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Title page

**Pilot experience of simultaneous robotic-assisted partial nephrectomy for bilateral renal tumors —
single center analysis**

Authors:

Taiyo Otoshi, Takeshi Yamasaki, Yuki Yoshi Hirayama, Junji Uchida

Department of Urology, Osaka City University Graduate School of Medicine

1-4-3 Asahi-machi, Abeno-ku, Osaka 545-8585, Japan

Correspondence:

Taiyo Otoshi

Email: sun.otoshi@gmail.com

Abstract

Bilateral renal tumors accounts for approximately 3% of renal tumors. However, surgical treatment methods for bilateral renal tumors have not yet been established. It is imperative to balance the need for curative surgery with the goal of maximal functional preservation in patients with bilateral synchronous renal tumors. Therefore, partial nephrectomy may be the optimal surgical treatment for bilateral synchronous renal tumors. We conducted a retrospective, observational study to analyze the clinical outcome of simultaneous robotic-assisted partial nephrectomy (RAPN) for bilateral renal tumors at our institution between 2016 and 2019. A total of 8 patients were enrolled and the number of renal masses in the 16 kidneys was 18. There was no positive surgical margin after RAPN in our case series and no local recurrence or metastasis during the follow-up period. The only complication of simultaneous RAPN in the present case series was that one patient experienced acute kidney injury after operation without need for dialysis therapy. Our study suggests that simultaneous RAPN for bilateral renal tumors might be feasible both for the preservation of renal function and for oncological outcome such as negative surgical margin..

Keywords: bilateral renal tumors, simultaneous, robotic-assisted partial nephrectomy

Introduction

Bilateral renal tumors accounts for approximately 3% of renal tumors [1]. Patients with bilateral synchronous sporadic renal tumors are a distinctive subpopulation and display different biological behaviors than those of hereditary bilateral renal tumors [2,3]. Surgery is the best method for treating bilateral sporadic renal tumors since its prognosis is similar to that of unilateral sporadic renal tumors . However, surgical treatment methods for bilateral renal tumors have not yet been established.

When bilateral radical nephrectomy is performed, it is necessary to introduce dialysis treatment after surgery; however, this greatly impairs the patient's quality of life. Previous reports suggest that chronic kidney disease and a rapid decline of estimated glomerular filtration rate (eGFR) increase the risk of cardiovascular events and death [4]. Minimizing the loss of renal function associated with surgery is especially crucial for patients with bilateral renal tumors. It is imperative to balance the need for curative surgery with the goal of maximal functional preservation in patients with bilateral synchronous renal tumors . Therefore, partial nephrectomy may be the optimal surgical treatment for bilateral synchronous renal tumors .

The superiority of either the simultaneous or staged surgical procedure for patients with bilateral synchronous renal tumors remains controversial. However, the simultaneous procedure may be advantageous for these patients because of reduced surgical procedures, shorter overall hospitalization, faster overall recovery, and less medical costs compared with the staged surgical procedure. In contrast, staged bilateral nephrectomy has been reported to be efficient in preserving renal function.

Recently, robot-assisted partial nephrectomy (RAPN) has become a reliable procedure to overcome the technical difficulties of laparoscopic partial nephrectomy (LPN) [5], permitting a broader application of laparoscopic treatment of renal masses. It may be possible for simultaneous RAPN for bilateral renal tumors to overcome the disadvantage of simultaneous surgical procedures, such as longer total operation time and risk of postoperative renal deterioration.

There are very few reported cases of bilateral renal tumors simultaneously treated with RAPN [6,7]. In our pilot study, we summarize our experience of simultaneous RAPN for bilateral renal tumors and investigate the safety and efficacy of this surgical procedure based on the perioperative outcomes.

