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Original Article

Contrast-enhanced and conventional ultrasound images of renal wounds after partial nephrectomy

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Abstract: Objectives: To observe the features of conventional ultrasound (US) and contrast-enhanced ultrasound (CEUS) images of renal wounds after minimally-invasive partial nephrectomy (MIPN) and evaluate their severity using these two modalities. Methods: This prospective, observational study included 120 patients who underwent MIPN from April to December 2019 in our hospital. The postoperative US images were evaluated and classified, and contrast extravasation characteristics of CEUS were recorded. The correlation between the classification system and perioperative factors was analyzed. Results: Eighty-five patients underwent US and CEUS after MIPN. Conventional US images were classified into three grades according to the surface morphology of renal wounds and overall shape of the kidney around the incision. Univariable and multivariable analyses indicated that the N component of the R.E.N.A.L. score and the resection range were preoperative and intraoperative factors, respectively, related to the US image grades (UIGs). A deep location and expanded excision contributed to an increased UIG. The extravasation rate increased with the UIG (Spearman correlation rho=0.247, *P*=0.022), and a higher UIG prolonged the length of extravasation. The depth of the tumor and resection range were related to the UIG. Conclusions: US and CEUS were feasible and repeatable methods that reflect the morphologic changes of renal wounds after MIPN and may be useful for evaluating their severity.

Keywords: Ultrasonography, CEUS, partial nephrectomy, minimally invasive, surgical wound

Introduction

Renal cancer accounts for 2% to 3% of all malignant disease worldwide [1], and its incidence has been increasing in recent years due to incidental detection by common imaging procedures such as ultrasound (US). Partial nephrectomy (PN) is the recommended standard treatment for T1-stage renal cancer, because it can maintain renal function without compromising oncological outcome [2]. Compared to an open approach, minimally-invasive PN (MIPN) is usually preferred in the form of laparoscopic partial nephrectomy (LPN) or robotic partial nephrectomy (RPN) [3], even though some disadvantages exist, such as an altered surgical field and a steep learning curve [4, 5]. Postoperative management, including restricted activity and drainage, mainly focuses on avoiding wound-healing complications such as hemorrhage and urine leakage. Postoperative management follows various principles in different centers based on experience and clinical retrospective analyses [6]. However, no morphologic or imaging evidence exists to indicate the severity of renal wounds after surgery. The morphology of postoperative kidney defects depends on the size and depth of the mass and also is correlated with the suture method, which is a critical step to avoid wound complications [7, 8]. Thus, morphologic evaluation may indicate the stability and recovery of the wound.

Conventional US and contrast-enhanced ultrasound (CEUS) have been widely used to diagnose abdominal organ trauma [9, 10]. CEUS can detect contrast agent extravasation, which is considered a significant indicator of active hemorrhage [11, 12]. The contrast agent used in CEUS imaging consists of tiny gas microbubbles surrounded by stabilizing shells. The microbubbles' diameter is similar to that of red blood cells, which could theoretically allow the microbubbles to extravasate into the interstitial space through vascular injury. Gregory et al. [13] injected indigo carmine into porcine renal arteries to observe whether extravasation occurred from the sutured wound after PN. Similarly, microbubbles as the intravascular media may also extravasate from the renal wound. The purpose of our study was to observe the features of CEUS and conventional US images of renal wounds after MIPN and evaluate their severity using these two modalities.

Materials and methods

Ethics approval

This prospective, observational, unpaired study was performed according to the principles of the 1964 Declaration of Helsinki and was approved by the ethics committee of the First Affiliated Hospital of Anhui Medical University (PJ2019-17-19). Written informed consent for CEUS and the use of related data for future research were obtained from each patient before the procedure, and all patient details were de-identified. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [14].

Patients

All consecutive patients treated using LPN or RPN at the First Affiliated Hospital of Anhui Medical University from April 2019 to December 2019 were evaluated according to the inclusion and exclusion criteria. Before surgery, contrast-enhanced computed tomography (CT) or magnetic resonance imaging was used to diagnose masses as T1N0M0 according to the Tumor Node Metastasis classification.

