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Comparison of Acute Kidney Injury After Robot-Assisted Laparoscopic Radical Prostatectomy Versus Retropubic Radical Prostatectomy

A Propensity Score Matching Analysis

Eun-Young Joo, MD, Yeon-Jin Moon, MD, Syn-Hae Yoon, MD, Ji-Hyun Chin, MD, PhD, Jai-Hyun Hwang, MD, PhD, and Young-Kug Kim, MD, PhD

Abstract: Acute kidney injury (AKI) is associated with extended hospital stay, a high risk of progressive chronic kidney diseases, and increased mortality. Patients undergoing radical prostatectomy are at increased risk of AKI because of intraoperative bleeding, obstructive uropathy, older age, and preexisting chronic kidney disease. In particular, robot-assisted laparoscopic radical prostatectomy (RALP), which is in increasing demand as an alternative surgical option for retropubic radical prostatectomy (RRP), is associated with postoperative renal dysfunction because pneumoperitoneum during RALP can decrease cardiac output and renal perfusion. The objective of this study was to compare the incidence of postoperative AKI between RRP and RALP.

We included 1340 patients who underwent RRP (n = 370) or RALP (n = 970) between 2013 and 2014. Demographics, cancer-related data, and perioperative laboratory data were evaluated. Postoperative AKI was determined according to the Kidney Disease: Improving Global Outcomes criteria. Operation and anesthesia time, estimated blood loss, amounts of administered fluids and transfused packed red blood cells, and the lengths of the postoperative intensive care unit and hospital stays were evaluated. Propensity score matching analysis was performed to reduce the influence of possible confounding variables and adjust for intergroup differences between the RRP and RALP groups.

After performing 1:1 propensity score matching, the RRP and RALP groups included 307 patients, respectively. The operation time and anesthesia time in RALP were significantly longer than in the RRP group (both $P < 0.001$). However, the estimated blood loss and amount of administered fluids in RALP were significantly lower than in RRP (both $P < 0.001$). Also, RALP demonstrated a significantly lower incidence of transfusion and smaller amount of transfused packed red blood cells than RRP (both $P < 0.001$). Importantly, the incidence of AKI in RALP was significantly lower than in RRP (5.5% vs 10.4%; $P = 0.044$). Furthermore, the length of hospital stay in RALP was also significantly shorter ($P < 0.001$).

The incidence of AKI after RALP is significantly lower than after RRP. RALP can therefore be a better surgical option than RRP in terms of decreasing the frequency of postoperative AKI.

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Abbreviations: AKI = acute kidney injury, eGFR = estimated glomerular filtration rate, KDIGO = Kidney Disease Improving Global Outcomes, NSAID = nonsteroidal anti-inflammatory drug, PSA = prostate-specific antigen, RALP = robot-assisted laparoscopic radical prostatectomy, RRP = retropubic radical prostatectomy.

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From the Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.
Correspondence: Young-Kug Kim, Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea (e-mail: kyk@amc.seoul.kr).
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INTRODUCTION

Radical prostatectomy is a standard surgical treatment for clinically localized prostate cancer.[1] Since retropubic radical prostatectomy (RRP) was developed in 1945,[2] it has been optimized as the surgical technique of choice to reduce short-term and long-term complications and improve functional results in terms of both urinary continence and erectile function.[3–6] Laparoscopic prostatectomy was developed and refined in 1999 with the intention of reducing the invasiveness of traditional open surgery and improving functional results, but the outcomes of laparoscopic prostatectomy patients were not much improved over RRP.[7–9] The development of robot-assisted laparoscopic radical prostatectomy (RALP) soon followed laparoscopic prostatectomy in an attempt to reduce the difficulty involved in performing complex laparoscopic urologic procedures. RALP has been known to be related to lower blood loss and blood transfusion rates and shorter hospital stays in comparison with RRP.[10] However, RALP requires a longer operation time and results in worse physiological changes due to pneumoperitoneum and the steep Trendelenburg position in comparison with RRP.[11,12] The glomerular filtration rate, renal blood flow, and urine output can thereby decrease with intraperitoneal carbon dioxide insufflation during RALP.[13–15]

Acute kidney injury (AKI) is increasingly recognized as a serious postoperative complication and is linked to increased health costs and adverse outcomes including progression to chronic kidney disease and death.[16,17] However, there have been no comparable studies to date on the evaluation of AKI between RRP and RALP. Therefore, we aimed in our current study to compare the incidence of postoperative AKI based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria between RRP and RALP using propensity score matching analysis.