Patients and methods

Between April 2016 and October 2019, 8 patients with bilateral synchronous sporadic renal tumors underwent simultaneous RAPN for bilateral renal tumors. The present study was approved by the ethics committee of Osaka City University Hospital (2019-046). Opt-out informed consent was obtained instead of written informed consent, and an opportunity to decline participation was also provided. All the

procedures were in accordance with the Helsinki Declaration of 2000.

The demographic profile (gender, age), renal function, and tumor characteristics before surgery were collected from electronic medical records. Estimated glomerular filtration rate (eGFR) was calculated using the modified Modification of Diet in Renal Disease equation using the new Japanese coefficient. The values of eGFR were measured before surgery, and 1 month after surgery. Change of eGFR from before surgery to 1 month after surgery was evaluated. All patients enrolled in this study received contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) for preoperative diagnosis.

The assessment of tumor complexity was performed by using the R.E.N.A.L. (radius, exophytic/endophytic properties, nearness of tumor to the collecting system or sinus in millimeters, anterior/posterior location relative to polar lines) score [8]. The complexity was defined as low, moderate, or high, if the score was 4-6, 7-9, and 10-12, respectively.

Surgical procedure

The surgical procedure was performed using the following steps. RAPN was performed in all patients using the transperitoneal approach. After reflection and retraction of the bowel, the ureter on the anterior surface of the quadratus lumborum muscle was identified, and the renal pedicle was exposed by lifting the kidney. This allowed for identification of the main branch of the renal artery. Only the renal artery was clamped, and selective arterial clamping was not performed. To mobilize the kidney to allow maximal ease of forceps manipulation, perirenal dissection was performed along the Gerota's fascia with consideration of the tumor location. A wide area was dissected to ensure that the tumor and surrounding normal renal parenchyma could be sufficiently identified. The Gerota's fascia immediately anterior to the tumor was resected along with the tumor. Thereafter, the location of the tumor was confirmed using laparoscopic ultrasound. Subsequently, hemostasis was achieved using renal artery clamps, and the resection was started. Collecting system closure was performed using 3-0 Vicryl interrupted sutures. Renorrhaphy was performed using continuous suturing with 2-0 V-Loc used on the parenchyma. After complete hemostasis was confirmed, a drain was placed under the diaphragm. Next, the patient position was conversely changed followed by movement of the robot apparatus to the opposite site, and the contralateral renal tumor was treated in the same manner.

Results

Patient demographics are described in Table 1. Patients' median (range) age was 56 (43-83) years and 4 men and 4 women were included. The median (range) body mass index (BMI) was 22.3 (19.7-32.8) kg/m². The preoperative median (range) eGFR was 82.5 (21.8-89.1) mL/min/1.73 m². Among the 8 patients enrolled, 18 tumors from 16 kidneys (1 patient had two tumors in the right kidney and two tumors in the

left kidney) were examined. The median (range) size of the tumors was 1.4 (0.9-9.0) cm. Regarding the R.E.N.A.L. score, low difficulty (4-6 points) was observed in 10 tumors, medium difficulty (7-9 points) in four tumors, and high difficulty (10-12 points) in four tumors. The pathological findings showed 14 clear cell carcinomas, 3 papillary carcinomas, and 1 angiomyolipoma. Tumor characteristics are also shown in Table 1. Ureteral catheters were inserted in three cases. Fifteen kidneys were temporarily clamped at the renal artery, and one kidney had no clamping. The median warm ischemic time for 16 kidneys was 13 minutes (range; 0-40 minutes). The median total operative time, the operative time for unilateral nephrectomy, and the median robot replacement time were 334 minutes (range; 199-576 minutes), 140 minutes (range; 67-303 minutes), and 25 minutes (range; 20-31 minutes), respectively. The median estimated blood loss was 90 mL (5-400mL). Perioperative details are summarized in Table 2.

