



Natural history of asymptomatic renal artery pseudoaneurysm after robot-assisted partial nephrectomy

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Background: We assessed the natural history of renal artery pseudoaneurysm (RAP) after robot-assisted partial nephrectomy (RAPN).

Methods: From May 2016 to September 2020, 106 patients underwent RAPN for renal tumors at our institution. Among 100 patients, excluding 6 who were ineligible for contrast-enhanced computed tomography (CE-CT), 4 underwent renal artery selective embolization (RAE), of which 2 cases were emergency RAE within 7 days after RAPN and the other 2 were prophylactic RAE 8 or more days after RAPN. In 98 patients examined for the clinical course of asymptomatic RAP managed by surveillance, excluding the 2 who underwent emergency RAE, routine CE-CT was performed at 7 days, 1 month and 3 months after RAPN. Factors influencing the occurrence of RAP among these 98 patients, including the 2 who underwent emergency RAE and excluding the 2 who underwent prophylactic RAE, were analyzed by logistic regression analysis.

Results: Median [interquartile range (IQR), range] observation period, age, radiographic tumor size, and maximum diameter of RAP were 20.8 (23.9, 3.0–57.6) months, 63 (18, 22–84) years, 23 (11, 9–48) mm, and 6.6 (5.2, 3.0–16.0) mm, respectively. CE-CT detected 28 RAPs in 23 (23.0%) of 100 patients by 7 days after RAPN and routine CE-CT detected 25 RAPs in 21 (21.4%) of 98 patients excluding 2 who underwent emergency RAE at 7 days after RAPN. RAP was diagnosed by routine CE-CT in 21 (21.4%), 1 (1.0%), and 0 (0%) patients at 7 days, 1 month, and 3 months after RAPN, respectively. In univariate analysis, age [odds ratio (OR) 0.144: 69–84 vs. 22–56 years old, $P=0.0179$], R.E.N.A.L [radius (tumor size as maximal diameter), exophytic/endophytic properties of tumor, nearness of tumor deepest portion to collecting system or sinus, anterior/posterior descriptor and location relative to polar line] nephrometry score (OR 1.374, $P=0.0382$), warm ischemic time (OR 1.085, $P=0.0393$), and renorrhaphy time (OR 1.055, $P=0.0408$) were significantly associated with the occurrence of RAP. In multivariate analysis, only age (OR 0.124, $P=0.0148$) was a significant factor.

Conclusions: Asymptomatic RAP up to 15 mm in diameter resolved spontaneously 3 months after RAPN. Young age (under 56 years) may be a factor in the development of RAP.

Keywords: Kidney neoplasms; comorbidity; robotics; age; pseudoaneurysm

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Introduction

Partial nephrectomy (PN) has been successful in reducing mortality in patients with small renal cancer through both the achievement of promising oncological outcomes and reducing cardiac events associated with the protection of renal function, which is still controversial. PN has now replaced radical nephrectomy as the gold standard treatment for these cancers (1,2). The procedure initially evolved from open PN (OPN) to laparoscopic PN (LPN), while in recent years, robot-assisted PN (RAPN) has become more common. Progress towards less invasive and safer surgery has been steady, supported by technological development and ingenuity such as in the use of 3D models (3-5). One of the most stressful and life-threatening complications for patients who undergo PN is renal artery pseudoaneurysm (RAP) (6). Previous studies have reported incidence rates of RAP after PN of 1–5% (6). The frequency of RAP increased from 1.00% with OPN to 1.96% with LPN (7). A review study reported that RAP after PN occurred at mean 14.9 days, but since it may appear within 1–90 days, care should be taken for up to about 3 months after surgery (8). The etiology of RAP after PN is believed to be direct injury

to a segmental branch of the renal artery. Recent studies demonstrated incidence rates of asymptomatic unruptured RAP on contrast-enhanced computed tomography (CE-CT) after PN of 15.0% and 21.7% (9,10). Accordingly, the frequency of asymptomatic unruptured RAP is likely higher than expected, which would in turn indicate that RAP in RAPN has not been fully evaluated.

Here, we report the natural course of RAP by assessing postoperative renal condition with routine CE-CT after RAPN regardless of the presence or absence of clinical symptoms and factors affecting the occurrence of RAP.

We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/tau-21-384>).

