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- Aysun POSTACI[1]
- Burak ERSAK[2]

CORRESPONDANCE

[1]Aysun POSTACI

Phone : +905323520383
e-mail : aysunposta@yahoo.com

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[1] Ankara City Hospital, Department of Anesthesiology and Reanimation, Ankara, Turkey

[2] Ankara City Hospital, Department of Gynecologic Oncology Surgery, Ankara, Turkey

RESEARCH

POSTOPERATIVE ACUTE KIDNEY INJURY IN GERIATRIC GYNECOLOGIC ONCOLOGY PATIENTS AFTER MAJOR OPEN ABDOMINAL SURGERY: A RETROSPECTIVE COHORT STUDY

Abstract

Introduction: This investigation's purpose was to determine the incidence of acute kidney injury, the associated risk factors, and the 90-day outcomes and kidney function of geriatric patients who underwent major open abdominal gynecologic oncologic surgery.

Materials and Method: This retrospective cohort study involved patients aged ≥ 65 years who underwent major open abdominal gynecologic oncologic surgery.

Results: The postoperative incidence of acute kidney injury in gynecologic oncologic surgical procedures was 22.1%, with a transient nature observed in 72% of patients. The in-hospital mortality rate was 4 %. Kidney function on the 90th day after acute kidney injury development revealed that estimated glomerular filtration rate regressed by over 25% in 6 patients (24%). Acute kidney injury development was associated with surgical time, intraoperative bleeding volume, bowel procedures, the presence of ascites, intraoperative hypotension, vasopressor use, postoperative diuretic use, postoperative hypoalbuminemia, prolonged post-anesthesia care unit, and hospital stay ($p < 0.05$). A logistic regression analysis of the risk factors for acute kidney injury revealed that surgery duration was a significant one ($p < 0.05$).

Conclusion: Postoperative acute kidney injury is an important postoperative complication associated with the development or progression of chronic kidney disease. This leads to a prolonged stay in the post-anesthesia care unit and in the hospital. Although acute kidney injury is frequently transient in geriatric patients following major open abdominal gynecologic oncologic surgery, developing preventive measures, encouraging team collaboration, and monitoring serum creatinine concentration in the early postoperative period are critical in complex surgical procedures.

Keywords: Postoperative Complications; Acute Kidney Injury; Geriatrics.

INTRODUCTION

Acute kidney injury (AKI) is a condition characterized by a sudden loss of kidney function, resulting in urea and other nitrogenous waste products accumulating in the blood. Initially referred to as acute kidney failure in the 1950s, the term has evolved over time, and the condition has been called acute kidney damage since 2004. Since 2012, acute kidney injury has been defined as a sudden (in hours) reduction in kidney function encompassing both injury (structural damage) and impairment (loss of function) function (1,2).

When diagnosing postoperative AKI (PO-AKI), the Kidney Disease Improving Global Outcomes (KDIGO) guideline has established criteria for defining the condition as a kidney disease (1-3). PO-AKI is an independent risk factor for both in-hospital and long-term mortality. It also indicates an increased risk of chronic kidney disease (CKD) and progression to cardiovascular events (4-6). PO-AKI can occur in 6.7% to 39.3% of patients undergoing noncardiac surgery. AKI etiologies and mechanisms are multifactorial. This is a common postoperative complication, especially in geriatric patients, due to decreases in preoperative renal reserve, multiple comorbidities, and polypharmacy (5-10).

AKI occurring in the postoperative period can sometimes be transient (< 48 hours) and rapidly reversible. Alternatively, AKI may be persistent, with structural tubular damage and dysfunction. Recent studies have shown that even transient AKI is associated with increased hospital stay duration, morbidity, and mortality in hospitalized patients (9,11,12).

Few studies in the literature have investigated the incidence and risk factors of PO-AKI after major open abdominal gynecologic oncological surgery in geriatric patients. This study conducted a retrospective analysis of the incidence of AKI, risk factors associated with its occurrence, 90-day outcomes, and kidney function of geriatric patients who underwent major open abdominal gynecologic oncologic surgery.

MATERIALS AND METHODS

Study design and patients

In this retrospective, single-center cohort study, data were collected from 113 geriatric patients aged 65 years and older who underwent major open abdominal surgery in the gynecologic oncologic surgery clinic between January 2021 and March 2022. Their preoperative American Society of Anesthesiologists (ASA) scores from I–III were evaluated (Figure 1) after obtaining approval from our hospital's Ethics Committee for Clinical Research (E1-22-2381).