There was no positive surgical margin after RAPN in our case series and no local recurrence or metastasis during the follow-up period. The only complication of simultaneous RAPN in the present case series was that one patient (case 3) experienced acute kidney injury after operation. In this case, contrast-enhanced CT revealed a 9.5 cm mass at the middle portion and a 1.8 cm mass at the upper segment of the right kidney and a 4.8 cm mass and 1.4 cm mass at the middle portion of the left kidney (Figure 1). Although the preoperative level of eGFR in this patient was 84.2 mL/9.5min/1.73 m², his renal function decreased to 7.21 mL/min/1.73 m² of eGFR at day 4 after the operation. However, his renal function recovered spontaneously without temporary renal replacement therapy. He was discharged on the 14th day postoperatively. The eGFR was 48.8 mL/min/1.73 m² at 1 month after the surgery.

The median preoperative eGFR and eGFR on postoperative day (POD) 30 was 82.5 (21.8-89.1) mL/min/1.73 m² and 62.4 (20.2-90) mL/min/1.73 m², respectively and the change in eGFR preoperatively and POD 30 was -7.4 (-35.4-2.1) mL/min/1.73 m². The renal function on POD 30 decreased slightly compared with that before surgery, but there were no significant differences (Figure 2).

Discussion

In our present case series study, we summarized 8 cases of simultaneous RAPN for synchronous bilateral renal tumors. There were no patients with positive surgical margins of renal tumor after operation. Furthermore, only one patient experienced acute kidney injury after surgery without need for dialysis therapy. Our study suggested that simultaneous RAPN for bilateral renal tumors might be feasible both for preservation of renal function and for oncological outcome such as negative surgical margin..

The optimal treatment strategies for patients with synchronous bilateral renal tumors have not yet been established. It is important to take preservation of renal function into consideration when treatment for bilateral renal tumors is conducted. Although there are some reports in which percutaneous cryoablation

as a local treatment allowed for conservation of renal function after the treatment, there are limited data on the extension of ablative techniques to treat bilateral renal tumors. In general, surgery is the standard treatment for localized renal cancer. However, for patients who underwent bilateral nephrectomy, renal replacement therapy such as dialysis would be required after surgery; this significantly impairs their quality of life and leads to a higher risk of cardiovascular disease. Previously, the main treatment options for bilateral renal tumors have been bilateral partial or unilateral nephrectomy plus unilateral partial resection [9,10,11]. In terms of better quality of life and greater longevity, bilateral partial nephrectomy may be an appropriate treatment for patients with synchronous bilateral renal tumors if feasible. In recent years, RAPN has become commoner as nephron-sparing surgery due to the encouraging outcomes reported in terms of safety, feasibility, and efficacy of this procedure. RAPN is superior to LPN in terms of the rate of conversion to total nephrectomy, preservation of renal function, shorter hospitalization, and ischemic time [12]. In addition, a previous meta-analysis reported that RAPN resulted in decreased bleeding and less eGFR reduction compared to open partial nephrectomy [13]. Thus, the robotic approach for nephron-sparing surgery has already overcome the technical difficulties of LPN and led to minimization of nephron loss compared with open partial nephrectomy or LPN. RAPN may become the standard procedure for bilateral renal tumors in the future if appropriate patient selection is undertaken and surgeons develop skills in robotic renal surgery. In this study, the proportion of cases obtaining a high difficulty score (10-12 points) was 22%. RAPN may be safely performed even in cases with a high R.E.N.A.L score, as in previous reports.

We performed simultaneous RAPN for a patient with multiple tumors,-including T1b and T1a in the right kidney and T2 and T1a in the left kidney (case 3). The patient's renal function deteriorated temporarily to chronic kidney disease (CKD) stage 4, but it recovered spontaneously without dialysis treatment. Because RAPN can also reduce nephron loss to a minimum [14], simultaneous RAPN for bilateral renal tumors may be an optimal surgical procedure for highly difficult cases with high R.E.N.A.L. scores and multiple tumors in one kidney.

