

〈Regular Article〉

Outcomes of robot-assisted partial nephrectomy in the treatment of renal cell carcinoma at Kawasaki Medical School Hospital

Tomohiro FUJII, Yoshiyuki MIYAJI, Shin OHIRA, Hirofumi MORINAKA,
Seitetsu SUGIYAMA, Masaichiro FUJITA, Shinjiro SHIMIZU, Syohei TSUKIMORI,
Mikako KAIFU, Ryoei HARA, Atsushi NAGAI

Department of Urology, Kawasaki Medical School

ABSTRACT Robot-assisted partial nephrectomy (RAPN) was introduced in our hospital for treating small renal cell carcinoma in May 2018; we examined treatment outcomes in 24 patients (25 kidneys) who had undergone this procedure till 2019. The median observation period was 11 months (range, 1-17 months). The patients' age range was 43-77 years (median, 68 years). Fourteen men and 10 women underwent the procedure. Their BMI was 17.9-39.7 (median, 24.1) kg/m². In one patient, RAPN was performed twice at different times for treating bilateral renal cancer. The right kidney was affected in 12 cases and the left kidney in 13 cases. The clinical cancer stage was T1a in 20 cases and T1b in 5 cases. Tumor sizes were 0.9-6.2 cm (median, 2.5 cm), and RENAL nephrometry scores were 4-10 (median, 7). The transperitoneal approach was used in 22 cases, and the retroperitoneal approach in 3. The operating durations were 147-358 min (median, 225 min), console durations were 59-394 min (median, 152 min), and renal ischemia durations were 8-54 min (median, 21 min). Blood loss was 10-700 ml (median 10 ml), and none of the patients underwent blood transfusion. The histopathological analysis of the resected tumors revealed clear cell renal cell carcinoma in 20 cases, chromophobe renal cell carcinoma in 2 cases, and papillary renal cell carcinoma, angiomyolipoma, and leiomyoma in 1 case each. All margins were negative. The postoperative hospital stay lengths were 5-14 days (median, 9 days). The postoperative deterioration in renal function was mild, and there were no severe complications. In the early stages after its introduction, RAPN was safely performed and allowed for the preservation of renal function. We plan to continue studying more cases going forward.

doi:10.11482/KMJ-E202046027 (Accepted on March 4, 2020)

Key words : Renal cell carcinoma, Robot-assisted partial nephrectomy, Early outcomes

INTRODUCTION

In the field of urology, laparoscopic surgeries

for urinary tract diseases have been established as minimally invasive means to obtaining positive

Corresponding author
Tomohiro Fujii
Department of Urology, Kawasaki Medical School, 577
Matsushima, Kurashiki, 701-0192, Japan

Phone : 81 86 462 1111
Fax : 81 86 463 4747
E-mail: tfujii@med.kawasaki-m.ac.jp

outcomes. A randomized controlled trial examining small renal tumors showed partial nephrectomy was similar to radical nephrectomy in terms of safety and cancer control¹⁾ and superior to radical nephrectomy in terms of preserving renal function²⁾, improving postoperative quality of life, reducing non-cancer-related mortality, and prolonging overall survival^{3, 4)}. Japanese guidelines have recommended that partial nephrectomy should be performed if it is technically feasible. Robot-assisted partial nephrectomy (RAPN) was first reported by Gettman *et al.* and is now performed in many facilities worldwide; positive therapeutic outcomes have been reported using this technique⁵⁾. In Japan, health insurance began covering this procedure from 2016; therefore, the number of patients undergoing this procedure has rapidly increase since then. Our hospital introduced RAPN in May 2018. By the end of September 2019, it was performed on 24 patients (25 kidneys). In this study, we conducted a clinical investigation of the therapeutic outcomes after the introduction of RAPN.