The study exclusion criteria were defined as geriatric patients who met any of the following criteria: surgical duration of ≤ 2 hours, AKI in the past 3 months, end-stage renal disease (i.e., an estimated glomerular filtration rate [eGFR] of ≤ 15 mL/min/1.73 m^2), a hospital stay of less than 4 days, less than 4 serum creatinine (sCr) measurements during hospitalization, and a missing or incomplete medical history.

Data collection and variables

For the study, patient information was obtained from anesthesia pre-intra-postoperative records, the hospital medical information system, the Republic of Turkey Ministry of Health e-nabiz application, and files and discharge records from the gynecologic oncologic surgery service. The following clinical data were collected:

1. Preoperative disease states, including hypertension, diabetes mellitus, ischemic heart disease (CHD), congestive heart failure, and other comorbidities, as well as patient demographic data.
2. Laboratory values, including hemoglobin, sCr, estimated eGFR, and serum

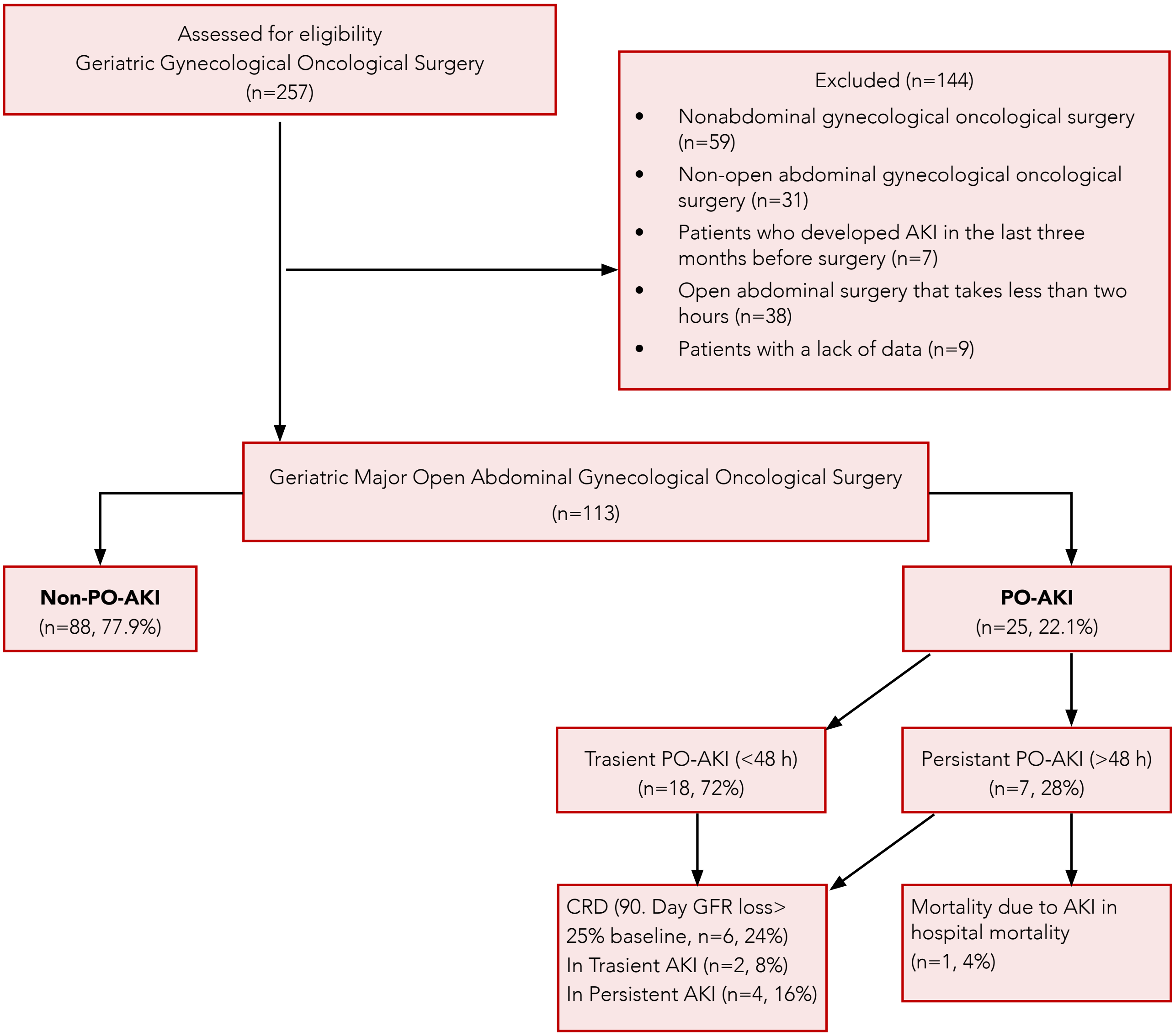

Figure 1. Patient selection and work flow chart.

albumin concentration, were measured preoperatively, postoperatively for the first three days, at discharge from the hospital, and 90 days after discharge.

3. Drugs were used preoperatively, intraoperatively, and postoperatively, including chemotherapy, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, diuretics, acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NSAIDs), vasoactive drugs, and furosemide.

4. The type and duration of surgery (in minutes), amount of ascitic discharge (in mL), blood loss (in mL), blood transfusion (in units), the total amount of crystalloid and colloid

infused (in mL), amount of fluid infused throughout the operation (in mL/h), bowel procedures, length of stay hospital and post-anesthesia care unit (PACU) duration (from the day of operation to discharge).

5. The ASA scores and General Surgery Acute Kidney Injury Risk Index were calculated and recorded (13).

Definition and calculation of kidney dysfunction

This study's primary aim was to determine the incidence and risk factors for PO-AKI considering sCr, according to KDIGO (2). The secondary outcome was to determine the risk factors associated with AKI, in-hospital mortality, hospital stay duration, and kidney function on the 90th day after hospital discharge.

Acute kidney injury staging

