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Comparison of incidence of acute kidney injury after robot-assisted radical prostatectomy with that after open retropubic and extraperitoneal laparoscopic radical prostatectomies in patients with prostate cancer

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Abstract

Background: We retrospectively evaluated the postoperative renal function in patients who had undergone radical prostatectomy to compare the incidences of postoperative acute kidney injury (AKI) among the patients who had undergone robot-assisted radical prostatectomy (RARP), retropubic radical prostatectomy (RRP), and extraperitoneal laparoscopic radical prostatectomy (exLRP).

Materials and methods: Patients with prostate cancer who had undergone radical prostatectomy at our institution between 2008 and 2014 were included. Robot-assisted radical prostatectomy was performed using an intraperitoneal approach in a 25-degree Trendelenburg position, whereas other procedures were performed with the patient in the supine position. We evaluated the serum creatinine levels and estimated glomerular filtration rates immediately after surgery and on postoperative day 1. We evaluated the incidence of AKI after prostatectomy using the Acute Kidney Injury Network criteria of the Kidney Disease: Improving Global Outcomes guidelines.

Results: A total of 150 consecutive patients were included, with each of the 3 groups (RARP, RRP, and exLRP) comprising 50 patients. Postoperative AKI was observed in 15 (30.0%), 1 (2.0%), and 3 (6.0%) patients in the RARP, RRP, and exLRP groups, respectively. Stage 1 AKI was observed in all the patients except one. The incidence of AKI in RARP group was significantly higher than that in the other groups ($p < 0.001$). In the RARP group, the serum creatinine level was significantly elevated immediately after the surgery; however, it returned to baseline on postoperative day 1. Surgical procedures were the only independent factor associated with AKI incidence.

Conclusions: This study suggest that compared with RRP and exLRP, RARP is associated with a higher incidence of postoperative AKI, although most patients recover rapidly. Intra-abdominal pneumoperitoneum may contribute to AKI onset.

Keywords: Acute kidney injury; Renal function; Prostatectomy

1. Introduction

Radical prostatectomy is the standard treatment for patients with localized prostate cancer and provides favorable long-term oncological outcomes.[1,2] Conventional retropubic radical prostatectomy (RRP) is an invasive procedure associated with extensive bleeding and perioperative complications.[3] To reduce the invasiveness, a laparoscopic procedure for radical prostatectomy has been introduced.[4] Furthermore, robot-assisted radical prostatectomy (RARP) was developed with technical innovations and is commonly used because the intuitive movement of the robotic arms with a 3-dimensional view of the surgical field has led to a shortened learning curve [3,5,6] and oncological and functional outcomes equivalent to or better than those of RRP and laparoscopic radical prostatectomy.[7,8]

In RARP, the intra-abdominal approach in the Trendelenburg position provides a wide working space and is commonly used.[9–11] However, the Trendelenburg position and pneumoperitoneum reduce renal perfusion and may impair renal function.[12,13]

Here, we evaluated the perioperative changes in renal function in patients who had undergone RARP to identify the incidence of postoperative acute kidney injury (AKI) and compared it with that in patients who had undergone extraperitoneal laparoscopic radical prostatectomy (exLRP) and RRP.

2. Materials and methods

This study included patients with prostate cancer who underwent radical prostatectomy at the Sapporo Medical University Hospital, Sapporo, Japan, between 2008 and 2014. Retropubic radical prostatectomy and exLRP were performed between 2008 and 2012. Robot-assisted radical prostatectomy was introduced in 2013. Patients who received transfusions immediately after the surgery and those lacking data were excluded from the study. All data, including preoperative and perioperative parameters, were retrospectively collected.

Robot-assisted radical prostatectomy was performed using a robotic system (Da Vinci Si, Intuitive Surgical Inc., CA, USA) according to the Vattikuti Institute technique.[9] After placing the transabdominal ports, a pneumoperitoneum was created using CO_2 insufflation at 12–15 mm Hg and the patients were positioned in a 25-degree

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Table 1

Patient characteristics.

