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ORIGINAL INVESTIGATION

Comparison of plasma neutrophil gelatinase-associated lipocalin (NGAL) levels after robot-assisted laparoscopic and retropubic radical prostatectomy: an observational study

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KEYWORDS
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Abstract
Background and objectives: Patients undergoing radical prostatectomy are at increased risk of Acute Kidney Injury (AKI) because of intraoperative bleeding, obstructive uropathy, and older age. Neutrophil Gelatinase-Associated Lipocalin (NGAL) may become important for diagnosis of postoperative AKI after urogenital oncosurgery. The objective of this study was to evaluate and compare the efficacy of NGAL as a predictor of AKI diagnosis in patients who underwent Retropubic Radical Prostatectomy (RRP) and Robot-Assisted Laparoscopic Prostatectomy (RALP) for prostate cancer.
Methods: We included 66 patients who underwent RRP (n = 32) or RALP (n = 34) in this prospective, comparative, nonrandomized study. Patients' demographic data, duration of surgery and anesthesia, amount of blood products, vasopressor therapy, intraoperative blood loss, fluid administration, length of hospital stay, creatinine, and plasma NGAL levels were recorded.
Results: Intraoperative blood loss, crystalloid fluid administration, and length of hospital stay were significantly shorter in RALP. There was no statistically significant difference between the groups in terms of intraoperative blood transfusion. Postoperative creatinine and plasma NGAL levels were increased in both groups. The 6-h NGAL levels were higher in RRP ($p = 0.026$). The incidence of AKI was 28.12% in RRP and 26.05% in RALP, respectively. The NGAL level at 6 hours was more sensitive in the early diagnosis of AKI in RALP.

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Conclusion: Although postoperative serum NGAL levels were increased in both RRP and RALP, the 6-h NGAL levels were higher in RRP. RALP was associated with fewer intraoperative blood loss and fluid administration, and shorter length of hospital stay.

Introduction

Retropubic Radical Prostatectomy (RRP) is the most commonly used surgical treatment for clinically localized prostate cancer because of its low morbidity, good tumour control, and good functional results. However, patients undergoing RRP are at increased risk for postoperative Acute Kidney Injury (AKI) because of higher amount of intraoperative bleeding, obstructive uropathy, and advanced age.[1] Robot-Assisted Laparoscopic Prostatectomy (RALP) has been developed as an alternative to RRP in recent years because of better surgical visualization, less surgical adverse events, intraoperative blood loss, postoperative pain, and shorter length of hospital stay.[2] However, RALP requires a longer surgical time and may lead to worse physiological changes compared to RRP due to pneumoperitoneum and prolonged steep Trendelenburg position.[3,4] Cardiac output, glomerular filtration rate, renal blood flow, and urine output may decrease due to intraperitoneal carbon dioxide insufflation during RALP.[1]

Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a small molecule of 25 KD weight from the lipocalin family, which is expressed from renal tubular cells. It has been shown that urine and plasma levels of NGAL were increased after tubular damage[5] and become altered before creatinine or oliguria signals a reduction in kidney function.[6] In the literature, it is stated that NGAL can be used as a biomarker for early recognition of AKI after liver transplantation,[7,8] after cardiac surgery,[9] in adult critically ill patients,[10] and after robotic surgery.[11] It has also been studied in pediatric populations.[12,13]

AKI is one of the most important postoperative complications and is associated with adverse outcomes, including chronic renal failure and death, and increased health costs.[14,15] There are a limited number of studies using NGAL for early detection of AKI after prostatectomy. NGAL may become important for diagnosis of postoperative AKI after urogenital oncosurgery. Therefore, we aimed to evaluate and compare the efficacy of NGAL as a predictor of diagnosing AKI in patients who underwent RRP and RALP for prostate cancer.