The study classified AKI in accordance with the established criteria set forth by the KDIGO guidelines. Specifically, AKI staging was based on sCr levels, as defined by KDIGO. According to the sCr levels defined by KDIGO, AKI is defined if either there is an increase in sCr by ≥ 0.3 mg/dL within 48 hours or an increase in sCr to ≥ 1.5 times the baseline. Therefore, AKI was classified into stages, considering that the baseline sCr was defined as the most recently measured sCr before surgery. The classification was as follows: stage 1a if there was (a) an increase in sCr 1.5–1.9 times baseline, stage 2 if there was (b) an increase in sCr 2.0–2.9 times baseline, and stage 3 if there was either (c) an increase in sCr ≥ 3 times or the initiation of RRT (1). Furthermore, transient AKI was defined when there is an increase in sCr meeting the sCr criteria of the highest stage maintained for ≤ 48 hours, and persistent AKI was defined when there is an increase in sCr satisfying the sCr criteria of AKI for > 48 hours (11,12). In this study, if sCr was not measured within the 90th day after discharge, the first sCr measured after day 90 was taken as a baseline for the post-discharge process.

Chronic kidney disease

Chronic kidney disease (CKD) is defined as a preoperative eGFR level of < 60 mL/min/1.73 m^2. CKD progression is defined as worsening of the eGFR category with a ≥25% reduction from baseline at 90 days in eGFR according to the 2012 Clinical Practice Guidelines for the Assessment and Management of Chronic Kidney Diseases: KDIGO (2).

Statistical analyses

The IBM SPSS 20 program for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Mean standard deviation, median, minimum, and maximum values were given in descriptive statistics for continuous data, and number and percentage values were given in discrete data. The Kolmogorov-Smirnov test was used to examine the conformity of the data to the normal distribution. The Mann-Whitney U test was used to compare continuous data between the non-AKI and AKI groups. Chi-square and Fisher's exact tests were used for group comparisons (cross tables) of nominal variables. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

In our study, the data of 113 out of 257 female patients aged 65 and over who had gynecological cancers surgery between January 2021 and March 2022 were analyzed, whereas 114 were excluded from the study (see Figure 1). The demographic characteristics of the patients, their medication status, and features specific to operations are seen in Table 1. Furthermore, PO-AKI was detected in 22.1% of the patients, as indicated in Table 2. Transient PO-AKI (PO-AKI time < 48 hours) was

Table 1. Preoperative medical status, baseline kidney functions, demographic and surgery characteristics of the patient with non-AKI and AKI.