	RRP group (n = 50)	exLRP group (n = 50)	RARP group (n = 50)	p
Age, yr (IQR)	65 (60–69)	68 (62–70)	66 (63–70)	0.25
BMI, kg/m^2 (IQR)	23.1 (21.2–24.4)	23.9 (22.6–25.3)	24.0 (22.2–26.2)	0.13
Prostate volume, mL (IQR)	27.8 (23.5–44.4)	30.2 (24.1–39.5)	29.2 (23.4–40.6)	0.89
Preoperative hemoglobin, g/dL (IQR)	14.4 (13.8–15.0)	14.4 (13.4–15.3)	14.2 (13.4–15.0)	0.79
eGFR, mL/min/1.73m^2 (IQR)	80.1 (72.9–86.9)	72.8 (64.1–81.7)	70.4 (62.9–76.5)	0.00024
Underlying diseases (%)				
Diabetes	1 (2.0)	8 (16.0)	6 (12.0)	0.06
Hypertension	18 (36.0)	17 (34.0)	21 (42.0)	0.69
IHD	2 (4.0)	3 (6.0)	6 (12.0)	0.28
CKD	2 (4.0)	10 (20.0)	10 (20.0)	0.02
Preoperative medication (%)				
CCB	10 (20.0)	12 (24.0)	16 (32.0)	0.38
ARB	7 (14.0)	11 (22.0)	17 (34.0)	0.06
ACEI	2 (4.0)	0 (0)	1 (2.0)	0.36
Diuretics	2 (4.0)	0 (0)	3 (6.0)	0.24
β-blockers	1 (2.0)	0 (0)	3 (6.0)	0.17

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CCB = calcium channel blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; exLRP = extraperitoneal laparoscopic radical prostatectomy; IHD = ischemic heart disease; IQR = interquartile range; RARP = robot-assisted laparoscopic radical prostatectomy; RRP = retropubic radical prostatectomy.

Trendelenburg position. Retropubic radical prostatectomy and exLRP were performed using a retroperitoneal approach with the patient in the supine position. After placing the retroperitoneal ports for exLRP, pneumoperitoneum was created using CO_2 insufflation at 8–10 mm Hg. In all the procedures, pelvic lymph node dissection in a limited region was performed concomitantly. Patients who underwent RARP in 2015 and beyond were not included in this study because extended lymph node dissection, which we had never performed during RRP or exLRP, was introduced.

The preoperative level of serum creatinine (sCr) was used as the baseline. Serum creatinine was measured immediately after the completion of surgery and on postoperative day (POD) 1. Serum samples were collected within 24 hours of surgery on POD 1. Acute kidney injury was determined according to the definition of the Kidney Disease: Improving Global Outcomes [14] as follows: stage 1, an absolute increase in the sCr level of at least 0.3 mg/dL or an increase in the sCr level of 1.5–1.9-fold from baseline or a urine output less than 0.5 mL/kg/hr for 6–12 hours; stage 2, an increase in sCr level of 2.0–2.9-fold from baseline or a urine output <0.5 mL/kg/hr for ≥12 hours; and stage 3, an increase in sCr level of >3.0-fold from baseline or a urine output <0.3 mL/kg/hr for ≥24 hours, or anuria for ≥12 hours. The estimated glomerular filtration rate (eGFR) was calculated as follows: eGFR (mL/min/1.73m^2) = $194 \times Cr^{-1.094} \times age^{-0.287}$ (in women: $\times 0.739$).[15]

Continuous variables were compared using the Kruskal-Wallis test and one-way analysis of variance. Categorical variables were compared using the χ^2 test. The sCr levels immediately after surgery and on POD 1 were compared with those at the baseline using the Wilcoxon signed-rank test. Univariate and multivariate logistic regression analyses were performed to assess the association between the clinical variables and postoperative AKI. The p value less than 0.05 was considered statistically significant. All statistical analyses were performed using EZR, which is a graphical user interface for R (version 2.13.0; The R Foundation for Statistical Computing, Vienna, Austria).[16] EZR is a modified version of R Commander (version 1.6–3) that is designed to add statistical functions frequently used in biostatistics.

All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee of the institution at which the study was conducted (Sapporo Medical University no. 342-57) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Because this was an observational and not a prospective intervention study, the ethics committee waived the need for written informed consent. We announced the commencement of this study on our Web site (http://web.sapmed.ac.jp/uro/) with the proviso that participants could withdraw later.

3. Results

A total of 150 consecutive patients were included, with each of the 3 groups (RARP, RRP, and exLRP) comprising 50 patients. The patient characteristics are shown in Table 1. No significant differences

Table 2

Intraoperative outcomes.

	RRP group	exLRP group	RARP group	p
Operation time, min (range)	233 (179–383)	255 (198–387)	251 (190–479)	0.02
Duration of pneumoperitoneum, min (range)	–	237 (181–376)	205 (148–455)	0.00083
Amount of bleeding, mL (range)	1387 (150–5150)	1015 (100–3250)	150 (20–1250)	<0.0001
Amount of intravenous fluid, mL (range)	3100 (1850–8200)	3375 (2000–5550)	1975 (1100–3400)	<0.0001
No. transfusions (%)	6 (12.0)	5 (10.0)	0 (0)	0.08

exLRP = extraperitoneal laparoscopic radical prostatectomy; RARP = robot-assisted laparoscopic radical prostatectomy; RRP = retropubic radical prostatectomy.

Table 3

Incidence of postoperative AKI.