Methods

Study design

The study was approved by the Ethics Committee of the University of Health Sciences (10/1), Antalya Training and Research Hospital, and registered in the NCT03607279 Clinical Research Database (clinicaltrials.gov). Written informed consent was obtained from all patients included in the study. This study followed the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[16]

A prospective, comparative, nonrandomized study enrolled 90 consecutive male patients who were 80 years of age or younger and were fully continent, potent, and candidates for radical prostatectomy by a retropubic or robot-assisted approach between January 2017 and August 2017. Patients aged between 18 and 80 years with American Society of Anesthesiologists (ASA) physical status I–III and without pre-existing chronic renal disease defined by Kidney Disease Improving Global Outcomes (KDIGO) classification[17] were included in the study. Exclusion criteria included: patient's refusal to participate, pre-existing renal disease, heart failure, and necessity for emergency surgery.

Patients' demographic data (age, height, weight, BMI, Charlson comorbidity index, ASA, comorbidities, and smoking), duration of surgery and anesthesia, amount of blood and blood products used intraoperatively, length of hospital stay, need for vasopressor therapy, intraoperative fluid treatment, perioperative creatinine (baseline, first, second, and third postoperative day), and NGAL (baseline, 6 hours, and 12 hours after induction of anesthesia) levels were recorded.

Preoperative care

Routine preoperative evaluation included electrocardiography, chest X-Ray, and blood analysis. One day before the surgery, a clear liquid diet was started, and patients stopped taking anything orally after midnight preceding the surgery. Although a full bowel preparation was not necessary, preoperative laxatives were used on the day before surgery. Preoperative antacid and antibiotic prophylaxis were applied according to the standard hospital care.

Anesthesia technique

On arrival in the operating room, a 16G peripheral venous catheter was placed. Patients were under standard monitoring including invasive blood pressure (via the 20G catheter in the radial artery), five-lead electrocardiography, and pulse-oximetry. After premedication with 0.04 $mg.kg^{-1}$ intravenous (IV) midazolam, anesthesia was induced with 2 $\mu g.kg^{-1}$ fentanyl, 1.5 $mg.kg^{-1}$ IV propofol, and 0.6 $mg.kg^{-1}$ rocuronium. Anesthesia was maintained with 50% oxygen in air and 0.8–1.5 age-adjusted minimum alveolar anesthetic concentration of desflurane. The patients were ventilated in the volume-controlled mode (Primus, Drager, Luebeck, Germany). Ventilator settings were set with the tidal volume of 6–8 $mL.kg^{-1}$ and with the inspiratory/expiratory ratio of 1:2, and 4–7 cmH_2O positive end-expiratory pressure.

Following tracheal intubation, invasive arterial blood pressure, end-tidal CO_2, diuresis, body core temperature, and hemoglobin concentration were also monitored. Fluids were administered using crystalloid (Hartmann's solution) and colloid (hydroxyethyl starch, 6%). When ureterovesical anastomosis was completed in patients undergoing RALP and the patient was returned to the supine position, intravenous fluid was provided with 1-L bolus Ringer lactate solution followed by 150 $mL.h^{-1}$ infusion for the next 12–24 hours, depending on the patient's volume status. During surgery, systolic blood pressure was maintained at or above 90 mmHg. Intraoperative analgesia was provided with IV remifentanil infusion. Repeated injections of rocuronium were administered, if necessary. End-tidal CO_2 was maintained between 30 and 35 mmHg by ventilatory parameters adjusted after creating CO_2 pneumoperitoneum. Intravenous 1000 mg paracetamol and 100 mg tramadol was administered to all patients approximately 30 minutes before reversal of anesthesia for postoperative analgesia. At the end of the surgery, cuff leak test was applied to all patients and neostigmine and atropine were administered for antagonizing muscle block.

All patients were awakened in the operating theatre and were then moved to the postanesthesia care unit. Criteria for discharge from the postanesthesia care unit were that patients must be awake, cooperative, hemodynamically stable, have an acceptable respiratory pattern, and have the recovery of motor functions.