METHODS

Following approval by the institutional review board of Asan Medical Center, the records of all patients who underwent

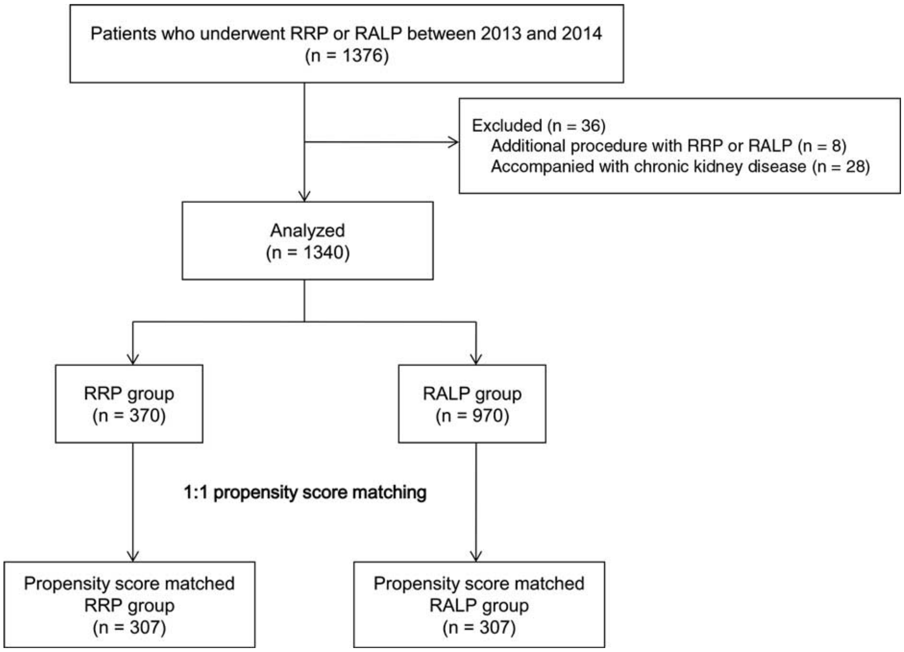

FIGURE 1. Study flow diagram. RALP = robot-assisted laparoscopic radical prostatectomy, RRP = retropubic radical prostatectomy.

RRP or RALP at Asan Medical Center, Seoul, Republic of Korea between January 2013 and December 2014 were searched. Of the 1376 searched patients, we excluded those who underwent additional procedures (n = 8) or had any history of chronic kidney disease (n = 28). A final cohort of 1340 patients was included in the present study (Figure 1).

Anesthetic Technique

Routine monitorings, including electrocardiography, noninvasive blood pressure monitoring, and pulse oximetry were performed before induction. General anesthesia was induced with propofol and rocuronium and maintained by sevoflurane-nitric oxide or sevoflurane-remifentanil. Following tracheal intubation, the invasive arterial blood pressure, body temperature, and hemoglobin concentration were additionally monitored. Fluids were administered using crystalloid (Hartmann's solution or Plasmalyte) and colloid (Volulyte). Systolic arterial blood pressure was maintained at 90 mm Hg or more during surgery. If systolic arterial blood pressure was less than 80 mm Hg, vasoactive drugs (ephedrine, phenylephrine, or norepinephrine) were administered. The hemoglobin concentration was maintained at 7 g/dL or more; if the hemoglobin concentration was less than 7 g/dL, a packed red blood cell transfusion was planned.