	Non-AKI		AKI		p value
	Mean ± SD Median (Range)		Mean ± SD Median (Range)		
Age (year)	72.16±5.96 71 (65-89)		72.12±5.08 72 (65-83)		0.822 [a]
BMI kg/m^2	32.33±6.45 30 (17-50)		32.20±6.79 31 (22-45)		0.936 [a]
Duration of surgery (min)	258.98±79.16 247.5 (135-490)		308.00±84.53 315 (180-480)		**0.014** [a]
Preoperative AKI risk score	3.45±0.98 3 (0-5)		3.60±0.76 4 (2-5)		0.600 [a]
Baseline creatinine (mg/dL)	0.83±0.21 0.79 (0.51-1.42)		0.85±0.19 0.84 (0.55-1.39)		0.543 [a]
Baseline Hb (gr/dL)	12.24±1.64 12 (8.8-16.3)		11.80±1.74 11.6 (8.8-15.1)		0.278 [a]
Baseline GFR (mL/kg/ 1.73 m^2)	73.09±17.16 75 (37-106)		70.88±16.69 70 (36-96)		0.536 [a]
Type of Surgery	**n**	**%**	**n**	**%**	**p value**
Endometrial Cancer	48	54.5	11	44.0	0.326 [b]
Ovarian Cancer	32	36.4	13	52.0	
Cervical Cancer	8	9.1	1	4.0	
HT					
No	15	17.0	3	12.0	0.759 [b]
Yes	73	83.0	22	88.0	
DM					
No	49	55.7	18	72.0	0.143 [b]
Yes	39	44.3	7	28.0	
CAD					
No	59	67.0	20	80.0	0.213 [b]
Yes	29	33.0	5	20.0	
HF					
No	79	89.8	24	96.0	0.454 [b]
Yes	9	10.2	1	4.0	

Table 1 continued.

Table 1. Preoperative medical status, baseline kidney functions, demographic and surgery characteristics of the patient with non-AKI and AKI.

Preoperative use of nephrotoxic drugs					
No	79	89.8	21	84.0	
Yes	9	10.2	4	16.0	0.480 [b]
ACEIs/ARBs					
No	27	30.7	8	32.0	
Yes	61	69.3	17	68.0	0.900 [b]
Diuretics					
No	30	34.1	9	36.0	
Yes	58	65.9	16	64.0	0.859 [b]
Preop chemo. drug use					
No	76	86.4	19	76.0	
Yes	12	13.6	6	24.0	0.225 [b]
Acetyl salicylic acid					
No	66	75.0	18	72.0	
Yes	22	25.0	7	28.0	0.762 [b]
Beta blockers					
No	57	64.8	15	60.0	
Yes	31	35.2	10	40.0	0.661 [b]
Baseline GFR ml/min/1.73 m^2					
<60	22	25.0	8	32.0	
≥60	66	75.0	17	68.0	0.484 [b]

AKI: acute kidney injury, HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, HF: heart failure, ACEIs: angiotensin converting enzyme inhibitors, ARBs: angiotensin receptor blockers, a: $p > 0.05$ not significantly different with Mann Whitney U test, b: $p > 0.05$ not significantly different with Chi-Square test/Fisher's Exact test.

detected in 72% of geriatric patients with AKI. The KDIGO distribution of patients with AKI is shown in Table 2.

In-hospital mortality was detected due to AKI in one of 7 patients who developed postoperative persistent AKI (mortality n=1, 4%) (Figure 1). Mortality was not detected in any of the patients in the transient AKI group.

While testing 90-day kidney functionality, a more than 25% decline in GFR was detected in 24% (n=6) of the geriatric patients with PO-AKI, 8% (n=2) of patients with transient AKI, and 16% (n=4) of patients with persistent AKI (Figure 1). There was no significant difference between the groups of patients who developed and did not develop AKI with preoperative baseline eGFR < 60 mL/

Table 2. Comparison of intraoperative and postoperative data of patients with non-AKI and AKI.