Methods

Patient population

From May 2016 to September 2020, 106 patients underwent RAPN for renal tumors at Jichi Medical University Hospital. As shown in *Figure 1*, six patients were excluded from the present analysis because they were ineligible for CE-CT due to asthma, allergy to contrast medium, or renal dysfunction. Among the 100 remaining patients, four underwent renal artery selective embolization (RAE). Two patients underwent emergency RAE due to ruptured RAP diagnosed by following the clinical course—the first with a decrease in blood pressure and progression of anemia 4 hours after RAPN and the second with fever 4 days after RAPN and a blood test showing anemia—and did not undergo routine CE-CT at 7 days after RAPN. The other two patients with RAP confirmed by routine CE-CT on the 7 days of RAPN underwent prophylactic RAE due to their social situation, namely difficulty in visiting the hospital if the RAP ruptured. Finally, in 98 patients examined for the clinical course of asymptomatic RAP managed by surveillance, excluding 2 who underwent emergency RAE, routine CE-CT was carried out 7 days, 1 month and 3 months after RAPN. Factors influencing the occurrence of RAP among these 98 patients, including 2 who underwent emergency RAE and excluding 2 who underwent prophylactic RAE, were analyzed by logistic regression analysis. Tumor and RAP size were determined by CT, and perioperative complications were graded by the Clavien-Dindo classification (11). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of Jichi Medical University (A19-199)

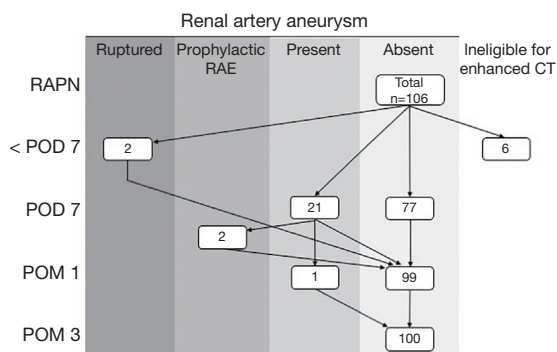


Figure 1 Clinical course of RAP in 106 patients. Among 106 patients who had undergone RAPN, 6 were excluded as ineligible for CE-CT. Ninety-eight completed routine CE-CT scans 7 days, 1 month and 3 months after RAPN, while 2 had emergency CE-CT scans. On POD7, 21 patients had RAPs, of which only 1 case remained at POM1. Within 1 week after routine CE-CT scans at 7 days, 2 patients underwent prophylactic RAE. No patient had RAPs at POM3. Abbreviations: RAP, renal artery pseudoaneurysm; RAPN, robot-assisted partial nephrectomy; CE-CT, contrast-enhanced computed tomography; RAE, renal artery selective embolization; POD, postoperative day; POM, postoperative month.

and withdrawal of consent to the use of medical data was by the opt-out system.

Surgical technique

All operations were performed using the da Vinci Si robotic platform (Intuitive Surgical, Inc., Sunnyvale, CA, USA). Six or seven ports were placed, of which two or three were for the assistant surgeons. Surgeries were performed by two surgeons (operator and assistant). The approach was chosen depending on the tumor location. The transperitoneal approach is generally used for lesions located anteriorly, while the retroperitoneal approach is used for lesions located posteriorly. In general, an extra arm was used. No ureteral catheters were used. An intraoperative ultrasonography probe (L43K; Hitachi, Tokyo, Japan) was used to confirm the margins of the tumor. Briefly, the renal hilum was dissected, allowing the clamping of individual renal arteries. The resection margin was delineated with ultrasound guidance. In the clamping method, bulldog clamps were used for total or partial renal artery clamping. After confirming that blood flow to the kidney was decreased by ultrasonography or by the renal parenchyma macroscopically turning from red to white, the tumor was bluntly dissected and enucleated and/or resected with a thin margin so as to preserve the normal parenchyma as much as possible. Some blood vessels flowing into and out of the tumor were sectioned after placement of hemolock clips by the assistant surgeon. The next procedure is parenchymal renorrhaphy (inner and outer layer sutures). The tumor bed was repaired with an inner running suture (15 cm 3-0 V-Loc 180 CV23; Covidien, New Haven, CT, USA); this repair was also conducted in cases in which the collecting ducts were released or renal sinus fat was exposed during tumor resection. After inner suturing, the clamps were removed (early unclamping). The outer continuous suture (20 cm 2-0 V-Loc 180 GS21; Covidien, New Haven, CT, USA) with hemolock clips placed at exit points was then done while repeating the procedure of sliding the hemolock clips after tightening the suture as needed. For hemostasis, absorbable hemostats (largely SURGICEL; Johnson & Johnson, Tokyo, Japan) were applied to the surface after renorrhaphy was completed.