Hypotension was defined as a reduction of more than 20% of baseline values and promptly treated with ephedrine IV 5–10 mg and bolus fluid application. If the treatment was insufficient, IV vasopressor therapy was planned to be started. The hemoglobin concentration was maintained at > 7 $g.dL^{-1}$; if the patient's hemoglobin concentration was $\leq$ 7 $g.dL^{-1}$, a packed red blood cell transfusion was planned.[1] Anesthesia time was defined as the time that the patient entered the operating room until the delivery of the patient to the postanesthesia care unit.

Surgical procedures

Both RALP and RRP were performed according to the standard protocols by our urology clinic. All patients had clinically localized carcinoma of the prostate and underwent RRP or RALP. The choice of surgical approach was according to patient preference after discussion of the risks, benefits, and alternatives with the attending surgeon. No demographic, clinical, or oncological criteria were used to select the surgical approach. Surgical time was defined as the time between the first incision and the end of surgery.

For RALP, robotic interventions were performed using da Vinci surgical robot (Intuitive Surgical, Mountain View, CA), which is designed for transform, filter, and transmit the surgeon's hand movements into precise movements of the instruments. Da Vinci surgical robot consists of a 3D high-resolution visualization system and special instruments that allow the surgeon to operate with advanced vision, precision, and control.[2]

RRP procedures were performed through a lower midline abdominal incision by the surgeon at the supine position. For RALP, the patients were placed in a modified lithotomy position. After adequate positioning of the patient, pneumoperitoneum was created by intraperitoneal insufflation of CO_2 with an insufflation pressure of 15 mmHg. After the trocar cannulas were placed, patients were placed in the steep Trendelenburg position (approximately 45 from horizontal). Intraperitoneal pressure was maintained at 12 mmHg during the induced pneumoperitoneum. At the end of the procedure, the table was brought back to the normal position and the pneumoperitoneum was released.

Postoperative analgesia was provided with paracetamol 1000 mg orally at 8-h intervals. A clear liquid diet was started at the earliest postoperative period and diet was advanced as bowel function returned. Fluid boluses (500 mL of Ringer Lactate) were administered to patients with urine output below 0.5 mg $mL.h^{-1}$. To reduce the incidence of deep vein thrombosis, subcutaneous low molecular weight heparin and early ambulation were administered. When the patients were hemodynamically stable and drains were removed, patients were discharged from hospital.

Measurement of NGAL

Five milliliters venous blood was collected into tubes (Becton Dickinson Vacutainer SST II Advance Plus, lot 7163845 Plymouth, UK) that contained a spray-dried clot activator and gel separator. The samples were maintained at room temperature for a minimum of 30 minutes to allow the blood to clot and then were centrifuged at 2500 RPM for 15 minutes at 4 °C to separate serum. Plasma specimens were aliquoted and maintained at -20 °C until NGAL levels were assessed.

Plasma human NGAL levels were measured using a commercially available ELISA kit (Affymetrix-eBioscience, Vienna, Austria) (%CV < 10, analytical sensitivity 6.5 $pg.mL^{-1}$, assay range 7.81–500 $pg.mL^{-1}$). The assays employed the solid-phase sandwich ELISA (enzyme-linked immunosorbent assay) technique. Plasma levels of NGAL were determined at baseline (preoperative), 6 hours, and 12 hours after induction of anesthesia. The cut-off value for NGAL plasma level for the diagnosis of AKI was considered 150 $ng.mL^{-1}$.[3]

Primary and secondary aims

The primary aim of this study was to evaluate and compare the efficacy of NGAL as predictor of diagnosing AKI in patients who underwent RRP and RALP for prostate cancer. AKI was defined based on the KDIGO criteria[17] for AKI within 48 hours after surgery (the presence of any of the following events: an increase in serum creatinine level $\geq$ 0.3 $mg.dL^{-1}$ within 48 hours, or increase in serum creatine $\geq$ 1.5 times baseline or urine output < 0.5 $mL.kg^{-1}.h^{-1}$ for 6 hours). Because the urine output was measured on a daily basis (not on an hourly basis), the urine output criterion was not included in the current study. The secondary aim was to compare intraoperative blood loss, fluid administration, and length of hospital stay.