	Non-AKI		AKI		p value
	Mean ± SD Median (Range)		Mean ± SD Median (Range)		
Bleeding during surgery (mL)	502.84±531.12 250 (50-3000)		742.00±689.60 600 (100-3500)		**0.016** [a]
Total use of crystalloids during surgery (mL)	3244.32±980.01 3400 (1000-5700)		3584.00±1184.07 3500 (1700-6000)		0.284 [a]
Total use of colloids during surgery (mL)	682.73±286.29 500 (100-1500)		682.35±327.74 500 (100-1500)		0.976 [a]
Total urine output during surgery (mL)	462.32±289.30 400 (90-1500)		499.60±338.43 400 (150-1400)		0.986 [a]
Total use of fluid during surgery (mL/h)	882.25±257.12 845 (400-1741)		817.12±232.42 825 (338-1299)		0.329 [a]
Length of stay in PACU (days)	1.50±0.85 1 (1-5)		2.88±2.61 2 (1-13)		**0.001** [a]
Length of stay in hospital (days)	7.06±3.28 6 (4-22)		11.08±6.17 9 (5-27)		**<0.001** [a]
	n	**%**	**n**	**%**	**p value**
Blood product					
No	64	72.7	15	60.0	0.221 [b]
Yes	24	27.3	10	40.0	
Bowel procedures					
No	79	89.8	18	72.0	**0.045** [b]
Yes	9	10.2	7	28.0	
Intraabdominal fluid (ascites)					
No	80	90.9	18	72.0	**0.022** [b]
Yes	8	9.1	7	28.0	
Blood product					
No	64	72.7	15	60.0	0.221 [b]
Yes	24	27.3	10	40.0	
Bowel procedures					
No	79	89.8	18	72.0	**0.045** [b]
Yes	9	10.2	7	28.0	

Table 2 continued.

Table 2. Comparison of intraoperative and postoperative data of patients with non-AKI and AKI.

Hypotension during surgery					
No	70	79.5	17	56.0	**0.017** [b]
Yes	18	20.5	11	44.0	
Use of norepinephrine during surgery					
No	86	97.7	21	84.0	**0.021** [b]
Yes	2	2.3	4	16.0	
Use of ephedrine during surgery					
No	70	79.5	14	56.0	**0.017** [b]
Yes	18	20.5	11	44.0	
AKI stage distribution	**n**	**%**			
KDIGO stage					
1	17	15			
2	6	5.3			
3	2	1.8			
PO-AKI					
No	88	77.9			
Yes	25	22.1			
PO-AKI duration time					
≤ 48 hour	18	72.0			
> 48 hour	7	28.0			

PO: postoperative, PACU: post-anesthesia care unit, a: $p > 0.05$ not significantly different with Mann Whitney U test, b: $p > 0.05$ not significantly different with Chi-Square test/Fisher's Exact test.

min/1.73 m^2 as visible in Table 1. In the group of patients who developed PO-AKI, the mean surgical time was longer, and the amount of intraoperative bleeding was significantly higher. In addition, PO-AKI was found to be significantly higher in patients who underwent a surgical bowel procedure, had abdominal ascites, developed intraoperative hypotension, and needed vasopressor support. AKI stage of the patients who developed PO-AKI see in Table 2. It is statistically significant that the length of hospital and PACU stay were longer, postoperative diuretic use was higher, and the decrease in postoperative serum albumin level was higher in patients who developed PO-AKI compared to patients who did not develop AKI (Table 2). As a result of the logistic regression analysis created with the effective risk factors for PO-AKI, it was determined that the duration of surgery was an effective risk factor for AKI and a 1-minute increase in the surgical time increased the incidence of PO-AKI 1.007 times [($p < 0.05$), Table 3]. The distribution graph of the serum creatinine values of the patients at the control, postoperative 1-3rd day, discharge, and 90th day after discharge is shown in Figure 2.

Table 3. Logistic regression analysis of risk factors for PO-AKI.

Variable	B	OR	95 % CI		p value
Duration of surgery (min)	0.007	1.007	1.001	1.014	0.031*
Bleeding during surgery (mL)	0.000	1.000	0.999	1.001	0.843
Bowel procedures	0.050	1.051	0.240	4.596	0.947
Intraabdominal fluid (ascites)	1.337	3.809	0.982	14.782	0.053
Hypotension during surgery	0.891	2.438	0.816	7.280	0.110

B: Regression coefficient, OR: Odds Ratio, CI: Confidence Interval, * p < 0.05 significantly different with logistic regression analysis.