In this study, we undertook simultaneous RAPN for patients with preoperative CKD, indicated by eGFR of 21.8 mL/min/1.73 m². After simultaneous RAPN, eGFR only decreased by a small degree (-1.6 mL/min/1.73 m²) (Case 8). We speculated that this patient could avoid progression of renal insufficiency because of the low R.E.N.A.L. score. Moreover, RAPN can preserve renal function compared to conventional methods. The preoperative renal dysfunction would not necessarily be a limitation for simultaneous RAPN in patients with bilateral tumors and low R.E.N.A.L scores, although it is necessary to monitor the long-term renal function of patients who had undergone RAPN.

The superiority of either the simultaneous or sequential procedure for bilateral renal tumors is still highly debated [15,16]. Previous reports showed that the sequential procedure was the standard treatment in many

facilities. Lowrance et al. reported that the period of decline in renal function could be minimized by the staged procedure, and patients could avoid dialysis treatment [11]. The staged procedure may actually be safer in terms of preserving renal function. However, there are some reports demonstrating that there was no significant elevated risk in the requirement for dialysis after the simultaneous procedure. Recently, Mason et al. reported 76 cases, including 75 laparotomy cases and one LPN case, treated with simultaneous bilateral partial nephrectomy at the Mayo Clinic[2]. Eight cases (10.8%) experienced acute renal failure during the perioperative period, but there were no patients requiring dialysis therapy. However, there was a median decrease in eGFR values before and after surgery of $-19 \text{ mL/min/1.73 m}^2$. The authors recommended the staged procedure for patients with bilateral synchronous sporadic renal tumors and impaired renal function. The Mayo Clinic has traditionally preferred to treat these patients with the simultaneous transperitoneal procedure rather than the staged approach [17,18]. The simultaneous procedure may be prioritized if technically feasible because of the merit of reducing hospitalization costs and completing the procedure with only a single general anesthesia. Mir et al. reported that RAPN costs \$12,000 [19], which is relatively similar to the cost in Japan. The simultaneous procedure can have a significant financial benefit for these patients. Therefore, the simultaneous procedure may be better for bilateral synchronous sporadic renal tumors if it is technically feasible.

This study had several limitations. First, this was a retrospective study with a small sample of only 8 patients, which affects the generalizability of the results. Moreover, this was not a comparative study of the simultaneous versus the staged procedure. However, this may be the first case series study on simultaneous RAPN for bilateral renal tumors. In the future, larger and long-term studies investigating the changes in the postoperative renal function and tumor recurrence should be conducted to confirm the safety and efficacy of this procedure.

In conclusion, surgical treatment methods for bilateral renal tumors have not yet been established. Our pilot study demonstrates that simultaneous RAPN for bilateral renal tumors might be feasible for the preservation of renal function and also for cancer control.

Declarations:

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Authors' contributions

All authors contributed to the conception and design.

All surgeries were performed by Takeshi Yamasaki.

The first draft of the manuscript was written by Taiyo Otoshi.

All authors read and approved the final manuscript.

Conflicts of interest

All authors have no conflicts of interest.

Ethics approval

All procedures performed in this study involving human participants were in accordance with the ethics committee of Osaka City University Hospital (2019-046) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Figure legends

Figure 1 Renal tumors in a patient complicated by acute renal failure

The patient of Case 3.

Contrast-enhanced CT, arterial phase, coronal image.

A: Right kidney tumor was 9 cm and located in the upper pole.

R.E.N.A.L score: 3-3-2-3, total 11 points

B: Left kidney tumor was 4.5 cm and located in the upper pole.