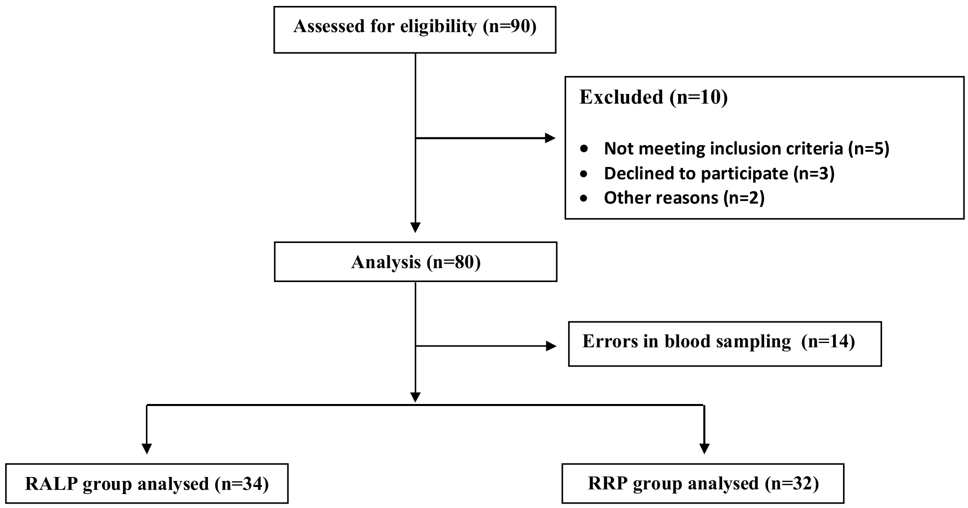

Figure 1 Patients' flow chart.

Statistical analyses

The sample size was calculated using G-power (G*Power 3.1, Düsseldorf, Germany) 3.1.9.2 software. A pilot study of 10 patients per group suggested a 41.51 ng.mL^{-1} difference in mean NGAL levels and SD of 56.61 between the groups. Consequently, a power calculation (α = 0.05 and β = 0.2) indicated a minimum of 31 patients for each group. Hence, 40 patients were included per group to replace any dropouts.

Statistical analysis was performed using SPSS version 24 statistical software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean $\pm$ standard deviation for normally distributed data or median (interquartile range) for not normally distributed data, and categorical data were presented as absolute frequencies and percentages. All numerical data were tested for normal distribution by the Kolmogorov-Smirnov test. Differences between mean values for normally distributed variables were compared using Student's *t*-test. Non-normally distributed variables and ordinal variables were compared with the Mann-Whitney *U* test and the Wilcoxon rank sum test. The chi-squared test and Fisher's exact test were used for categorical data where appropriate. Repeated measures of variance (ANOVA) were used to test for any change in values among the study time points. At each time point, the NGAL values for each patient were recorded, and these values were correlated with the patients who matched and did not meet the definition of AKI. All confidence intervals were constructed with 95% statistical confidence. A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 90 patients were asked to participate in the study. Five patients did not meet the inclusion criteria, three patients declined to participate in the study, and two surgeries were cancelled. Fourteen patients were excluded from analysis because of errors in blood sampling. Data from the remaining 66 patients, 34 in the RALP group and 32 in the RRP group, were analyzed for the study (Fig. 1).

There were no statistically significant differences between the two groups with respect to age, height, weight, Body Mass Index (BMI), Charlson Comorbidity Index, ASA physical status, and comorbidities (Table 1).

No statistically significant differences were found between the two groups in terms of duration of surgery and anesthesia. Moreover, 15.6% of RRP patients received Red Blood Cell (RBC) transfusions intraoperatively, while none of the RALP patients received RBC transfusion. No patient in both groups needed vasopressor therapy in the intraoperative period. The amount of use of intraoperative crystalloid fluids was statistically higher in RRP group (p = 0.0001). The amount of use of intraoperative colloid fluids was similar in both groups (p = 0.929). The length of hospital stay was also significantly shorter in the RALP group (p = 0.001). The intraoperative blood loss was statistically higher in the RRP group (p = 0.04) (Table 2).