SUBJECTS AND METHODS

This study was approved by the Ethics Committee of Kawasaki Medical School and Kawasaki Medical School Hospital (approval number 3,742). All authors have no conflict of interest which should be declared. Twenty-four patients (25 kidneys) diagnosed with renal cell carcinoma who underwent RAPN using the Davinci Xi surgical system from May 2018 to the end of September 2019 were included. We retrospectively examined their characteristics, surgical and perioperative outcomes, pathological results, therapeutic outcomes, and postoperative renal function.

All patients are evaluated 3-dimensional reconstruction images using preoperative computed tomography before surgery.

Surgery was performed as follows. In the lithotomy position, the tip of a 5 Fr ureteral catheter

was placed inside the renal pelvis to supply an indigo carmine-saline solution, and was fixed to the urethral catheter outside the body with silk thread. The patient was then placed in the lateral decubitus position.

The surgical procedure was performed by dissecting around the kidney outside Gerota's fascia, identifying and dissecting the renal artery and vein, and then securing the renal artery with vascular tape. After dissecting the fat around the tumor, the tumor was identified using robot-assisted intraoperative ultrasonography, the resection line was marked, indigo carmine-saline drip was started from the ureteral catheter, and the renal artery was clamped with bulldog forceps. Sharp and blunt dissection of the tumor was then performed. Depending on the patient condition, hemostasis of the resection surface was performed with a combination of methods including soft coagulation, inner sutures of the base of the resection surface of the tumor, application or drops of a fibrinogen + thrombin preparation, spraying a starch-derived absorbent local hemostatic material, and suturing of the renal parenchyma on the resection surface. After these procedures, the renal artery was unclamped, and after confirming the absence of bleeding, a drainage tube was inserted and the operation was finished. Two surgeons performed the procedures; however, the assistants and nurses were not fixed. The median follow-up period was 13 months (range, 3-19 months).

RESULTS

The age range of the patients was 43-77 years (median, 68 years); there were 14 men and 10 women. In 1 patient, RAPN was performed twice for bilateral renal cancer at different times. The patients' BMI range was 17.9-39.7 (median, 24.1) kg/m². The right kidney was affected in 12 patients and the left kidney in 13. The clinical stage was T1a in 20 patients and T1b in 5. The tumor sizes were

0.9-6.2 cm (median, 2.5 cm) and tumor location sites were 3 in the upper pole, 13 in the middle, and 9 in the lower pole (Table 1). RENAL nephrometry scores were 4-10 (median, 7) and the details were shown in Table 2. Three patients had undergone appendicitis surgery, 1 had undergone robot-assisted radical prostatectomy, and 1 had undergone

contralateral RAPN.

The transperitoneal approach was used in 22 patients and the retroperitoneal approach in 3. Pneumoperitoneum was performed at 8-15 mmHg. The number of ports was 6 with the transperitoneal approach and 4 with the retroperitoneal approach after dilation of the retroperitoneal space. Fig. 1 shows the port positions with the right transperitoneal approach.

The operating durations were 147-358 min (median 225 min), console durations were 59-304 min (median, 152 min), and renal ischemia durations were 8-54 min (median 21 min) except 1 case of no clamp of renal artery. Blood loss was 10-700 ml (median, 10 ml), and none of the patients underwent blood transfusion. No patients were transitioned to the open procedure. The postoperative hospital stays were 5-14 days (median, 9 days) (Table 3). Histopathological analysis revealed that the resected tumors were a clear cell renal cell carcinoma in 20 patients, chromophobe renal cell carcinoma

Table 1. Characteristics of patients (24 cases, 25 kidneys)

Age (years) : 43 - 77 (median, 68)
Sex : Male 14, Female 10
BMI : 17.9 - 39.7 (median, 24.1)
Tumor side : Right 12, Left 13
Clinical T stage : T1a 20, T1b 5
Tumor location : upper pole 3, middle 13, lower pole 9

Table 2. RENAL nephrometry score (n=25)