CT imaging and analysis

CT technique

CT examinations were carried out using multi-detector

row CT scanners, such as SOMATOM Definition Flash, SOMATOM Definition AS, and SOMATOM Sensation 64 (Siemens, Erlangen, Germany). Our institutional triphasic renal CT protocol consisted of acquisition of an unenhanced CT image of the upper abdomen, followed by a corticomedullary phase acquisition of the upper abdomen and a delayed nephrographic phase acquisition of the entire abdomen and pelvis. A fixed 100- or 120-kVp technique was used for all three phases, with automated tube current modulation and a variable tube current of 100–500 mA. Slice thickness is 2.5–3 mm in all phases. Patients were administered 540–600 mgI/kg of nonionic iodine contrast agent at a fixed intravenous injection rate of 2.5–3.0 mL/s with the use of a power injector. The timing of the corticomedullary phase was established by bolus tracking (30–40 s after injection). The nephrographic phase image was acquired 80 s after the corticomedullary phase image acquisition (110–120 s after injection).

CT image evaluation

All acquired images were transferred to our clinically-used server and evaluated with a picture archiving and communication system (PACS; Synapse, Fujifilm Medical Systems, Tokyo, Japan) with 2-megapixel high resolution liquid crystal display. A single experienced diagnostic radiologist who had no knowledge of the surgical or clinical results reviewed axial and coronal multiplanar reformatted images (3 mm) of multiphase images, and assessed vascular complications, such as RAP, irregularity of renal arteries and contrast extravasation. RAP was defined as a saccular- or fusiform-shaped dilatation of the renal arterial branches compared with the surrounding normal renal arterial branches. Potential RAP smaller than 2 mm in diameter were excluded because of imaging limitations, such as slice-related pseudolesion or the possibility of renal artery stump dilation.

Statistical analysis

Categorical variables were expressed as frequencies and percentages, and differences were compared using the chi-square test and Mann-Whitney U test. Univariate analyses for the occurrence of RAPs were performed by logistic regression methods. Subsequent multivariate logistic regression analysis for the occurrence of RAPs was performed with factors whose P values greater than 0.1 in the univariate analysis. In the multivariate analysis, the inner suture time, which is a component of the renorrhaphy time,

was included in the warm ischemic time, so warm ischemic time was used as representative. All P values presented are two-sided. Statistical significance was calculated using StatView ver. 5 (Abacus Concepts, CA, USA), with P values of <0.05 considered to indicate statistical significance.

Results

Patient characteristics and perioperative outcomes are detailed in *Table 1*. A total of 2 operators and 8 assistants were involved in the surgery. There was no significant difference in the chi-square test between the operator (A vs. B) or surgical approach (transperitoneal vs. retroperitoneal) ($P=0.1248$) (data not shown). No patient required intraoperative blood transfusion or was converted to open surgery and nephrectomy. Urinary leakage was not observed. A positive surgical margin was found in one patient (1.0%) with chromophobe renal cell carcinoma (RCC). No patients, except those who underwent emergency RAE, experienced any signs of potential pseudoaneurysm, such as gross hematuria. A major complication of Clavien-Dindo grade 3 or higher was found in 4 patients with RAE. RAE was the only procedure with a Clavien-Dindo grade 3 or higher complication.

Figure 1 outlines the clinical course of RAPs. CE-CT detected 28 RAPs in 23 (23.0%) of 100 patients by 7 days after RAPN and routine CE-CT detected 25 RAPs in 21 (21.4%) of 98 patients (excluding 2 patients who underwent emergency RAE by 7 days after RAPN due to inability to measure the exact size of RAP) on 7 days of RAPN. By timing, 21 (21.4%), 1 (1.0%), and 0 (0%) of patients with RAP were diagnosed by routine CE-CT at 7 days, 1 month, and 3 months after RAPN, respectively. The median maximum diameter of RAP was 6.6 mm (interquartile range 5.2 mm; range, 3.0–16.0 mm). All of the RAPs were located on the interlobar, arcuate or interlobular arteries. The RAP sizes of the two patients who underwent prophylactic TAE were 12 and 16 mm, respectively. Five RAPs (12.4, 13.3, 14.3, 15.0, and 15.2 mm in diameter) with a size larger than 12 mm and smaller than 16 mm observed in 5 patients at 7 days after RAPN resolved spontaneously 1 month after RAPN. Among all patients, only one patient had RAP 1 month after RAPN, with an RAP size course of 4.8, 3.7, and 0 mm at 7 days, 1 month, and 3 months after RAPN, respectively. As shown in *Figure 2*, one patient with three RAPs (10.9 mm in *Figure 2A*, 14.3 mm in *Figure 2B*, and 6.0 mm in *Figure 2C*, as shown by a white arrow with a black border) found 7 days after RAPN resolved by 1 month

after RAPN.