Preoperative and postoperative creatinine and plasma NGAL levels are presented in Table 3. There was no statistical difference between the two groups in terms of creatinine values at any time point. The creatinine values on the first, second, and third postoperative days were significantly higher compared with the baseline values in RRP group (p = 0.036, p = 0.004, p = 0.018, respectively). Similarly, the creatinine values were significantly higher compared with the baseline values in RALP group (except third postoperative day) (p = 0.0001, p = 0.031, p = 0.092, respectively). According to the baseline levels, the plasma NGAL levels increased in 6 and 12 hours after induction of anesthesia in RRP group (p = 0.0001, p = 0.0001, respectively) and RALP group (p = 0.0001, p = 0.0001, respectively). Baseline and 12-h NGAL levels were similar in both groups (p = 0.259, p = 0.323, respectively). Moreover, the 6-h NGAL levels were higher in RRP group (p = 0.026). In accordance with KDIGO criteria, the incidence of AKI was 28.12% in RRP and 26.05% in RALP (p = 0.572), respectively.

The sensitivity of serum NGAL to detect AKI was greater at 12 hours in RRP group, whereas it was greater at 6 hours in RALP group (Table 4). When the cut-off value for the NGAL plasma level for the diagnosis of AKI was considered 150 ng.mL^{-1}, the sensitivity of NGAL in both groups was

Table 1 Demographic data.

	Group RRP (n = 32)	Group RALP (n = 34)	*p*-value
Age, years	66.1 ± 7.2	63.4 ± 6.1	0.100
Height, cm	172.1 ± 3.4	171.9 ± 4	0.819
Weight, kg	78.8 ± 3.7	79 ± 3.9	0.770
BMI, kg.m^{-2}	26.5 ± 0.4	26.7 ± 0.3	0.084
Charlson Comorbidity Index	2.4 ± 0.9	2 ± 0.7	0.090
ASAphsicalstatus, n (%)			
ASA I	4 (12.4)	5 (14.7)	0.323
ASA II	14 (43.8)	19 (55.9)	
ASA III	14 (43.8)	10 (29.4)	
Comorbidities, n (%)			
Arterial hypertension	12 (37.5)	16 (47.1)	0.296
Diabetes mellitus	4 (12.5)	6 (17.6)	0.407
CAD	8 (25)	8 (23.5)	0.558
Smoking, n (%)	9 (28.1)	8 (23.5)	0.442

Values are the mean ± standard derivation (SD) or the number (percentage).
BMI, Body Mass Index; ASA, American Society of Anesthesiologists; CAD, Coronary Artery Disease. $p < 0.05$ is statistically significant.

Table 2 Perioperative data.

	Group RRP (n = 32)	Group RALP (n = 34)	*p*-value
Duration of surgery, min	220 (180–300)	250 (200–395)	0.450
Duration of anesthesia, min	260 (205–340)	290 (240–352)	0.502
Hospital stay, days	10 (7–10)	7 (5–7)	0.001*
Intraoperative blood loss, mL	310 ± 176	190 ± 105	0.040*
Red blood cell transfusion, n (%)	5 (15.6)	0 (0)	0.088
Fluids administered			
Crystalloid, mL	2687 ± 669	1855 ± 447	0.0001*
Colloid, mL	93 ± 235	88 ± 260	0.929
Urine volume, mL			
Intraoperative	1495 ± 293.99	1580 ± 190.32	0.420
First day	1510 ± 354.96	1640 ± 214.47	0.335
Second day	2915 ± 710.30	3105 ± 462.15	0.484
Third day	3485 ± 401.42	3600 ± 434.60	0.546

Values are the mean ± standard derivation (SD), median (interquartile range) or the number (percentage). $p < 0.05$ is statistically significant.