Inclusion and exclusion criteria

The inclusion criteria for the study included patients who could cooperate with CEUS examinations and sign informed consent forms. The exclusion criteria consisted of a known history of allergies to medications, albumin, foods, or other blood products; age <18 or >80 years; grade IV cardiac function and/or intracardiac shunt; severe arrhythmia, acute respiratory distress syndrome, respiratory failure, and/or asthma; psychosis or epilepsy; and lack of cooperation.

Surgical technique

All PNs were performed using the Da Vinci Si Surgical System (Intuitive, Sunnyvale, CA, USA) or a laparoscope through a transperitoneal or retroperitoneal approach. Standard excision involving removal of a 5-mm rim of healthy tissue along with the tumor was carried out using cold-cut scissors [15]. When the pathologic size of the resected specimen was compared to the tumor size on preoperative imaging, we noted an increased loss of parenchymal mass during surgery for the excision of a >5 mm rim of tissue adjacent to the tumor in some patients, which was called "expanded excision". Renorrhaphy was performed using 3-0 V-Loc 180 sutures on V-20 needles (Covidien, Mansfield, MA, USA) with anchoring Hem-o-Lok clips in the loops of the sutures [16]. A drainage tube was routinely placed after surgery and was removed when the drainage volume was <50 ml/day. Bed rest with spinal positioning was required for 3 days postoperatively.

US imaging

A Mindray Resona 7 system (Mindray Medical, Shenzhen, China) and an SC-5-1U 3-5-MHz probe were used for US examinations. Perfluoropropane-albumin microsphere injection (Kangrun Pharmaceutical Co, Yueyang, China) and a low mechanical index of 0.08 were used for CEUS imaging. Preoperative conventional US scanning (grayscale and color Doppler scanning) was performed to determine the size and location of masses. One US specialist experienced in CEUS and one urology specialist with 3 years of experience in PN performed the examinations.

During CEUS, patients were requested to hold a spinal or lateral position with slow, shallow breathing. Coronal images of the kidneys were obtained with the US probe placed on the posterior axillary line. The morphological features of the renal incision were evaluated using conventional US. Then, an intravenous 2.5-ml bolus was injected via a peripheral intravenous cannula, followed by a 5-ml saline flush. A timer and video recorder were started immediately after the injection. The duration of the CEUS examination was at least 2.5 min, including the

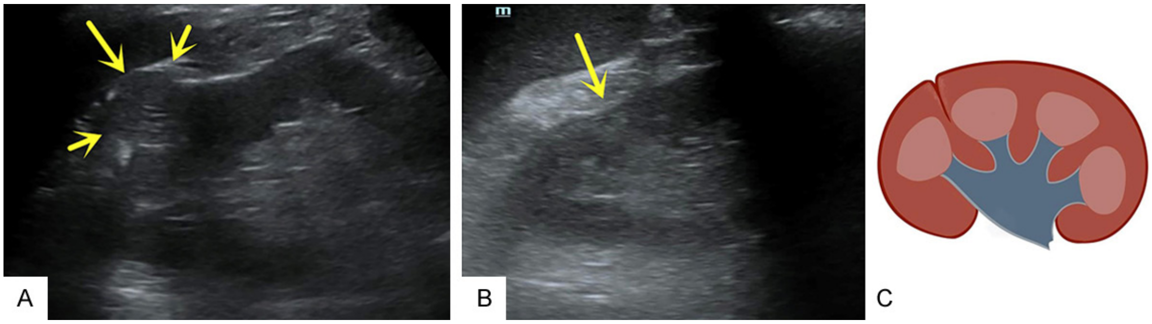

Figure 1. Grade 1 conventional ultrasound images. A 50-year-old man with a 2.5×2.0 cm solid tumor underwent a robotic partial nephrectomy (RPN). A. Conventional US displayed a hyperechoic mass located in the upper pole of the left kidney (arrows). B. At 24 hours after RPN, conventional US indicated a grade 1 wound: a normal kidney shape, regular anastomosed renal parenchyma, and a relatively smooth capsule (arrow). C. Diagrammatic representation of a grade 1 surgical renal wound.