R.E.N.A.L score: 2-3-3-3, total 11 points

Figure 2 Perioperative changes in renal function

Median (range) preoperative eGFR 82.5 (21.8-89.1) ml/min/1.73 m²

Median (range) POD1 eGFR 47.8 (17.17-91.35) ml/min/1.73 m²

Median (range) POD30 eGFR 62.4 (20.2-90) ml/min/1.73 m²

Table 1 Patient and tumor characteristics

PS, performance status

BMI, body mass index

Cr, serum creatinine

Table 2 Perioperative outcomes

PSM, positive surgical margin

POD, postoperative day

Cr, serum creatinine

CCC, clear cell carcinoma

RCC, renal cell carcinoma

AML, angiomyolipoma

Fig 1. Renal tumors in a patient complicated by acute renal failure

A

B

Fig 2. Perioperative changes in renal function

eGFR (ml/min/1.73 m²)

100

80

60

40

20

Preoperative
eGFR

Postoperative
eGFR (POD 1)

Postoperative
eGFR (POD 30)

POD, postoperative day

Table 1. Patients' characteristics

		Age, years	PS	BMI (kg/m ²)	Gender	Tumor size (cm)	T stage	R.E.N.A.L. score	PSM	Complications	Post operative CKD stage	Histological subtypes
Case1	(Right)	43	0	27.5	Female	1.4	T1a	4	(-)	none	2	CCC
	(Left)					1.4	T1a	4	(-)			CCC
Case2	(Right)	44	0	26.2	Male	5.8	T1b	10	(-)	none	2	CCC
	(Left)					2.6	T1a	9	(-)			CCC
Case3	(Right)	45	0	32.8	Male	9, 1.8	T2, T1a	11, 6	(-)	Acute renal failure	3	CCC
	(Left)					4.8, 1.4	T1b, T1a	11, 6	(-)			CCC
Case4	(Right)	55	0	20.4	Female	1.7	T1a	9	(-)	none	2	CCC
	(Left)					5.4	T1b	10	(-)			CCC
Case5	(Right)	62	0	22.8	Male	0.9	T1a	5	(-)	none	2	Papillary RCC
	(Left)					1.3	T1a	6	(-)			AML
Case6	(Right)	70	0	21.7	Female	1.2	T1a	5	(-)	none	3	Papillary RCC
	(Left)					1.2	T1a	5	(-)			Papillary RCC
Case7	(Right)	57	0	21.4	Male	1.3	T1a	5	(-)	none	2	CCC
	(Left)					1.1	T1a	7	(-)			CCC
Case8	(Right)	83	0	19.7	Female	2	T1a	7	(-)	none	4	CCC
	(Left)					2.2	T1a	6	(-)			CCC
median (range)		56 (43-83)		22.3 (19.7-32.8)		1.4 (0.9-9.0)						

Table 2. Perioperative outcomes

		Total operative time (min)	Each operative time (min)	Robot replacement time (min)	Estimated blood loss (ml)	Warm ischemic time (min)	Pre operative Cr (mg/dl)	Pre operative eGFR (ml/min/1.73 m ²)	Post operative Cr (mg/dl)	Post operative eGFR (ml/min/1.73 m ²)
Case1	(Right)	366	188	24	100	10	0.61	84.22	0.67	75.49
	(Left)		154			10				
Case2	(Right)	409	210	20	130	28	0.83	80.82	1.07	61.21
	(Left)		128			20				
Case3	(Right)	576	243	30	400	40	0.79	84.2	1.3	48.83
	(Left)		303			35				
Case4	(Right)	287	87	20	20	18	0.54	89.07	0.62	76.57
	(Left)		153			22				
Case5	(Right)	199	87	23	30	9	0.7	88.5	0.69	89.9
	(Left)		109			0				
Case6	(Right)	302	137	25	5	13	0.79	55.04	0.88	48.91
	(Left)		140			9				
Case7	(Right)	293	127	27	80	10	0.99	61.47	0.96	63.57
	(Left)		129			13				
Case8	(Right)	395	195	31	100	10	1.76	21.81	1.88	20.22
	(Left)		169			10				
median (range)		334 (199-576)		25 (20-31)	90 (5-400)	11.5 (0-40)	0.79 (0.54-1.76)	82.5 (21.8-89.1)	0.92 (0.62-1.88)	62.4 (20.2-90)