84.2% (95% CI: 60.4–96.6) and the specificity was 31.9% (95% CI: 19.0–47.1) at 6 hours. Moreover, the sensitivity was 78.9% (95% CI: 54.4–93.9) and the specificity was 38.3% (24.51–53.6) at 12 hours.

Discussion

This study showed that the NGAL levels after both RRP and RALP increased significantly in 6 and 12 hours according to the baseline levels. Furthermore, baseline and postoperative NGAL levels measured at 12 hours were similar in both groups, while those measured at 6 hours were higher in RRP than RALP. The amount of use of intraoperative crystalloid fluids, and intraoperative blood loss were significantly lower, and length of the hospital stay was significantly shorter in RALP.

In the literature, the relevant studies have shown that RALP provides better surgical visualization, less intraoperative bleeding, fewer operative adverse events, early patient discharge, less postoperative pain, and early patient mobilization compared to RRP.[4,18,19] A study by Joo et al. showed that intraoperative estimated blood loss, fluid treatment, length of hospital stay, and transfusion requirement were significantly lower in patients undergoing RALP.[1] In a retrospective study of 707 patients whose data were evaluated in 2009, D'Alanzo et al. reported that the estimated blood loss was significantly higher in RRP, the intraoperative red blood cell transfusion was significantly lower in RALP, and the RALP patients had less fluid therapy with shorter hospitalization.[20] Consistent with these studies, in this study, we found that the need for intraoperative crystalloid fluid therapy, the estimated amount of intraoperative bleeding, and the need for blood and blood products transfusion were less, and the duration of hospital stay was shorter in patients undergoing RALP when compared to the RRP.

Restricted fluid therapy is frequently used in RALP to reduce the effects of the Trendelenburg positioning combined with pneumoperitoneum on respiratory,

Table 3 Creatinine and NGAL levels.

	Group RRP (n = 32)	Group RALP (n = 34)	*p*-value
Creatinine, mg.dL^{-1}			
Baseline	1.09 ± 0.22[a,b,c]	1.05 ± 0.14[d,e,f]	0.405
1st postoperative day	1.22 ± 0.41[a]	1.21 ± 0.24[d]	0.879
2nd postoperative day	1.26 ± 0.44[b]	1.16 ± 0.32[e]	0.293
3rd postoperative day	1.28 ± 0.46[c]	1.10 ± 0.23[f]	0.058
NGAL, ng.mL^{-1}			
Baseline	122 ± 68.7[g,h]	105.8 ± 45.3[i, j]	0.259
6 h	251.2 ± 133.2[g]	192.5 ± 67.2[i]	0.026*
12 h	219.2 ± 141.5[h]	190.2 ± 90.9[j]	0.323

Values are the mean ± standard derivation (SD). $p < 0.05$ is statistically significant.
[a] $p = 0.036$ baseline vs. 1st postoperative day.
[b] $p = 0.004$ baseline vs. 2nd postoperative day.
[c] $p = 0.018$ baseline vs. 3rd postoperative day.
[d] $p = 0,0001$ baseline vs. 1st postoperative day.
[e] $p = 0.031$ baseline vs. 2nd postoperative day.
[f] $p = 0.092$ baseline vs. 3rd postoperative day.
[g] $p = 0.0001$ baseline vs. 6 h.
[h] $p = 0.0001$ baseline vs. 12 h.
[i] $p = 0.0001$ baseline vs. 6 h.
[j] $p = 0.0001$ baseline vs. 12 h.

Table 4 Specificity and efficacy of NGAL plasma levels at 6 hours and 12 hours in detecting AKI.