Table 2 shows patient characteristics and perioperative outcomes classified by the presence or absence of RAP managed by surveillance. Age ($P=0.0325$), R.E.N.A.L [radius (tumor size as maximal diameter), exophytic/endophytic properties of tumor, nearness of tumor deepest portion to collecting system or sinus, anterior/posterior descriptor and location relative to polar line] nephrometry score ($P=0.0410$), warm ischemic time ($P=0.0230$), renorrhaphy time ($P=0.0103$), and blood loss ($P=0.0128$) were significantly associated with the presence or absence of RAP.

Table 3 shows factors influencing the occurrence of RAP on logistic regression analysis using the five factors related to the presence or absence of RAP shown in *Table 2*. First, logistic regression analysis was performed on the five factors as continuous variables. In univariate analysis, R.E.N.A.L nephrometry score [odds ratio (OR) 1.374, $P=0.0382$], warm ischemic time (OR 1.085, $P=0.0393$), and renorrhaphy (inner and outer layer suture) time (OR 1.055, $P=0.0408$) were significantly associated with the development of RAP. In multivariate analysis using these three factors plus additional two factors with P values <0.1 in univariate analysis—age (OR 0.963, $P=0.0617$) and blood loss (OR 1.006, $P=0.0715$)—no significant factors were detected, but age showed a tendency to an association ($P=0.0643$). Therefore, a logistic regression univariate analysis was performed with classification by a median age of 63 years, which showed that younger age was a significant factor in the occurrence of RAP (OR 4.267, $P=0.0098$). Furthermore, on classification into three groups such that the number of cases in each group was almost equal, youngest age was significantly associated with the occurrence of RAP in both logistic regression univariate (OR 0.144, $P=0.0179$) and multivariate analysis (OR 0.124, $P=0.0148$).

Discussion

In this study, we found that RAPs occurring after RAPN resolved spontaneously after 3 months, and showed no recurrence at a median follow-up period of 21.6 months. We also found that the occurrence of RAP may associated with a patient age younger than the predominant age of renal cancer, namely under age 56 years.

Pseudoaneurysm can arise from various arteries and is an undesirable complication after treatment of various organs and disorders. Although the cause has not been elucidated, or such characteristics as whether it occurs only in certain persons or in persons who originally

Table 1 Patient characteristics and perioperative outcomes

Characteristic or variable	Data
Patients (men/women), n	98 (61/37)
Age, median (IQR, range), year	63 (18, 22–84)
BMI, median (IQR, range), kg/m ²	24.2 (6.0, 15.6–46.1)
ASA-PS, median (IQR, range)	2 (0, 1–3)
Comorbidity	
Smoking/hypertension/diabetes mellitus/dyslipidemia/urinary protein, n	55/57/32/40/10
Anticoagulant or Antiplatelet therapy, n	13
Preoperative eGFR, median (IQR, range), mL/min/1.73 m ²	70.3 (28.0, 30–114)
eGFR at POD7, median (IQR, range), mL/min/1.73 m ²	68.5 (28.0, 30–114)
eGFR reduction rate at POD7, median (IQR, range), %	4.3 (17.4, –30.0 to 36.2)
eGFR at POM1 eGFR, median (IQR, range), mL/min/1.73 m ²	69.0 (27.5, 32–113)
eGFR reduction rate at POM1, median (IQR, range), %	4.5 (15.1, –24.2 to 100.0)
Tumor side, left/right, n	46/52
Tumor size, median (IQR, range), mm	23 (11, 9–48)
R.E.N.A.L. nephrometry score, median [IQR, range]	7 [3, 4–10]
R.E.N.A.L. nephrometry score, low [4–6]/moderate [7–9]/high [10–12], n	47/48/3
Hilar lesion, n	16
Operator, A/B, n	77/21
Surgical approach, transperitoneal/retroperitoneal, n	71/27
Renal artery clamp, total/selective	90/8
Operating time, median (IQR, range), min	188 (57, 123–345)
Console time, median (IQR, range), min	131 (41, 59–285)
Warm ischemic time, median (IQR, range), min	14.9 (8.7, 5.5–39.7)
Tumor resection time, median (IQR, range), min	7.7 (4, 2–72)
Renorrhaphy time, median (IQR, range), min	21 (10, 5–50)
Blood loss, median (IQR, range), mL	50 (80, 3–700)
Resected tissue weight, median (IQR, range), g	9.7 (11.1, 1.0–55.7)
Pathological stage, T1a/T3a, n	83/2
Fuhrman grade, grade 1/grade 2/grade 3/grade 4, n	31/49/5/0
Tumor histology	
Malignant, n	85
Clear cell RCC/papillary RCC/chromophobe RCC/mucinous tubular and spindle cell carcinoma, n	77/5/2/1
Benign, n	13
Angiomyolipoma/oncocytoma/others, n	5/5/3
Positive surgical margin, n	1
Observation period, median (IQR, range), month	20.8 (23.9, 3.0–57.6)