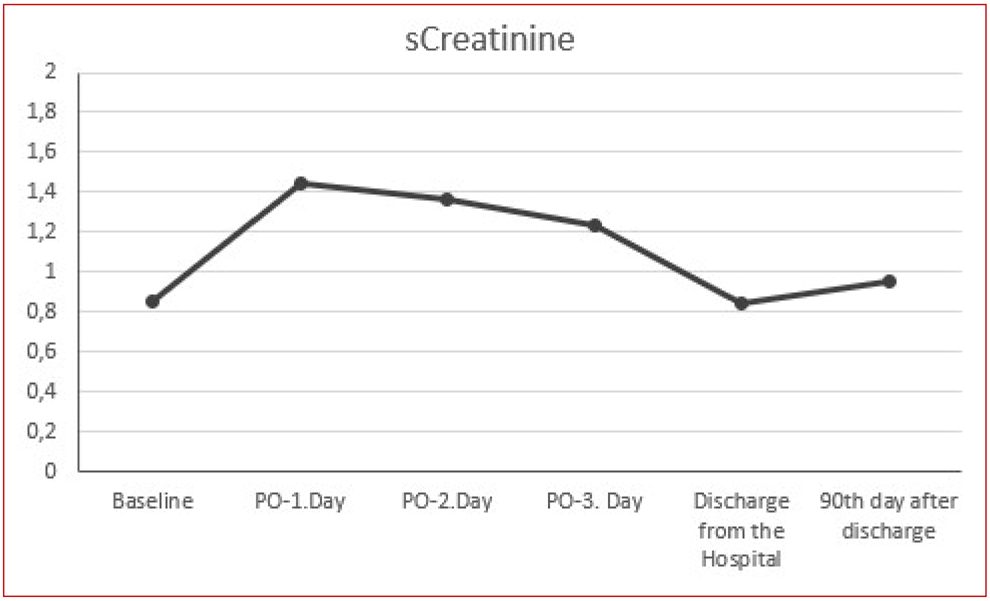

Figure 2. The curve of sCr levels of geriatric patients who participated in the study.

DISCUSSION

In our study, it was determined that the incidence of PO-AKI following gynecologic oncologic surgery among geriatric patients was 22.1%. PO-AKI was considered transient (< 48 hours) in 72% of the patients, whereas it was considered persistent (> 48 hours) in 28% of the patients. The development of PO-AKI was associated with surgical time, amount of intraoperative bleeding, patients undergoing bowel procedures, presence of intra-abdominal acid, intraoperative hypotension, vasopressor use, postoperative diuretic use, postoperative hypoalbuminemia, and prolonged PACU and hospital stay length.

Previous studies reported incidences of AKI as a common type of organ injury that occurs in patients who have undergone noncardiac surgery, with a frequency ranging from 3% to 39% (4,12,14,15). Studies demonstrated that the incidence of AKI is increasing in the geriatric patient population due to the aging population and the corresponding increasing comorbidities, increasing prevalence of CKD and diabetes, polypharmacy, intravenous contrast agent use for imaging, and cardiovascular intervention procedures (6,7,9,10). AKI seen in 23–40% of elderly patients has a correlation between both CKD and mortality risk (6,9). The keys to recovering AKI prognosis are early diagnosis and early intervention.

Shen et al. analyzed AKI incidence at 5.76% for patients aged above 75 who had undergone major abdominal surgery in their retrospective cohort study, and it was demonstrated that the development of PO-AKI was higher in female patients (n = 22, 66.7%). Shen et al. found that the independent risk factors were older age, intraoperative hypertension, baseline GFR, serum albumin level, and the use of Hydroxyethyl starch (HES) + Non-steroidal anti-inflammatory drugs (NSAIDs) (6).

Privratsky et al. investigated PO-AKI incidence and risk factors according to age and gender in a multicenter retrospective study done in noncardiac, non-kidney/urologic surgery. In their study, it was determined that the incidence of PO-AKI was less prevalent in female patients aged below 50 (3.7%) than female (6.5%) and male (8.3%) patients aged above 50 and male patients below 50 (5.9%) (3). While the mean age of women over 50 was 66.7 years, emergency patients were included in this study. However, in our study, the mean age was 72.15, and only patients who underwent gynecological oncological surgery were included; therefore, this may explain the higher incidence of AKI in our study.

In a randomized controlled study with geriatric patients who underwent noncardiac surgery, Wu et al. evaluated the relation between PO-AKI and 3-year mortality and the incidence of PO-AKI was 15.5 %. In their study, the patients with AKI consisted of 85% with Stage 1, 10% with Stage 2, and 5% with Stage 3; however, it was not associated with 3-year mortality in elderly patients who underwent noncardiac surgery (16).