		NGAL levels	AKI (+)	AKI (-)	Sensitivity % (95%CI)	Specifity % (95%CI)
6hours						
Group RRP (n = 32)	NGAL < 150	109.7 ± 52.8	2	7	80 (44.3–97.4)	31.8 (13.8–54.8)
	NGAL > 150	306.6 ± 111.2	8	15		
Group RALP	NGAL < 150	109.9 ± 28.8	1	8	88.8 (51.7–99.7)	32 (14.9–53.5)
(n = 34)	NGAL > 150	222.2 ± 49.7	8	17		
12hours						
Group RRP (n = 32)	NGAL < 150	121.2 ± 70.5	1	8	90 (55.5–99.7)	36.3 (17.2–59.3)
	NGAL > 150	257.5 ± 144.6	9	14		
Group RALP	NGAL < 150	111.1 ± 26.1	3	10	66.6 (29.9–92.5)	40 (21.1–61.3)
(n = 34)	NGAL > 150	239.2 ± 81.5	6	15		

Values are the mean ± Standard Derivation (SD), the number or % (95% CI).

cardiovascular, and cerebrovascular systems, to prevent peroperative pharyngeal, laryngeal, and facial edema and to increase the surgical vision.[21,22] Considering the administration of a restricted fluid treatment, to create a better surgical area by ensuring less urine output, and intraoperatively less estimated blood loss, the need for intraoperative fluid and blood treatments is less in RALP, compared to RRP.[4,20,23] The requirement of crystalloid fluid treatment and the need for blood and blood product transfusion are less in the RALP group in our study, and these findings consistent with previous studies. However, this fluid restriction applied during RALP may also cause a slight increase in patients' serum creatinine levels in the postoperative period.[20] In our study, serum creatinine levels were found to be higher in both groups compared to the baseline values. In the study of Orsolya et al., similar to our results, it was stated that serum creatinine levels increased significantly on the postoperative first day compared to the baseline values, and then they tended to decrease.[11]

In retrospective and/or nonrandomized prospective studies, the duration of surgery and anesthesia in RALP was found significantly longer when compared to RRP.[2,21] Yonekura et al. reported that RALP surgery was associated with longer pneumoperitoneum time and duration of anesthesia than conventional laparoscopic radical prostatectomy.[24] Nevertheless, the duration of surgery and anesthesia varied in the studies according to the experience of the surgical team. As a matter of fact, it is clearly stated in the literature that the duration of surgery in the laparoscopic approaches is influenced by the experience of the surgical team, and this duration is shortened with increasing experience.[25]

A long-term steep Trendelenburg positioning combined with pneumoperitoneum is required during RALP. In particular, the use of pneumoperitoneum pressures above 15 mmHg may cause decreased cardiac output, renal blood flow, glomerular filtration rate, and urine output. The renin–angiotensin–aldosterone system, which is activated due to these physiological changes, leads to a further decrease in blood flow, and thus further deterioration of renal function.[26–28] In a study of Joo et al, the incidence of postoperative AKI after RALP and RRP was evaluated according to the KDİGO criteria and they showed that the incidence of AKI was statistically lower in patients undergoing RALP (5.5% in RALP and 10.4% in RRP, $p = 0.004$).[1] In our study, although not statistically significant, the incidence of postoperative AKI was higher in RALP. Duration of anesthesia and surgery was longer in our study than in the study by Joo et al. In the literature, there is a study reporting the incidence of postoperative AKI as 37.5% after robotic urological oncosurgery.[11]

AKI is one of the most important causes of postoperative morbidity and mortality. The incidence of AKI after radical prostatectomy is not clear in the literature. However, it has been reported that patients with urological diseases are a high risk group for AKI due to reasons such as obstructive uropathy, advanced age, and current chronic kidney disease.[29] Early recognition of AKI is very important in terms of preventing renal failure and/or initiating early treatment. Serum creatinine level is the most commonly used parameter to evaluate renal function. However, both serum creatinine and urine output, which are the parameters used to identify AKI, have been shown to have limited sensitivity and specificity for predicting AKI.[30] Increases of serum creatinine levels are detected later than changes in glomerular filtration.[11] This leads to a delay in the early detection of AKI and consequently to preventive measures and delayed treatment. Moreover, serum creatinine levels are influenced by many factors such as aging and loss of muscle mass, which is significantly more prevalent in elderly patients. Therefore, the serum creatinine levels of the elderly can be lower than the normal values, often resulting in delayed or late diagnosis due to increased kidney injury pathologies being obscured, which all reveal the necessity to search for biomarkers of early injury, such as NGAL.[31–33]