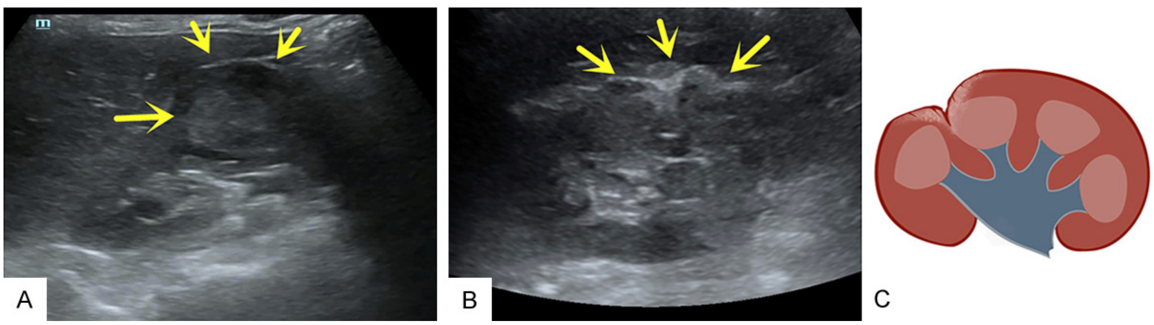

Figure 2. Grade 2 conventional ultrasound images. A 75-year-old woman with a 2.5×2.3 cm solid tumor underwent a robotic partial nephrectomy (RPN). A. Conventional US displayed a mass with heterogeneous echo located in the middle pole of the right kidney (arrows). B. At 24 hours after RPN, conventional US demonstrated a grade 2 wound: a relatively normal kidney shape, irregular anastomosed renal parenchyma, and a rugged capsule (arrows). C. Diagrammatic representation of a grade 2 surgical renal wound.

cortical phase (approximately 15-30 s post injection) and the medullary phase (approximately 30-70 s post injection). All videos and images were saved by the US system for subsequent analysis.

The first CEUS examination was performed on postoperative day 1. If contrast agent extravasation was absent, the length of extravasation (LOE) of the patient was defined as 1 day. If extravasation was present, repeated CEUS examinations were performed every 24 hours until extravasation was absent.

US image interpretation

The US examiner and another US specialist designed a classification system with three grades based on the postoperative conventional US images: grade 1: a normal kidney shape, regular anastomosed renal parenchyma, and a relatively smooth capsule (**Figure 1**); grade 2: a relatively normal shape, irregular anastomosed renal parenchyma, and a rugged capsule (**Figure 2**); grade 3: an abnormal kidney shape with loss of renal units and obvious hollowness on the surface (**Figure 3**). CEUS videos and images were carefully assessed to ensure the presence of contrast agent extravasation from the wound and to observe areas with perfusion defects adjacent to the renal incision. The LOE of each patient was recorded.

Statistical analysis

The baseline characteristics of patients and tumors, as well as surgical and postoperative factors, were recorded for analysis of their relationships to the US image grades (UIGs). Continuous variables were expressed as the mean ± standard deviation or median (interquartile range) for data with a non-normal distribution, and categorical variables were expressed as numbers (percentages). The Chi-