IQR, interquartile range; BMI, body mass index; ASA-PS, American Society of Anesthesiologists physical status; eGFR, estimated glomerular filtration rate; R.E.N.A.L., radius (tumor size as maximal diameter), exophytic/endophytic properties of tumor, nearness of tumor deepest portion to collecting system or sinus, anterior/posterior descriptor and location relative to polar line; RCC, renal cell carcinoma.

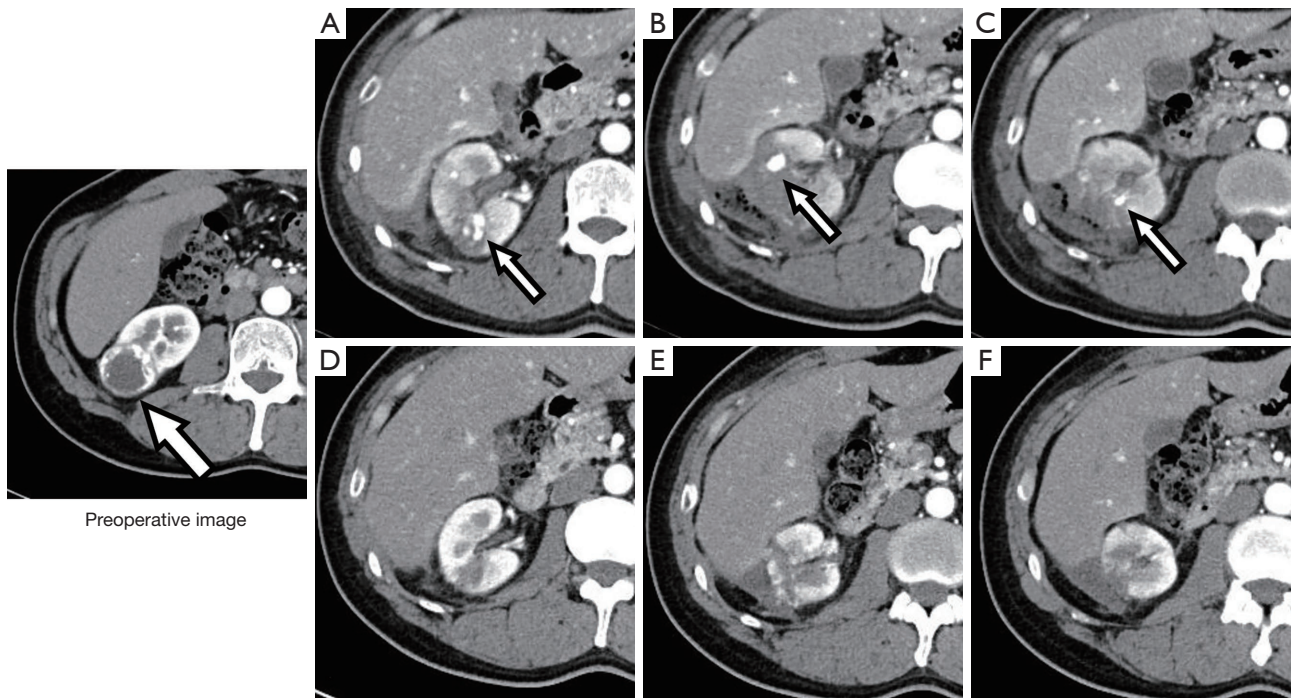


Figure 2 Contrast enhanced CT images. (A-C) Arterial phase CT images on POD7 after RAPN show multiple nodular enhancements that suggest RAPs. (D-F) Arterial phase CT images on POM1 show disappearance of RAPs. All three RAPs [10.9 mm in (A), 14.3 mm in (B) and 6.0 mm in (C); shown by a white arrow with a black border] found on POD7 after RAPN had resolved by 1 month after RAPN as shown in (D-F). Abbreviations: CT, computed tomography; POD, postoperative day; RAPN, robot-assisted partial nephrectomy; RAP, renal artery aneurysm; POM, postoperative month.