4-10 pts (median 7 pts)			
4pts : 1, 5pts : 3, 6pts : 5, 7pts : 5, 8pts : 5, 9pts : 4, 10pts : 2			
	1pt	2pts	3pts
R	20	5	0
E	7	16	2
N	7	7	11
(A : a 9, p 4, x 12)			
L	5	14	6

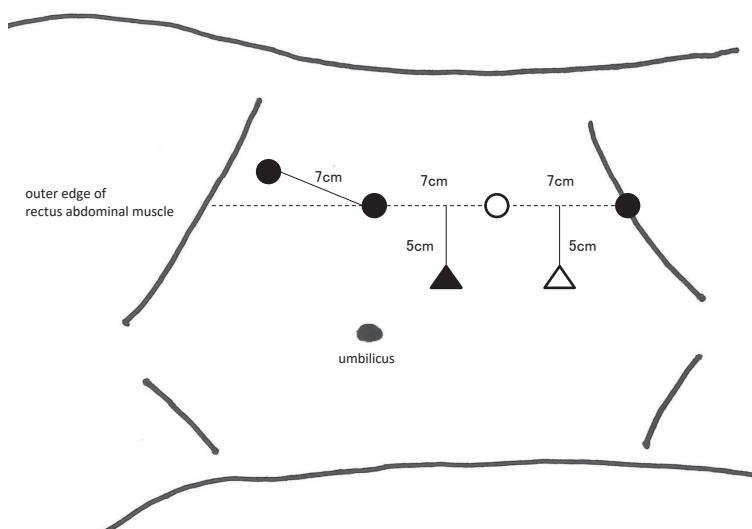


Fig. 1. Port site of right transperitoneal RAPN

- : camera port
- : port for Da Vinci
- △ : port for assistant
- ▲ : Air seal port for assistant

RAPN: robot assisted laparoscopic partial nephrectomy

Table 3. Intra/perioperative Results (n=25)

Operation time (min) : 147 - 358 (median, 225)
Console time (min) : 59 - 304 (median, 152)
Blood loss (ml) : 10 - 700 (median, 10)
Transfusion : none
Open conversion : none
Postoperative hospital stay (days) : 5 - 14 (median, 9)
Complications: intraoperative bleeding more than 600ml 2 (8%)

Table 4. Pathological results (n=25)

Renal cell carcinoma	
Clear cell renal cell carcinoma	20 (80%)
Chromophobe renal cell carcinoma	2 (8%)
Papillary renal cell carcinoma	1 (4%)
pathological stage : pT1a 17, pT1b 5, pT3a 1	
Fuhrman grade : grade1 3, grade2 10, grade3 10	
surgical margin : all negative	
Angiomyolipoma	1 (4%)
Leiomyoma	1 (4%)