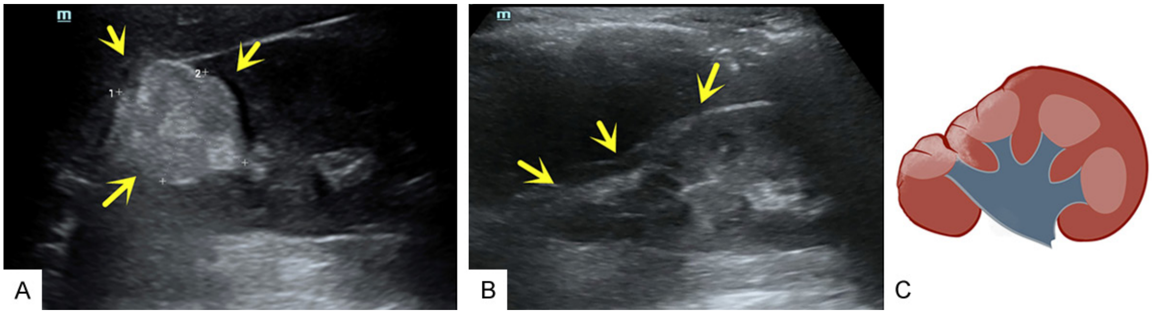

Figure 3. Grade 3 conventional ultrasound images. A 33-year-old woman with a 2.6×2.6 cm solid tumor underwent a robotic partial nephrectomy (RPN). A. Conventional US displayed a hyperechoic mass located in the upper pole of the right kidney (arrows). B. At 24 hours after RPN, conventional US demonstrated a grade 3 wound: an abnormal shape with loss of renal units and obvious hollowness on the surface (arrows). C. Diagrammatic representation of a grade 3 surgical renal wound.

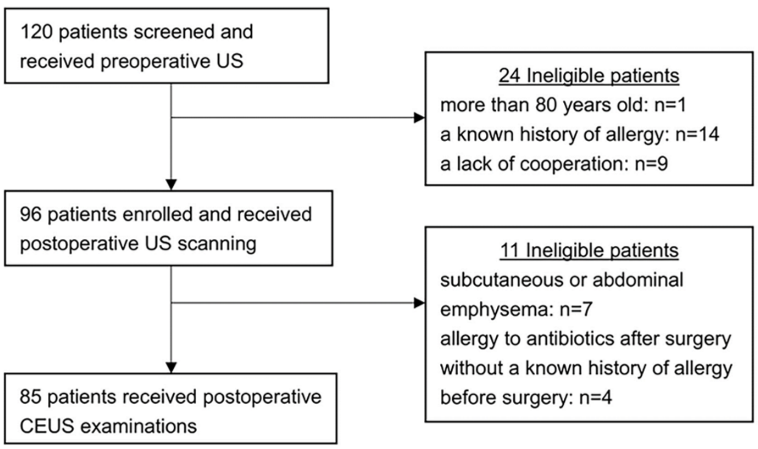

Figure 4. Flowchart of patient enrollment in this prospective study.

square test or Fisher's exact test, Mann-Whitney U and Kruskal-Wallis test, and one-way analysis of variance were used to analyze unordered categorical, ordered categorical, and continuous variables, respectively. The Kruskal-Wallis test was applied to analyze continuous variables with a non-normal distribution. Then, variables with a *P* value <0.05, age, side, and sex were included in the multivariable ordinal logistic regression model. IBM SPSS Statistics, Version 20.0 (IBM, Armonk, NY, USA) was used for data analysis, and a two-tailed value of *P*<0.05 was considered significant.

Results

Baseline patient characteristics

In total, 120 patients were screened and underwent preoperative US scanning. After surgery, 85 of 120 patients received CEUS examinations (**Figure 4**). Neither complications nor adverse reactions associated with CEUS were observed. Twenty-nine cases (29/85, 34.1%) were classified as grade 1, 41 cases (41/85, 48.2%) were classified as grade 2, and 15 cases (15/85, 17.6%) were classified as grade 3. The baseline patient and tumor characteristics are presented in **Table 1**, and surgical and postoperative factors are shown in **Table 2**.

Imaging

The renal wound was defined as a region of irregular heterogeneous echo with an unclear border on conventional US imaging and an uneven wound surface. Conventional US also detected hypoechoic or anechoic-free fluid around the wound. However, we could not precisely quantify the fluid volume because of its irregular distribution. A wider excision led to more loss of renal units, which was imaged as hollowness on the surface, and conspicuous volume loss.

CEUS showed a drip or a band-like spot outside of the sutured capsule during the cortical to the medullary phase (**Figure 5**). The parenchymal wound exhibited an irregular perfusion defect area or a delayed perfusion area.