Table 2 Patient characteristics and perioperative outcomes by the presence or absence of RAP

Characteristics or variables	RAP		P value
	Present (n=21)	Absent (n=77)	
Men/women, n	13/8	48/29	0.9711 [†]
Age, median (IQR, range), year	56 (8.8, 22–77)	65 (17.5, 35–84)	0.0325 ^{††}
BMI, median (IQR, range), kg/m ²	25.6 (5.9, 15.6–39.4)	24.2 (6.4, 16.6–46.1)	0.3985 ^{††}
ASA-PS, median (IQR, range)	2 (0, 1–3)	2 (0, 1–3)	0.6002 ^{††}
Comorbidity, +/-, n			
Smoking	8/13	47/30	0.0604 [†]
Hypertension	12/9	45/32	0.9148 [†]
Diabetes mellitus	5/16	27/50	0.3296 [†]
Dyslipidemia	8/13	32/45	0.7747 [†]
Urinary protein	2/19	8/69	0.9075 [†]
Anticoagulant or antiplatelet therapy, +/-, n	2/19	11/66	0.5685 [†]
Preoperative eGFR, median (IQR, range), mL/min/1.73m ²	70.0 (24.8, 44.0–114.0)	70.6 (31.0, 30.0–113.0)	0.4644 ^{††}

Table 2 (continued)

Table 2 (continued)

Characteristics or variables	RAP		P value
	Present (n=21)	Absent (n=77)	
eGFR at POD7, median (IQR, range), mL/min/1.73m ²	68 (22.0, 48–114)	69 (29.0, 30–114)	0.9379 ^{††}
eGFR reduction rate at POD7, median (IQR, range), %	6.6 (17.8, –15.2 to 27.6)	4.1 (17.3, –30.0 to 36.1)	0.1673 ^{††}
eGFR at POM1 eGFR, median (IQR, range), mL/min/1.73m ²	71.1 (31.8, 38.0–93.0)	69.0 (27.0, 32.0–113.0)	0.4170 ^{††}
eGFR reduction rate at POM1, median (IQR, range), %	1.3 (18.4, –8.0 to 21.7)	4.7 (14.2, –24.4 to 100.0)	0.8541 ^{††}
Tumor side, left/right, n	9/12	37/40	0.2603 [†]
Tumor size, median (IQR, range), mm	2.1 (0.9, 0.9–4.3)	2.4 (1.2, 1.0–4.8)	0.6724 ^{††}
R.E.N.A.L. nephrometry score, median [IQR, range]	8 [3, 4–10]	6 [3, 4–10]	0.0410 ^{††}
R.E.N.A.L. nephrometry score, low [4–6]/moderate [7–9]/high [10–12], n	6/13/2	41/35/1	0.0359 [†]
Hilar lesion, +/-, n	1/20	15/62	0.1058 [†]
Operator, A/B, n	16/5	61/16	0.7642 [†]
Surgical approach, transperitoneal/retroperitoneal, n	13/8	58/19	0.2224 [†]
Renal artery clamp, total/selective	20/1	70/7	0.5207 [†]
Collection system opening, +/-, n	5/16	9/68	0.1594 [†]
Renal sinus exposure, +/-, n	9/12	29/48	0.6650 [†]
Operating time, median (IQR, range), min	188 (45.0, 154–266)	188 (63.8, 123–345)	0.4232 ^{††}
Console time, median (IQR, range), min	139 (24.8, 64–211)	130 (53.5, 59–285)	0.4777 ^{††}
Warm ischemic time, median (IQR, range), min	20.0 (9.6, 7.8–29.1)	14.4 (7.2, 5.5–39.7)	0.0230 ^{††}
Tumor resection time, median [IQR, range], min	9 [3, 3–17]	7 [4, 2–72]	0.0525 ^{††}
Renorrhaphy time, median (IQR, range), min	27 (10.8, 14–43)	20 (9.5, 5–50)	0.0103 ^{††}
Blood loss, median (IQR, range), mL	50 (72, 10–700)	50 (86, 3–300)	0.0128 ^{††}
Resected tissue weight, median (IQR, range), g	12.6 (13.9, 3.4–55.7)	9.1 (11.6, 1.0–39.1)	0.1319 ^{††}
Tumor histology, malignant/benign, n	19/2	66/11	0.5685 [†]
Cell type, clear cell/non-clear cell, n	18/3	59/18	0.3681 [†]
Observation period, median (IQR, range), month	22.6 (24.6, 4.9–48.1)	20.5 (22.1, 3.0–57.4)	0.8727 ^{††}

[†], Chi-square test; ^{††}, Mann-Whitney U test. RAP, renal artery pseudoaneurysm; IQR, interquartile range; BMI, body mass index; ASA-PS, American Society of Anesthesiologists physical status; eGFR, estimated glomerular filtration rate; R.E.N.A.L., radius (tumor size as maximal diameter), exophytic/endophytic properties of tumor, nearness of tumor deepest portion to collecting system or sinus, anterior/posterior descriptor and location relative to polar line; RCC, renal cell carcinoma.