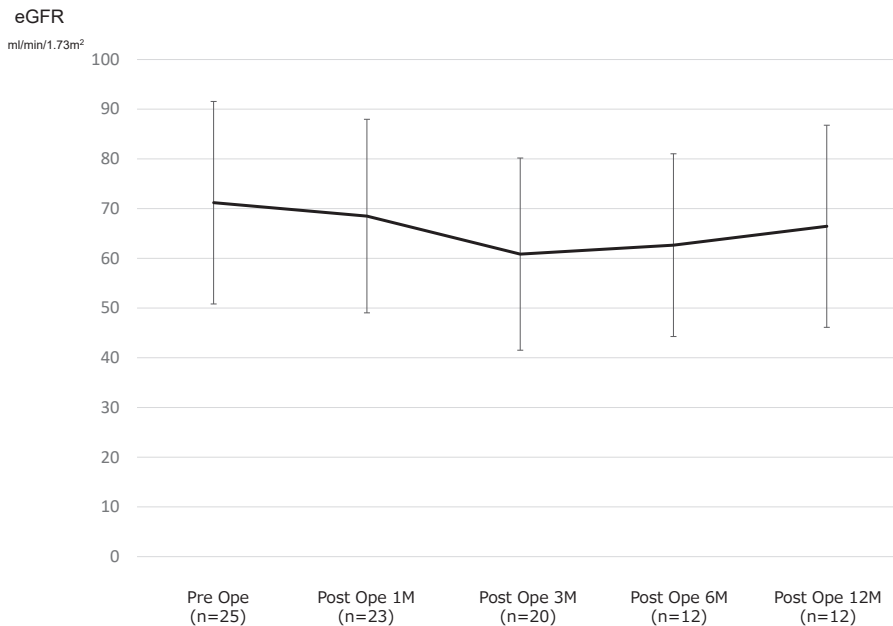


Fig. 2. Changes in postoperative renal function

in 2 patients, and papillary renal cell carcinoma, angiomyolipoma, and leiomyoma in 1 patient each. The pathological stage of renal cell carcinoma was pT1a in 17 cases, pT1b in 5 cases, and pT3a in 1 case. Regarding Fuhrman grade, grade 1 was 3 cases, grade 2 was 10 cases, and grade 3 was 10 cases. All margins were negative (Table 4). Although the observation periods were short, no recurrence or metastasis was observed.

Regarding postoperative renal function, the median eGFRs before and after 1, 3, 6, and 12 months were 71.2, 68.5, 60.9, 62.7, and 66.4 ml/min/1.73 m², respectively (Fig. 2). These represent

rates of decline of 3.8%, 14.5%, 11.5%, and 6.7%, respectively.

Regarding complications, intraoperative blood loss of ≥ 600 ml occurred in 2 patients; however, no severe Clavien-Dindo grade III or higher postoperative complications occurred.

DISCUSSION

Methods of performing partial nephrectomy for small renal cell carcinoma include open surgery, laparoscopic surgery, and RAPN. A comparison between open surgery and RAPN found the latter to be superior in terms of the amount of blood

loss, transfusion rate, length of hospital stay, re-hospitalization rate, postoperative renal function, overall mortality, and recurrence rate, while a comparison between laparoscopic surgery and RAPN found the latter to be superior in terms of the intraoperative ischemia time, rate of transition to open surgery, intraoperative and postoperative complications, positive margin rate, postoperative renal function, and overall mortality⁶⁾. Considering such findings, the number of patients undergoing partial nephrectomy has been increasing since RAPN was introduced⁷⁾. Our hospital introduced the Davinci Xi surgical system in November 2017 and started with robot-assisted radical prostatectomy.

At our hospital, patients with renal tumors up to 7 cm are indicated to undergo RAPN, though the procedure can be difficult depending on the location of the tumor. Kutikov *et al.* proposed the RENAL nephrometry score as a method for scoring the risk of complications; this system was based on anatomical characteristics in preoperative images. Possible complications included the difficulty of partial nephrectomy, blood loss, and opening to the urinary tract. This score is now used worldwide, with 12 points indicating the highest degree of difficulty and 10 points a high degree of difficulty⁸⁾. The patients we experienced had scores of 4-10 points, with a median score of 7 and 2 patients with scores of 10. In the future, we would like to create a more rigorous system for operating on such patients that considers the skill level of the surgeon and assistants. For contained tumors difficult to directly observe during surgery, we used 3-dimensional reconstruction images using preoperative computed tomography and robot-assisted intraoperative ultrasonography. All patients were resected safely with negative margins. There were no tumors in the renal hilum area that required dissection of renal blood vessels or the urinary tract, leaving this type of tumor as a topic for future study.

While either the transperitoneal or retroperitoneal approach can be used, there are no differences between them in terms of complications, transition to open surgery, warm ischemia time, blood loss, and positive margin rate⁹⁾. While either approach appears feasible, the location of the tumor in the kidney is important. The retroperitoneal approach is particularly useful for tumors in the posterior and lateral kidney¹⁰⁾. Initially, after RAPN was introduced, we used the transperitoneal approach in all patients; however, in 3 recent patients with tumors on the posterior kidney, we used the retroperitoneal approach. Although approaching the renal hilum is easy with this method, manipulations must be performed close to the camera, and the procedure can be difficult owing to reasons such as the small working space. Going forward, we plan to use the transperitoneal approach on anterior tumors, the retroperitoneal approach on posterior tumors, and leave the decision up to the surgeon for the best approach on lateral tumors.