Surgical Technique

The key procedures for RRP and RALP were performed according to the standard protocols of our institution.[18] For RRP, a lower midline abdominal incision was made and the endopelvic fascia was opened from the base of the prostate to the apex. For RALP, pneumoperitoneum was established using a Veress needle, and 6 trocars were inserted. For RALP, the prostate was dissected using the antegrade approach. In both surgeries, bilateral pelvic lymph node dissection was performed, and the neurovascular bundles were spared for all potent patients. After the surgical specimen was removed, vesicourethral anastomosis was performed using a 20-Fr urethral catheter.

Data Collection and Measurement

We collected information regarding the baseline characteristics and laboratory, intraoperative, and postoperative data from the computerized patient record system at our institution (Asan Medical Center Information System Electronic Medical Records). The baseline characteristics included age, height, weight, body mass index, comorbidities (eg, hypertension, diabetes mellitus, cardiac disease, and cerebrovascular disease), and the use of prescribed medications (beta-blockers and nonsteroidal anti-inflammatory drugs). Cardiac disease included ischemic heart disease and heart failure. Heart failure was defined as a history of any type of heart failure that was diagnosed by a cardiologist regardless of medication or decreased ejection fraction (ie, ejection fraction $< 40\%$). Cerebrovascular disease was defined as a history of carotid artery stent or angioplasty, transient ischemic attack, stroke, or cerebral hemorrhagic event. Data on the status of patient's cancer including prostate-specific antigen (PSA) level and Gleason score were collected. The estimated glomerular filtration rate (eGFR), hematocrit, albumin, uric acid, and C-reactive protein levels were collected as preoperative laboratory data. eGFR was calculated using the 4-variable (age, sex, race, and serum creatinine) Modification of Diet in Renal Disease Study equation: $\text{eGFR} = 186 \times \text{serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times [0.742 \text{ if female}] \times [1.210 \text{ if African-American}]$.[19]

Intraoperative data included operation time, anesthesia time, estimated blood loss, volume of administered fluids, volume of transfused packed red blood cells, and the use of vasoactive drugs. The operation time was defined as the time between first incision and the end of the operation. Anesthesia time was defined as the time from anesthesia induction to tracheal extubation. Estimated blood loss was evaluated by the amount of lost red cell mass, which was calculated using the perioperative change in the hematocrit and transfused red cell mass using the following equation: lost red cell mass (mL) = papatient's estimated blood volume (mL) × (preoperative hematocrit in % − postoperative hematocrit in %) + (transfused packed red blood cell in units × 250 (mL) × 0.6).[20]

Primary and Secondary Endpoints

The primary endpoint of this study was the comparison of the incidences of AKI based on the KDIGO criteria between RRP and RALP. According to KDIGO criteria, AKI is defined as an increase in serum creatinine by 0.3 mg/dL or more within 48 hours or an increase in the serum creatinine by 1.5 times or more within the prior 7 days.[21] However, in the present study, the urine output criterion was not included due to the inconsistency in urine output measurement. The secondary endpoints included the lengths of postoperative intensive care unit and hospital stay.

Statistical Analysis

Before propensity score matching, we compared data between the RRP and RALP groups using the Chi-square test or Fisher exact test for categorical variables and the student *t* test or Mann–Whitney *U* test for continuous variables, as appropriate. Data are presented as the mean ± standard deviation, or number (percentage), as appropriate. We performed 1:1 propensity score matching analysis to reduce the influence of possible confounding variables and adjust intergroup differences between RRP and RALP groups. To determine the propensity score, a multiple logistic regression model was run using the following 17 variables: age, height, weight, body mass index, hypertension, diabetes mellitus, cardiac disease, cerebrovascular disease, taking beta-blockers or nonsteroidal anti-inflammatory drugs, PSA level, Gleason score, preoperative eGFR, hematocrit, albumin, uric acid, and C-reactive protein (Table 1). After performing 1:1 propensity score matching, continuous variables were compared using the paired *t* test or Wilcoxon signed-rank test, as appropriate, and categorical variables were compared using the McNemar test. Here, $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS for Windows (version 21; IBM Corp, Armonk, NY).