In recent years, NGAL has been one of the most promising biomarkers in the early detection of AKI. A meta-analysis by Haase et al. clearly shows that NGAL is a useful marker for early detection of AKI, both serum and urinary NGAL levels are similar in diagnosis, and the NGAL levels have a prognostic value for clinical outcomes such as mortality and renal replacement therapy.[34] The NGAL sensitivity and specificity measured at 6 hours were 84.2% and 31.9%, respectively, and those measured at 12 hours were 78.9% and 38.3%, respectively, when the cut-off value for the diagnosis of AKI was 150 $ng.mL^{-1}$. Similar to the results of our study, the study of Orsolya et al., examining the efficacy of plasma NGAL levels after RALP, found that the NGAL levels measured at 6 hours were more sensitive in detecting AKI compared to those measured at 12 hours, and the sensitivity and specificity of the NGAL levels measured to detect AKI at 6 hours were 81.82% and 55.17%, respectively, while those measured at 12 hours were found to be 72.73% and 62.07%, respectively, when the cut-off value for the diagnosis of AKI was 150 $ng.dL^{-1}$.[11] In a study by Cruz et al., conducted on evaluating the plasma NGAL levels for the early detection of AKI in adult patients in ICU, the sensitivity of plasma NGAL in the first 48 hours was found to be 73% and its specificity was 81% when the cut-off value was 150 $ng.mL^{-1}$.[10]

The study showed that NGAL evaluation through time is different between RRP and RALP. We found that NGAL levels measured for RALP at 6 hours and NGAL levels measured for RRP at 12 hours were more significant in detecting AKI. In a previous study, patients undergoing urogenital laparoscopic surgery had higher postoperative NGAL levels at both 6 and 12 hours, serum NGAL was peaked at 6 hours, and this increase was significantly at 6 hours when compared to 12-hours serum NGAL levels.[35] This may be explained to the intrinsic differences between RRP and RALP on renal physiology during surgery. RALP often requires pneumoperitoneum with an intra-abdominal pressure of more than 15 mmHg. However, high intra-abdominal pressures applied during RALP can decrease cardiac output, renal blood flow, glonmerular filtration rate, and urine output.[1] Moreover, a restricted fluid treatment, to create a better surgical area during RALP, may also contribute to renal impairment.[20] The incidence of AKI after RRP may result from the decreases in cardiac output and renal perfusion, and increased oxidative stress that are associated with a larger amount of blood loss during surgery. Furthermore, red blood cell transfusion during RRP may also contribute to the incidence of AKI after RRP.[1]

This study has several limitations. First, serum creatinine changes were based on AKI definition. Evaluations of more sensitive definitions of AKI, using markers other than serum creatinine, may be useful to confirm the results of this study. Second, the patient population in the study was a relatively elderly patient group. Therefore, the findings of this study are not generalized to the whole population. Third, the design of the study is a prospective but nonrandomized trial. A prospective randomized trial is needed to confirm our findings. Finally, although plasma NGAL may be useful in early diagnosis of renal injury, simultaneous urinary NGAL levels could also be more significant.

In conclusion, the results of our study showed that the NGAL levels increased significantly after both RRP and RALP. Although the NGAL values measured at 12 hours were better in detecting the AKI after RRP, those measured at 6 hours were much better in detecting AKI after RALP. Intraoperative blood loss, and the amount of use of intraoperative crystalloid fluids were lower and length of hospital stay was shorter in RALP. Although not statistically significant, the incidence of AKI was found to be higher in RRP. Controlled randomized trials with larger sample groups will support the findings of our study.

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Conflicts of interest

The authors declare no conflicts of interest.

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