have a vascular lesion (12), and how often it disappears spontaneously, it is believed to commonly occur during surgical vascular injury and its healing process. Regarding the etiology of RAP after PN, Singh and Gill proposed two mechanisms: (I) inadvertent vascular injury during tumor resection, and (II) vascular injury during parenchymal renorrhaphy (13). Previous reports demonstrated that the retroperitoneal approach, tumors buried in the renal

parenchyma, tumor complexity, and renal sinus exposure affected the development of RAP, suggesting that treating deep kidneys with tumor complexity within a narrow surgical field increases the risk of RAP (7,14,15). In our study, surgical approach and renal sinus exposure did not affect the presence or absence of RAP (Table 2). In contrast, high R.E.N.A.L. nephrometry scores, which indicate tumor complexity, affected the presence or absence of RAP

Table 3 Factors influencing the occurrence of RAP by logistic regression analysis

Category	Incidence of RAP, n [%]	Univariate			Multivariate A			Multivariate B		
		Odds ratio	95% CI	P value	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
R.E.N.A.L. nephrometry score	21 [100]	1.374	1.017–1.857	0.0382	1.304	0.923–1.842	0.1328	1.412	0.987–2.020	0.0587
Blood loss	21 [100]	1.006	1.000–1.012	0.0715	1.005	0.999–1.012	0.1070	3.571	0.959–13.291	0.0577
Warm ischemic time	21 [100]	1.085	1.004–1.172	0.0393	1.029	0.935–1.131	0.5587	1.022	0.929–1.125	0.6517
Renorrhaphy time	21 [100]	1.055	1.002–1.111	0.0408	–	–	–	–	–	–
Age	21 [100]	0.963	0.924–1.004	0.0617	0.960	0.920–1.002	0.0643	–	–	–
Age > median (vs. ≤ median)	5 [24] vs. 16 [71]	4.267	1.419–12.831	0.0098	–	–	–	–	–	–
Age, years old										
22–56, n=34	11 [52]	Reference	–	–	–	–	–	Reference	–	–
57–68, n=33	8 [35]	0.669	0.229–1.956	0.4627	–	–	–	0.812	0.254–2.598	0.7257
69–84, n=31	2 [13]	0.144	0.029–0.716	0.0179	–	–	–	0.124	0.023–0.665	0.0148

In the multivariate analyses, the inner suture time, which is a component of renorrhaphy time, is included in the warm ischemic time, so warm ischemic time was used as a representative. Multivariate A is a multivariate analysis in which factors are used as continuous variables, while multivariate B is a multivariate analysis in which only the factor of age is categorized. CI, confidence interval; RAP, renal artery pseudoaneurysm; BMI, body mass index; eGFR, estimated glomerular filtration rate; R.E.N.A.L., radius (tumor size as maximal diameter), exophytic/endophytic properties of tumor, nearness of tumor deepest portion to collecting system or sinus, anterior/posterior descriptor and location relative to polar line; RCC, renal cell carcinoma.

(Table 2) and were a significant factor in the occurrence of RAP (Table 3). The same tendency was seen when only the “E” component of the R.E.N.A.L. nephrometry scores was examined (data not shown). Supporting the vascular injury hypothesis, previous reports have shown that early unclamping might reduce the risk of RAP after RAPN or LPN (14,16,17). Kondo *et al.* stated that early unclamping can provide information regarding arterial bleeding from the resected bed before renal parenchymal suture. As arterial bleeding from the resected bed is controlled by the inner suture rather than the renal parenchymal suture, additional inner suturing should provide hemostasis of arterial bleeding with early unclamping (16). Early unclamping was also adopted, but the incidence of RAP (23%) was higher than that reported by Kondo *et al.* (11%) (16). The present study is a review of all cases from the start of RAPN at our university hospital; this difference in outcomes may be related to technical proficiency in renorrhaphy, followed by the significant association of longer renorrhaphy time with both the presence or absence of RAP and the occurrence of this complication (Tables 2,3). In addition, with regard to OPN, Ota *et al.* reported the safety and effectiveness of the soft-coagulation system for

PN without parenchymal renorrhaphy, excluding hilar tumors (18). The soft coagulation system of the VIO 300D was used with the effect level set at 7 and output of 80 W, using a ball-type electrode to increase the contact area with the resection bed. Tachibana *et al.* also showed that the non-renorrhaphy (inner layer sutures only) technique using the soft-coagulation system may produce a lower risk of RAP than renorrhaphy (inner and outer layer sutures) (19). Similarly, for RAPN in patients with cT1a renal tumors, RAP did not occur with hemostasis by soft coagulation only, namely with inner sutures and without outer sutures (20,21). Thus, the soft coagulation system may help prevent the development of RAP occurring following surgical resection.