RESULTS

A total of 1340 patients who underwent RRP (n = 370) or RALP (n = 970) were included in the current analyses. Age, height, weight, presence of cardiac disease, PSA, preoperative hematocrit, and albumin level demonstrated statistically significant differences between RRP and RALP groups (Table 1). After performing 1:1 propensity score matching analysis, there were no significant differences in demographic data, cancer-related data, or preoperative laboratory data between the RRP (n = 307) and RALP (n = 307) groups (Table 1). The operation time and anesthesia time in the RALP group were significantly longer than in the RRP group (both $P < 0.001$) (Table 2). However, the estimated blood loss and amount of administered fluids in the RALP group were significantly lower than in the RRP group (both $P < 0.001$) (Table 2). Also, the RALP group demonstrated a lower incidence of transfusion and smaller amount of transfused packed red blood cells than the RRP group (both $P < 0.001$) (Table 2). Importantly, the incidence of AKI in the RALP group was significantly lower than in the RRP group (5.5% [n = 17] vs 10.4% [n = 32]; $P = 0.044$) (Figure 2). Furthermore, the length of hospital stay in the RALP group was

TABLE 1. Demographic data, cancer-related data, and preoperative data between the RRP and RALP patients

	Before propensity score matching			After propensity score matching		
	RRP group (n = 370)	RALP group (n = 970)	*P*	RRP group (n = 307)	RALP group (n = 307)	*P*
Age, y	67.6 ± 6.2	64.9 ± 7.4	<0.001	67.1 ± 5.9	67.0 ± 6.6	0.753
Height, cm	165.5 ± 6.4	166.7 ± 5.7	0.001	165.9 ± 6.3	165.6 ± 5.5	0.519
Weight, kg	67.1 ± 8.5	68.9 ± 8.4	<0.001	67.5 ± 8.4	67.2 ± 7.6	0.536
Body mass index, kg/m^2	24.5 ± 2.8	24.8 ± 2.6	0.071	24.5 ± 2.7	24.5 ± 2.5	0.851
Hypertension	175 (47.3%)	436 (44.9%)	0.440	144 (46.9%)	135 (44.0%)	0.521
Diabetes mellitus	66 (17.8%)	138 (14.2%)	0.100	48 (15.6%)	47 (15.3%)	1.000
Cardiac disease	20 (5.4%)	86 (8.9%)	0.036	18 (5.9%)	15 (4.9%)	0.720
Cerebrovascular disease	18 (4.9%)	32 (3.3%)	0.176	12 (3.9%)	9 (2.9%)	0.648
Medication						
Beta-blockers	30 (8.1%)	93 (9.6%)	0.402	30 (9.8%)	19 (6.2%)	0.126
NSAIDs	32 (8.6%)	93 (9.6%)	0.597	26 (8.5%)	27 (8.8%)	1.000
PSA, ng/mL	9.5 ± 12.7	7.5 ± 6.5	0.003	7.6 ± 6.4	7.9 ± 6.3	0.467
Gleason score	7.18 ± 1.03	7.06 ± 0.95	0.058	7.08 ± 0.98	7.10 ± 0.94	0.801
eGFR, mL/min/1.73 m^2	77.8 ± 12.3	76.8 ± 11.8	0.196	76.7 ± 12.4	76.6 ± 11.3	0.925
Hematocrit, %	39.1 ± 4.4	40.2 ± 4.0	<0.001	39.7 ± 4.2	39.6 ± 4.3	0.673
Albumin, g/dL	3.98 ± 0.36	4.06 ± 0.30	<0.001	4.01 ± 0.32	4.02 ± 0.31	0.587
Uric acid, mg/dL	5.5 ± 1.3	5.6 ± 1.2	0.157	5.5 ± 1.3	5.6 ± 1.3	0.159
C-reactive protein, mg/dL	0.25 ± 0.62	0.21 ± 0.54	0.176	0.22 ± 0.55	0.19 ± 0.30	0.356

Data are expressed as a mean ± standard deviation, or number of patients (%), as appropriate.
eGFR = estimated glomerular filtration rate, NSAID = nonsteroidal anti-inflammatory drug, PSA = prostate-specific antigen, RALP = robot-assisted laparoscopic radical prostatectomy, RRP = retropubic radical prostatectomy.