	RRP group	exLRP group	RARP group	p
Overall (%)	1 (2.0)	3 (6.0)	15 (30.0)	<0.001
Stage 1	1 (100)	3 (100)	13 (86.7)	
Stage 2	0	0	2 (13.3)	
Stage 3	0	0	0	
Immediately after operation	0	3	14	
Stage 1	0	3	13	
Stage 2	0	0	1	
Stage 3	0	0	0	
POD 1	1	1	1	
Stage 1	1	1	1	
Stage 2	0	0	0	
Stage 3	0	0	0	

AKI = acute kidney injury; exLRP = extraperitoneal laparoscopic radical prostatectomy; POD = postoperative day; RARP = robot-assisted laparoscopic radical prostatectomy; RRP = retropubic radical prostatectomy.

were observed in patient age, body mass index, prostate volume, preoperative hemoglobin level, or preoperative medications among the 3 groups. The eGFR was significantly higher in the RRP group than in the other groups. The prevalence of underlying comorbidities was not significantly different among the groups, except that for chronic kidney disease, which was significantly lower in the RRP group than in the other groups. The intraoperative parameters are shown in Table 2. The operative time was significantly shorter in the RRP group than in the exLRP group. The duration of pneumoperitoneum was significantly shorter in the RARP group than in the exLRP group. The amount of bleeding and volume of intraoperative fluid administered were significantly lower in the RARP group than in the other groups. None of the patients in the RARP group required a transfusion.

The incidence of AKI after surgery was significantly higher in the RARP group than in the RRP and exLRP groups, although most AKI cases were stage 1 (Table 3). The sCr levels decreased to baseline on POD 1 in all patients in the RARP group, except for one (Fig. 1). Complete recovery was observed on POD 7 in the patients who developed AKI on POD 1. Therefore, drug-induced nephrotoxicity was suspected (data not shown). Univariate and multivariate analyses of the association between the clinical variables and AKI are shown in Table 4. The surgery type was the only factor associated with the incidence of postoperative AKI.

4. Discussion

During the last decade, the incidence of AKI, represented by a sudden deterioration of renal function, with small changes in sCr and requiring renal replacement therapy, has increased. In 2012, the Kidney Disease: Improving Global Outcomes guidelines for AKI were released [14] that proposed a definition of AKI based on 2 major criteria: the risk, injury, failure, loss, end-stage renal disease, [17] and Acute Kidney Injury Network.[18]

Acute kidney injury occurs predominantly after a major surgery and is associated with prolonged hospital stay [19] along with increased mortality [20] and costs.[21] Postoperative AKI associated with cardiovascular surgery, the incidence of which ranges from 20% to 40%, is common and well studied.[22–24] Postoperative AKI is also observed after nonvascular general abdominal surgeries. We previously reported that the incidence of postoperative AKI after radical cystectomy was 33%, although most cases were low grade and could be resolved.[25] This relatively high incidence is explained by the longer operative time and greater blood loss associated with radical cystectomy. The incidence of postoperative AKI is reportedly 1%–6% in nonvascular general abdominal surgery.[15,26]

Recent studies have reported a relatively high incidence of postoperative AKI immediately after the completion of RARP. Sato et al.[27] and Naito et al.[28] reported that the incidence of AKI was 46.9% and 13.4%, respectively and that most AKI cases resolved on POD 1. However, RRP was rarely associated with postoperative AKI.[28] Our results were consistent with the results of these studies. In contrast, Joo et al.[29] reported opposite results; in the propensity score matching analysis, patients who had undergone RARP had a significantly lower incidence of postoperative AKI than those who had undergone RRP. However, the evaluation time was not shown in the report. The evaluation of patients on POD 1 and not POD 0 would result in a lower incidence of postoperative AKI after RARP, as observed by us and other researchers.[27,30]

In our study, RARP was associated with a significantly higher incidence of postoperative AKI, compared with both RRP and exLRP. The specific characteristics of RARP include high intra-abdominal