The so-called trifecta – cancer control, intraoperative and perioperative complications, and preservation of renal function – is being commonly used as an indicator of RAPN outcomes. Regarding cancer control, while we had no patients with recurrence or metastasis, the observation period was short and it was not worth evaluating. Therefore, we examined the complications and postoperative renal function.

We compared our outcomes to those of previous reports^{11, 12)}. Previous studies reported median operation durations of 118 and 140 min, which are shorter than the 225 min noted in our patients. However, our recent cases have shown durations been below 200 min, which indicates that the procedures are gradually getting shorter. Previous reports demonstrated blood loss to be 120 and 440 ml. While the median amount in our patients was only 10 ml, we did experience blood loss of 700 ml, indicating that we need to be careful about

indications and surgical manipulations. Warm ischemia time of the affected kidney may affect postoperative renal function, and renal function decreased when this lasted longer than 25 min¹³. In previous reports, the median durations were 20 and 27 min, while for our patients, it was 21 min. The positive margin rate was 0%, both in previous reports and in our patients. Similarly, no patients were transitioned to open surgery and there were no Clavien-Dindo grade III or higher severe complications. Ramirez *et al.* performed a detailed examination of complications in 545 patients with T1a renal tumors who underwent RAPN¹⁴. They reported bleeding and other intraoperative complications in 1.7% of patients and Clavien-Dindo grade III or higher complications in 5.5%. Although our report is only on outcomes in a small number of cases for a short period of time, intraoperative bleeding of ≥ 600 ml, which normally requires blood transfusion, occurred in 2 patients (8%), which is slightly higher than that reported in previous studies and indicates that our surgical techniques need to improve. Postoperatively, no Clavien-Dindo grade III or higher complications occurred, which, for outcomes relatively soon after introducing RAPN, indicates that the procedure is being performed to an acceptable degree of safety.

Regarding postoperative renal function, there have been few reports on long-term outcomes, leaving the actual state of postoperative renal function unclear. Kim *et al.* reported long-term outcomes of renal function in 195 patients who underwent RAPN. They reported that eGFR levels were lowest at 3 months after surgery, after which they gradually increased, recovering to 95% of preoperative levels by 5 years postoperatively. New-onset stage III or IV chronic kidney disease (CKD) occurred after RAPN in 3.2% of patients¹⁵. While there were only 8 patients with $eGFR \geq 60$ ml/min/1.73 m² who were followed-up for at least 1 year in the present study, none developed CKD of stage III or

higher, which, despite the short observation period, indicates that renal function was postoperatively maintained. Postoperative renal function is mainly determined by the warm renal ischemia time. Successful methods for minimizing the impact of ischemia on normal renal parenchyma include the early unclamping method, in which the renal artery is immediately unclamped after resecting the renal tumor and inner suturing of the base of the resection surface is done¹⁶, and the selective clamp method, in which only the arteries that flow into the tumor are clamped¹⁷. In the future, we plan to incorporate these methods to help preserve postoperative renal function and further improve outcomes.

CONCLUSION

We examined the outcomes of robot-assisted partial nephrectomy for renal cell carcinoma at our hospital. Although the operation times were somewhat long, the other results were similar to those reported previously, indicating the procedure was introduced safely.