TABLE 2. Intraoperative data for propensity score matched patients who underwent RRP or RALP

	All patients (n = 614)	RRP group (n = 307)	RALP group (n = 307)	P^*
Operation time, min	162.9 ± 42.5	144.4 ± 37.3	181.5 ± 39.0	<0.001
Anesthesia time, min	197.1 ± 43.5	177.5 ± 37.2	216.7 ± 40.3	<0.001
Estimated blood loss, mL	227.9 ± 172.4	274.9 ± 184.2	180.9 ± 145.4	<0.001
Fluids administered, mL/kg	27.1 ± 11.3	28.9 ± 12.1	25.3 ± 10.2	<0.001
Red blood cell transfusion rate	28 (4.6%)	25 (8.1%)	3 (1.0%)	<0.001
Red blood cell transfused (unit)	0.1 ± 0.6	0.20 ± 0.78	0.02 ± 0.20	<0.001
Vasoactive drugs	201 (32.7%)	108 (35.2%)	93 (30.3%)	0.235

Data are expressed as a mean ± standard deviation, or number of patients (%), as appropriate.
RALP = robot-assisted laparoscopic radical prostatectomy, RRP = retropubic radical prostatectomy.
* All *P* values were determined by comparing the RRP and RALP groups.

significantly shorter than in the RRP group (7.0 ± 2.5 days vs 8.8 ± 3.0 days; $P < 0.001$). However, there were no significant differences in the lengths of stay in the intensive care unit between the groups.

DISCUSSION

In the present study, we found that the incidence of AKI after RALP was significantly lower than after RRP. The amounts of intraoperative blood loss and transfused packed red blood cells in RALP were also significantly lower, and the duration of hospital stay was significantly shorter in comparison with RRP.

Postoperative AKI is associated with increased costs, morbidity, and mortality and can increase the risk of progressive chronic kidney disease. Patients undergoing radical prostatectomy are at increased risk for AKI because of the common occurrences such as obstructive uropathy, older age, and preexistent chronic kidney disease, as well as intraoperative bleeding.[22] Nevertheless, the exact incidence of AKI after radical prostatectomy using validated criteria have never been determined. Our present study provides the first information on the incidence of AKI after radical prostatectomy according to the KDIGO criteria, which can detect even acute subclinical increases in serum creatinine or decreases in eGFR after surgery.

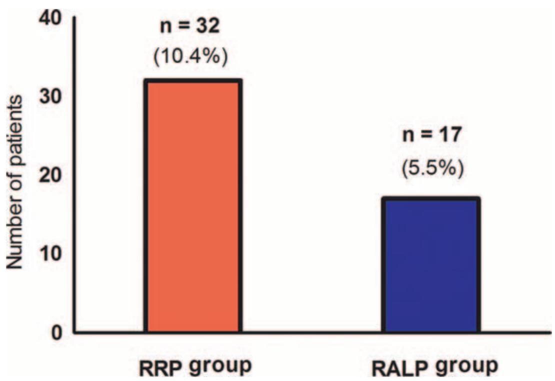

FIGURE 2. Incidences of postoperative AKI between the RRP and RALP groups. The incidence of AKI after RALP was significantly lower than after RRP. AKI = acute kidney injury, RALP = robot-assisted laparoscopic radical prostatectomy, RRP = retropubic radical prostatectomy.