Li et al. conversely determined AKI incidence to be 39.0% in a retrospective study in which they analyzed patients aged 75 and over who developed AKI according to the KDIGO criteria and were hospitalized in the geriatric clinic. In those patients, the percentage of transient AKI was 41.4%, while the percentage of persistent AKI was 58.6% (11).

Vaught et al. analyzed the incidence of AKI in adult patients undergoing major gynecological surgery according to the Risk, Injury, and Failure; and Loss; and End stage kidney disease. (RIFLE) criteria at 13%. While the incidence of AKI was 5% in patients undergoing benign tumor surgery, it was 18% in patients with malignancy. In this retrospective cohort study, the average age of the patients who developed AKI was 60 years. Non-abdominal surgery patients were also included in the study, which had a younger patient population than our study (17).

There are various perioperative risk factors for the development of PO-AKI (18-21). Wu et al. found PO-AKI to be directly proportional to surgical time, total fluid infusion amount, cardiac complications, and length of hospital stay (16). Li et al. alternatively reported low hemoglobin levels; high blood urea, nitrogen, and uric acid levels; and patients who underwent mechanical ventilation as risk factors for the development of PO-AKI (11). Furthermore, in Shen et al.'s study, age, serum albumin level, baseline GFR, intraoperative hypotension, and use of HES+NSAIDs and HES+ furosemide were independent risk factors for the development of PO-AKI (6). Shaw et al. examined the association between intraoperative hypotension thresholds (MAP thresholds were ≤ 75, ≤65, and ≤ 55 mmHg) and the following two AKI subtypes (persistent and delayed) in a retrospective multicenter cohort study, and intraoperative hypotension was associated with persistent but not delayed AKI (22). Since our study was retrospective, we did not have the opportunity to determine the threshold value for MAP. The rates of both persistent and transient AKI in the patients who developed and were treated for hypotension were significantly higher than in those who did not develop AKI.

Huepenbecker et al. reported that the percentage of AKI was higher after gynecologic surgery with enhanced recovery after surgery (ERAS) (13.1% versus 5.8%) in their study, in which they examined the incidence of PO-AKI after ERAS protocols in open gynecological surgery (23). In this study, bowel procedures, estimated blood loss, intraoperative PRBC transfusion, hypotension, vasopressor administration, surgical complexity of ovarian cancer, intraoperative administration, and higher mean intraoperative use of crystalloids and colloids were found in the patient group that developed PO-AKI as the factors that cause AKI. While the mean age of the patients who developed AKI in this study was 65, the mean age of the patients who developed PO-AKI was 72 in our study, and only patients with malignant and underwent open abdominal surgery were included in the study. The absence of reports of geriatric patients undergoing gynecologic oncologic major open abdominal surgery demonstrates that the incidence of PO-AKI is low in this patient population in our clinic.

Preoperative and/or postoperative hypoalbuminemia have been reported in studies of patients who developed AKI after major surgery (24,25). In our study, postoperative hypoalbuminemia developed at a higher rate in patients who developed AKI. In our study, the surgical complexity score was not considered; however, it can be interpreted that postoperative hypoalbuminemia may be associated with gynecologic oncologic surgical complexity.

Our study was a retrospective cohort study conducted at a single center covering the period from 2021 to 2022. While this allowed us to carefully examine the data from this specific center, we acknowledge that the narrow time range may limit the generalizability of our findings. Additionally, due to the restricted period, the sample size of the patients and the data collected may be relatively small. Nevertheless, we believe that our study provides valuable insights into this specific population and can serve as a foundation for further research in this area.

In conclusion, PO-AKI is a common but mostly temporary postoperative complication associated with chronic kidney disease, increased PACU and hospital stay in elderly patients after open abdominal gynecologic oncologic surgery. In order to ensure the prevention of the development of PO-AKI, it is imperative to ensure the continuity of oncological treatment in cancer patients and to prevent unwanted complications. It is important to reduce the incidence of AKI, especially in complex surgical procedures, by developing preventive strategies and team cooperation, ensuring the prevention of bleeding, avoiding unnecessary blood transfusion and nephrotoxic agents, ensuring hemodynamic stability, optimization of perioperative hydration, and close monitoring of sCr concentration in the early postoperative period.

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Disclosure Statement

The authors declare they have no conflict of interest related to the research.

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