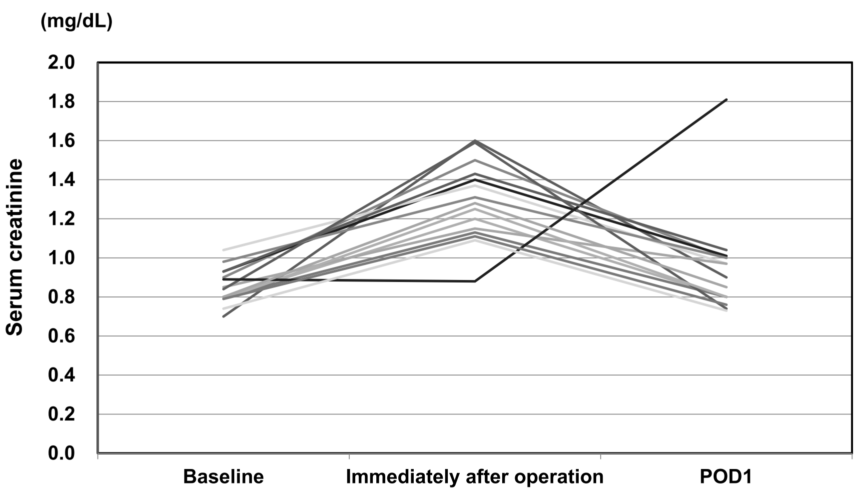

Figure 1. Time courses of serum creatinine levels in 15 patients with postoperative acute kidney injury in the robot-assisted laparoscopic radical prostatectomy group. POD = postoperative day.

Table 4

Univariate and multivariate analyses performed to assess the association between clinical variables and AKI.

	Univariate		Multivariate	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Type of surgery (RARP vs. others)	10.10 (2.96–44.6)	0.000017	6.93 (1.43–33.6)	0.016
Age (≥70 yrs)	2.45 (0.90–6.64)	0.08		
BMI (≥25 kg/m^2)	2.20 (0.83–5.85)	0.11		
Operation time (≥270 min)	0.56 (0.19–1.65)	0.29		
Amount of bleeding (≥500 mL)	0.15 (0.05–0.45)	0.000669	0.58 (0.13–2.60)	0.474
Preoperative hypertension	1.60 (0.54–4.74)	0.45		
Preoperative diabetes	1.07 (0.11–5.39)	1		
Preoperative CKD	1.10 (0.19–4.43)	1		

AKI = acute kidney injury; BMI = body mass index; CI = confidence interval; CKD = chronic kidney disease; OR = odds ratio; RARP = robot-assisted laparoscopic radical prostatectomy.

pressure caused by pneumoperitoneum and the Trendelenburg position. Extraperitoneal laparoscopic radical prostatectomy was performed with extraperitoneal insufflation of carbon dioxide; however, its effect on intra-abdominal pressure may be limited. An increase in intra-abdominal pressure leads to reduced renal perfusion and dysfunction.[13] Pneumoperitoneum may cause a significant increase in intra-abdominal pressure during laparoscopic procedures.[29] However, the effect of the Trendelenburg position on renal function remains unclear. This position increases cardiac volume load, which may affect renal perfusion. Hirose et al.[31] reported that a 6-degree Trendelenburg position caused a slight but non-significant reduction in creatinine clearance. There are no reports on the effects of the Trendelenburg position on renal function, although the effects of a combination of the Trendelenburg position and pneumoperitoneum have been evaluated.[32]

Acute kidney injury is defined by sCr levels and is associated with future cardiovascular events, progression of chronic renal disease, and overall mortality.[33] However, AKI is not always associated with irreversible damage to the renal parenchyma. In a population-based study by Sawhney et al.,[34] the prognostic effect of AKI was observed within 1 year after surgery and not beyond. Sato et al.[30] and Naito et al.[27] found no difference in postoperative renal function between patients with and without an episode of postoperative AKI after 1 year. Collectively, these findings indicate that AKI after RARP rarely has a clinical impact. However, further studies are needed to understand the impact of AKI after RARP on long-term clinical outcomes.

Our study has certain limitations. First, this study was conducted retrospectively with a small sample size. Second, RARP and other procedures were performed during different periods. Third, operative time might have influenced the incidence of AKI in patients who underwent RARP. This learning curve may be associated with AKI incidence. However, the effects of the RARP learning curve could not be evaluated in our study. Thus, further prospective studies with large cohorts and longer follow-up periods are necessary to validate our findings and clarify the impact of postoperative AKI after RARP.

In summary, the results of our study suggest that patients who undergo RARP have a higher incidence of postoperative AKI than those who undergo RRP and exLRP but is resolved by POD 1. Intra-abdominal pneumoperitoneum may be associated with AKI incidence. Although postoperative AKI after RARP is resolved by POD 1, further studies are required to determine its long-term clinical impact.

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Statement of ethics

This study was approved by the institutional research committee of the institution at which the study was conducted (Sapporo Medical University no. 342-57). Because this was an observational and not a prospective intervention study, the ethics committee waived the need for written informed consent. We announced the commencement of this study on our Web site (http://web.sapmed.ac.jp/uro/) with the proviso that participants could withdraw later. All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee of the institution at which the study was conducted (Sapporo Medical University no. 342-57) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest statement

No conflict of interest has been declared by the author.

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Author contributions

SS: Participated in research, data analysis, and writing the manuscript;
TT: Participated in data analysis and writing the manuscript;
TM: Participated in research design and data analysis;
KH, KK: Participated in data analysis;
NM: Supervised the research and participated in writing the manuscript.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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