4375)	4250 (2250-5875)	0.222
Colloid usage	Yes	49 (84.5)	6 (100)	0.582
	No	9 (15.5)	-	
Colloid amount, ml		500 (500-600)	850 (625-1000)	<.001
ES replacement	Yes	48 (82.8)	3 (50.0)	0.092
	No	10 (17.2)	3 (50.0)	
ES amount, ml		0 (0-0)	150 (0-975)	0.036
FFP amount, ml		0 (0-188)	250 (0-500)	0.122
Amount of intraoperative bleeding, ml		375 (150-688)	1250 (400-2100)	0.116
Intraoperative urine output amount, ml		625 (400-1313)	650 (275-763)	0.496
Intraoperative vasopressor usage	Yes	5 (8.6)	3 (50.0)	0.022
	No	53 (91.4)	3 (50.0)	
Nephrotoxic agents usage	Yes	50 (86.2)	6 (100)	1.000
	No	8 (13.8)	-	
Diuretic usage	Yes	15 (25.9)	1 (16.7)	1.000
	No	43 (74.1)	5 (83.3)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitneyww U test, and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant p-values are in bold. AKI: Acute kidney injury; ES: Erythrocyte Suspension; FFP: Fresh frozen plasma

Table 5. Postoperative parameters

Parameter		Non-AKI n=58	AKI n=6	p
APACHE-II score		5 (3-6)	6 (5.25-6.75)	0.110
Postoperative vasopressor usage	Yes	1 (1.7)	3 (50.0)	0.002
	No	57 (98.3)	3 (50.0)	
Postoperative diuretic usage	Yes	7 (12.1)	3 (50.0)	0.044
	No	51 (87.9)	3 (50.0)	
Postoperative complication	Yes	15 (25.9)	3 (50.0)	0.338
	No	43 (74.1)	3 (50.0)	
Length of stay in ICU, days		3 (2-4)	3 (2-13)	0.440
Creatinine at ICU discharge		0.57 (0.48-0.69)	0.9 (0.49-1.03)	0.150
Length of hospital stay, days		12 (10-18)	18 (9-23)	0.481
Creatinine at hospital discharge		0.65 (0.51-0.73)	0.78 (0.71-0.87)	0.064
Hospital mortality	Yes	1 (1.7)	-	1.000
	No	57 (98.3)	6 (100)	
Three-month mortality	Yes	2 (3.4)	1 (16.7)	0.259
	No	56 (96.6)	5 (83.3)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitney U test, and categorical variables were compared using Pearson's Chi-Square test or Fisher exact test. Statistically significant p-values are in bold. AKI: Acute kidney injury; APACHE-II: Acute Physiology and Chronic Health Evaluation II skoru; ICU: Intensive care unit.

DISCUSSION

In this study evaluating factors influencing the development of AKI in patients undergoing major abdominal surgery, advanced age, ACEI/ARB usage, aspirin usage, and frailty index, along with intraoperative vasopressor usage, ES usage, colloid usage, and postoperative vasopressor and diuretic usage, were observed to be significant risk factors. These findings suggest that during the perioperative period of major abdominal surgeries, various demographic and clinical parameters play a role in the development of AKI.

AKI is a serious health issue and among the leading causes of morbidity and mortality. Moreover, the presence of multiple risk factors requires a detailed analysis of these factors. In recent years, the increase in the elderly population and the consequent proliferation of comorbidities have led to encountering patient groups requiring surgical interventions at an advanced age more frequently.[18,19] In major abdominal surgeries, not only non-modifiable factors such as age but also modifiable factors (such as vasopressor, colloid, diuretic usage, etc.) necessitate a comprehensive perioperative analysis. An increase in the frailty index and the consequent rise in AKI incidence, particularly in the postoperative period, can be a commonly encountered situation.[20] In our study, we demonstrated that there is no correlation between the GNRI score and the PNI score with AKI in major abdominal surgeries where nutritional deficiency may be observed. However, several aspects including preoperative frailty, intraoperative management and events, and postoperative care may influence the risk of developing postoperative complications.[21] Therefore, we believe that the frailty index, which encompasses more than just nutrition, may be a more suitable prognostic factor for AKI in major abdominal surgeries. In our study, an increase in advanced age and frailty index was observed to be effective factors in the development of AKI. Therefore, comprehensive and multidisciplinary evaluation, especially in the frail patient population, is crucially important.