REFERENCES

- 1) Van Poppel H, Da Pozzo L, Albrecht W, *et al.*: A prospective, randomized EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol.* 59: 543-552, 2010
- 2) Huang WC, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, Scardino PT, Russo P: Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol.* 7: 735-740, 2006
- 3) Zini L, Perrote P, Capitanio U, Jeldres C, Shariat SF, Antebi E, Saad F, Patard JJ, Montorsi F, Karakiewicz PI: Radical versus partial nephrectomy: effect on overall and non-cancer mortality. *Cancer* 115: 1465-1471, 2009
- 4) Kim SP, Thompson RH, Boorjian SA, *et al.*: Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. *J*

- Urol. 188: 51-57, 2012
- 5) Gettman MT, Blute ML, Chow GK, Neururer R, Bartsch G, Peschel R: Robotic-assisted laparoscopic partial nephrectomy: technique and initial clinical experience with DaVinci robotic system. *Urology* 64: 914-918, 2004
 - 6) Cacciamani GE, Medina LG, Gill T, Abreu A, Sotelo R, Artibani W, Gill IS: Impact of Surgical Factors on Robotic Partial Nephrectomy Outcomes: Comprehensive Systematic Review and Meta-Analysis. *J Urol* 200: 258-274, 2018
 - 7) Kim SP, Gross CP, Meropol N, Kutikov A, Smaldone MC, Shah ND, Yu JB, Psutka S, Kiechle J, Abouassaly R: National treatment trends among older patients with T1-localized renal cell carcinoma. *Urol Oncol* 35: e115-e121, 2017
 - 8) Xia L, Zhang X, Wang X, Xu T, Qin L, Zhang X, Zhong S, Shen Z: Transperitoneal versus retroperitoneal robot-assisted partial nephrectomy: A systematic review and meta-analysis. *Int J Surg* 30: 109-115, 2016
 - 9) Choo SH, Lee SY, Sung HH, Jeon HG, Jeong BC, Jeon SS, Lee HM, Choi HY, Seo SI: Transperitoneal versus retroperitoneal robotic partial nephrectomy: matched-pair comparisons by nephrometry scores. *World J Urol* 32: 1523-1529, 2014
 - 10) Castillo OA, Rodriguez-Carlin A, Lopez-Fontana G, Mora Vidal I, Gomez R: Robotic partial nephrectomy: An initial experience in 25 consecutive cases. *Actas Urol Esp*. 36: 15-20, 2012
 - 11) Lemos GC, Apezato M, Borges LL, Colombo J: Robotic-assisted partial Nephrectomy: Initial experience in South America. *Int Braz J Urol*. 37: 461-467, 2011
 - 12) Dagenais J, Maurice MJ, Mourcade P, Kara O, Nelson R, Malcok E, Kaouk JH: The Synergistic Influence of Ischemic Time and Surgical Precision on Acute Kidney Injury After Robotic Partial Nephrectomy. *Urology*. 107: 132-137, 2017
 - 13) Ramirez D, Maurice MJ, Caputo PA, Nelson RJ, Kara O, Malcok E, Kaouk JH: Predicting complications in partial nephrectomy for T1a tumours: does approach matter? *BJU Int*. 118: 940-945, 2016
 - 14) Kim JH, Park YH, Kim YJ, Kang SH, Byun SS, Kwak C, Hong SH: Preoperative and long-term renal functional outcomes of robotic versus laparoscopic partial nephrectomy: a multicenter matched-pair comparison. *World J Urol*. 33: 1579-1584, 2015
 - 15) Kutikov A, Uzzo RG: The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol*. 182: 844-853, 2009
 - 16) Baumert H, Ballaro A, Shah N, Mansouri D, zafar N, Molinié V, Neal D: Reducing warm ischemia time during laparoscopic partial nephrectomy: a prospective comparison of two renal closure techniques. *Eur Urol*. 52(4): 1164-1169, 2007
 - 17) Shao P, Qin C, Yin C, Meng X, Ju X, Li J, Lv Q, Zhang W, Xu Z: Laparoscopic partial nephrectomy with segmental renal artery clamping: technique and clinical outcomes. *Eur Urol*. 59(5): 849-855, 2011