The results of our current analyses showed a postoperative AKI incidence of 5.5% after RALP and 10.4% after RRP. RALP often requires pneumoperitoneum with an intra-abdominal pressure of more than 15 mm Hg for better visualization of the surgical field and continues for more than 3 hours. Direct compression of the intra-abdominal vessels and renal parenchyma by pneumoperitoneum can decrease cardiac output, renal blood flow, the glomerular filtration rate, and urine output.[13–15] These physiologic changes consequently stimulate the renin-angiotensin system and further decreases renal blood flow.[23,24] All of these can contribute to the impairment of renal function. However, previous studies on this issue have reported that postoperative renal function is unaltered after RALP, even under using a pressure of 20 mm Hg for pneumoperitoneum.[25,26] However, these earlier reports analyzed the change in the creatinine clearance or the value of eGFR to measure the differences between preoperative and postoperative renal function, instead of using validated criteria. Also, those studies analyzed only patients that underwent RALP, so the outcomes were not comparable to patients who underwent RRP. In our present study, we used the KDIGO criteria to define AKI, and its incidence between RRP and RALP groups were compared using propensity score matching analysis to reduce the influence of confounding variables and adjust intergroup differences between groups. Therefore, we believe that our present results are highly reliable for the evaluation of AKI after radical prostatectomy.

There are several comparative studies between RRP and RALP in terms of surgical, oncological, and functional outcomes. In line with a previous report,[10] RALP demonstrated lower blood loss and blood transfusion rate in comparison with RRP. The steep Trendelenburg position for RALP under pneumoperitoneum improves visualization, and thus bleeding from the dorsal vein complex during surgery can be more easily controlled.[25] Furthermore, the tamponade effect by pneumoperitoneum also contributes to reduced blood loss.[27] Generally, anemia and blood transfusion are well-known important risk factors of renal injury after cardiac surgery.[28–31] The pathogenesis is unclear, but several mechanisms have been suggested: high vulnerability to hypoxic injury to the kidney and iron-mediated oxidative kidney injury.[32–35] A previous study of 8799 patients who underwent lower-extremity revascularization to investigate the effects of blood transfusion demonstrated that intraoperative blood transfusion was associated with renal failure, as well as morbidity and mortality.[36] Another study of 1034 cardiac surgery patients reported that the patients who received a nonleukoreduced red blood cell transfusion were at a higher risk of acute kidney injury and in-hospital mortality than the patients who received leukoreduced red blood cell transfusion.[37] Another retrospective study of trauma patients demonstrated that the transfusion of red blood cell stored for more than 14 days was associated with increased renal dysfunction and mortality.[38] In our current study, the higher incidence of AKI after RRP may result from the decreases in cardiac output and renal perfusion, diminished oxygen delivery, and increased oxidative stress to the kidney that are associated with a larger amount of blood loss during RRP. Furthermore, the higher incidence of red blood cell transfusion during RRP may also be responsible for the higher incidence of AKI.

Rhabdomyolysis and urinary tract obstruction can occur after robotic or nonrobotic radical prostatectomy and may be associated with development of AKI. Rhabdomyolysis can lead to glomerular filtration rate impairment. However, prostatectomy-related rhabdomyolysis is a very rare complication, and its incidence is reported to be 0.08%.[39] In our current study, none of the patients with postoperative AKI previously had rhabdomyolysis or urinary tract obstruction after RRP or RALP.

The inevitable limitation of our current study comes from its retrospective design. Many confounders such as age, body mass index, comorbidities, and preoperative anemia may affect the accurate evaluation of the incidence of postoperative AKI. Also, previous studies show that cancer characteristics (eg, PSA level, Gleason score) might predict the risk of complications.[40,41] Thus, we performed propensity score matching analysis for 17 confounding variables to minimize these biases. In addition, there are many difficulties in performing a randomized controlled trial to compare RALP and RRP because most patients are unwilling to accept the idea of randomization to a particular surgical treatment. Thus, propensity score matching analysis can be a reliable second-best strategy for comparing RALP and RRP.

In conclusion, postoperative AKI occurs at a lower incidence after RALP than RRP. This result provides valuable information on the additional benefit of RALP, which has many well-known advantages in comparison with RRP. Accordingly, RALP can be a better surgical option in terms of decreasing postoperative AKI than RRP.

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