Another important factor is the inevitable need for polypharmacy in this patient group due to comorbidities.[22] Especially the negative effects of ACEI/ARB, NSAIDs, and diuretic usage on renal functions are a well-known fact. This effect can lead to adverse outcomes both intraoperatively and postoperatively. However, there is no consensus on the mechanisms by which these drugs are associated with the risk of AKI development.[23,24] Adding multiple risk factors arising from major surgeries and significant, uncontrolled surgical stress response to this situation can further adversely affect already problematic renal functions. The results of this study suggest that ACEI/ARB usage in the preoperative period and diuretic usage in the postoperative period may be a risk factor for the development of AKI.

An interesting finding in our study is the positive correlation between aspirin usage and the development of AKI. Although aspirin use in cardiac surgery has been noted to limit increase bleeding risk in patients, it has also been suggested to reduce the incidence of AKI development and intraoperative myocardial infarction.[25-27] However, research investigating the relationship between aspirin usage and AKI is predominantly focused on cardiovascular surgery. Contrary to these studies, there is a need for more comprehensive research to understand why such a result was encountered in this study.

AKI development is largely attributed to reduced renal perfusion due to volume depletion, which is a significant concern, especially in major surgeries. Therefore, effective perioperative fluid management aiming to maintain renal perfusion is crucial. In recent years, goal-directed fluid therapy has gained significant importance. This practice is also among the main objectives of Enhanced Recovery After Surgery (ERAS) protocols, which have become increasingly important in recent years.[28] Perioperative fluid management plays a crucial role in preventing organ hypoperfusion. This process should begin with optimal fasting duration in the preoperative period and continue with a positive fluid balance consisting of crystalloids and colloids during the intraoperative period. In the postoperative period, it should be completed with early oral hydration and nutrient intake. Additionally, vasopressor usage should be considered if necessary. However, there are studies indicating that colloid usage may be associated with AKI, and therefore its usage should be limited.[29] In our study, the higher use of colloids during the intraoperative period in patients who developed AKI may suggest this, but it should be noted that this remains a topic of ongoing significant debate.

In a study, it was indicated that blood transfusion is associated with allergic reactions and may increase the incidence of AKI. Additionally, an increase in AKI incidence has been observed in patients receiving ES. This may be attributed to the kidneys being more sensitive to the inflammatory process associated with transfusion.[30] Additionally, patients undergoing surgery involving the use of blood and blood products may experience significant fluid shifts. These large fluid shifts can lead to hemodynamic instability, which in turn can cause AKI. The higher incidence of AKI development in patients receiving transfusions in this study is consistent with this result.

Limitations

The study has several limitations. Firstly, it was conducted at a single center and retrospectively. Due to the limited number of patients in the study, multicenter and prospective studies are needed to determine more precise results. Additionally, including only abdominal surgeries in the study may limit generalization.

CONCLUSION

The development of AKI following major abdominal surgeries is not only a significant cause of morbidity and mortality but also leads to substantial resource utilization. Detailed analysis of risks that may affect the perioperative period and efforts to limit them is crucial in reducing AKI incidence. Especially in elderly patients, frailty and age are significant factors that must be kept in mind. In addition, polypharmacy and perioperative medications can significantly impact renal function in patients undergoing major abdominal surgery. It is crucial to conduct a detailed evaluation of the drug treatments and consider potential dose adjustments to mitigate these effects. We believe that more comprehensive studies in this regard will be important in uncovering specific and potential risk factors for subgroups.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Ankara Bilkent City Hospital Clinical Researches Ethics Committee (Date: 17.03.2021, Decision No: E1/1605/2021).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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