In contrast, uterine arterial pseudoaneurysm occurs rarely following cesarean section, and may also occur due to factors other than surgical procedures (22). It is noteworthy that the target demographic for this condition is young fertile women. Moreover, lower age (<65.5 years) was reported to be an independent risk factor for the development of pseudoaneurysm after pancreaticoduodenectomy, while a systematic review reported a higher number of cases of ankle pseudoaneurysm among young adults, namely in 15 (65%) of 23 case reports

published from 1966 until 2018 (23,24). On the contrary, while a positive effect of aging on the occurrence of RAP after RAPN has been reported, little discussion of this association has appeared (16). In logistic regression analysis of the factors that influenced the occurrence of RAP in our study (Table 2), young population and factors involved in surgery such as tumor resection time, renorrhaphy (inner and outer layer sutures) time, blood loss, and R.E.N.A.L. nephrometry scores were significant factors in univariate analysis. In addition, there was no difference among patients in baseline characteristics by age (data not shown). These results support the hypothesis of RAP occurrence. In multivariate analysis, in contrast, the only significant factor was a young population age. Angiogenesis plays an important role in the repair of blood vessels and tissues, and the impairment of this process in older patients has been demonstrated (25,26). Taken together, younger age may contribute to the occurrence of RAP. A conclusive answer to the possible role of age in RAP will require evaluation in a larger number of patients and basic research on angiogenic factors.

As shown in Figure 1, the most impactful result of our study is that, regardless of cause, pseudoaneurysms of approximately 15 mm resolved spontaneously after 3 months, and showed no recurrence with a median observation period of 20.8 months. Accordingly, our results suggest indicators of causation and resolution in the natural history of RAP, namely potential target values for RAP size and observation period. The size of RAP at which resolution occur is consistent with the size reported for the spontaneous disappearance of uterine arterial pseudoaneurysm (27). In any case, our findings suggest that one method of preventing RAP might be hemostasis of the resected surface by soft coagulation with an inner layer suture (20,21). RAP is generally described as occurring about 2 weeks after surgery, but may occur anywhere up to 6 months after LPN or RAPN or 2 or more years after OPN, and long-term follow-up should therefore not be neglected (28,29). In addition, although routine postoperative CE-CT is harmful in terms of renal function, radiation exposure and cost, Kondo *et al.* have pointed out that the benefits can outweigh the harm given the complications and costs which occur after RAP rupture (16). Conversely, routine postoperative CE-CT may carry greater risk of overimaging, overdiagnosis, and overtreatment of asymptomatic RAP, as in our two patients who underwent prophylactic RAE for asymptomatic RAP diagnosed by routine CE-CT 7 days after RAPN. Further, the usefulness

of Doppler ultrasonography for the early detection of significant asymptomatic RAP has been reported (30). Against this background, we found that RAPs of 15 mm or less disappear spontaneously after 3 months, suggesting that routine early postoperative imaging including CE-CT is not required in the absence of clinical signs or symptoms such as gross hematuria.

This study has some limitations. First, it was a retrospective study with a small sample size at a single university hospital, hindering generalization of the results. Second, as many surgeons were involved as assistants, it was not possible to examine the effect of their proficiency in surgical techniques. Third, diagnosis of RAP was performed by a single radiologist, albeit one that was skilled in this procedure. Fourth, patients with renal impairment, allergy to contrast medium, or asthma were excluded from this study. Fifth, this study was initiated at a single university hospital in a situation where the natural history of RAP was unknown, and possible complications other than RAP were identified. We therefore planned to carefully follow the course of all consecutive patients and perform routine CE-CT without missing any cases. Patients who understood the above underwent RAPN, resulting in overimaging. Sixth, although age was detected as a factor in the development of RAP, we were unable to evaluate the mechanism of this effect. We are currently preparing basic research into this question. Further progress in this field awaits a larger multicenter, prospective, randomized study.

In conclusion, RAPs generated after RAPN were followed by routine CE-CT. Asymptomatic RAP up to 15 mm in diameter resolved spontaneously within 3 months after RAPN. Young age (under 56 years) may be a factor in the development of RAP. Although further research is needed on factors such as long-term follow-up and age, we suggest that current efforts to prevent RAP should consider the use of soft coagulation in the repair of resected surfaces.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of Jichi Medical University (A19-199) and withdrawal of consent to the use of medical data was by the opt-out system.

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