Univariable analysis of factors related to the UIGs

Regarding the preoperative clinical findings, only the N component of the R.E.N.A.L. nephrometry score, which represents the nearness

Table 1. Univariate analysis of the associations of patient and tumor characteristics with ultrasound image grade

Variable	Grade 1 (n=29)	Grade 2 (n=41)	Grade 3 (n=15)	*P* value
Age (years)	54.93±10.51	53±13	50±12.66	0.444
Sex				0.337
Male	17 (58.6)	19 (46.3)	8 (53.3)	
Female	12 (41.1)	22 (53.7)	7 (46.7)	
Side				0.364
Left	17 (41.5)	17 (41.5)	7 (17.1)	
Right	12 (27.3)	24 (54.5)	8 (18.2)	
BMI (kg/m^2)	25.14±3.84	23.68±3.38	24.1±3.59	0.244
Maximum diameter of tumor (cm)	2.84±1.09	3.14±1.14	3.43±1.63	0.307
Baseline eGFR (mL/min/1.73 m^2)	103.62±14.75	102.12±16.89	108.6±14.19	0.398
Baseline Cr (μmol/L)	67.69±14.99	68.54±14.92	64.82±15.6	0.716
Baseline Hb (g/L)	136.34±14.27	130.34±12.55	130±16.91	0.168
Charlson comorbidity index	1 (1-2)	1 (0-2)	1 (0-2)	0.807
R.E.N.A.L. score	6.45±1.764	7.1±1.67	7±1.47	0.265
Tumor complexity (%)[a]				0.163
Low	17 (58.6)	15 (36.5)	5 (33.3)	
Intermediate	11 (37.9)	22 (53.7)	9 (60)	
High	1 (3.5)	4 (9.8)	1 (6.7)	
R component				0.065
1	26 (89.7)	32 (78)	10 (66.7)	
2	3 (10.3)	9 (22)	5 (33.3)	
E component				0.099
1	19 (65.5)	14 (34.1)	6 (40)	
2	8 (27.6)	23 (56.1)	7 (46.7)	
3	2 (6.9)	4 (9.8)	2 (13.3)	
N component				0.011[b]
1	15 (51.7)	10 (24.4)	2 (13.3)	
2	6 (20.7)	14 (34.1)	8 (53.3)	
3	8 (27.6)	17 (41.5)	5 (33.4)	
A component				0.163
A	8 (27.6)	13 (31.7)	8 (53.3)	
P	13 (44.8)	16 (39)	2 (13.3)	
X	8 (27.6)	12 (29.3)	5 (33.4)	
L component				0.314
1	9 (31)	14 (34.1)	7 (46.7)	
2	8 (27.6)	15 (36.6)	5 (33.3)	
3	12 (41.4)	12 (29.3)	3 (20)	

Abbreviations: GUIs, grades of US images; BMI, body mass index; eGFR, estimated glomerular filtration rate; Cr, creatinine; Hb, hemoglobin; R.E.N.A.L.= (R)adius (tumor size as maximal diameter), (E)xophytic/endophytic properties of tumor, (N)earness of tumor deepest portion to collecting system or sinus, (A)nterior (a)/posterior (p) descriptor, and (L)ocation relative to polar lines; A, anterior; P, posterior; X, unknown A or P. Notes: Numbers are n (%) or mean ± standard deviation (SD) or median (Interquartile range); [a]low complexity is R.E.N.A.L. score 4-6, intermediate 7-9, and high 10-12; [b]Kruskal-Wallis test.

of the deepest portion of the tumor to the collecting system or sinus, was related to the UIG (**Table 1**, χ^2=9.043, *P*=0.011). A deep tumor location was associated with a higher UIG (Spearman correlation rho=0.22, *P*=0.043, Mantel-Haenszel χ^2=3.9, *P*=0.048). Regarding

Table 2. Univariate analysis of the association of surgical and postoperative factors with ultrasound image grade

Variable	Grade 1 (n=29)	Grade 2 (n=41)	Grade 3 (n=15)	*P* value
Surgical method				0.226
RPN	23 (79.3)	35 (85.4)	14 (93.3)	
LPN	6 (20.7)	6 (14.6)	1 (6.7)	
Surgical approach				0.942
Retroperitoneal	20 (69)	29 (70.7)	10 (66.7)	
Transperitoneal	9 (31)	12 (29.3)	5 (33.3)	
Seniority of surgeon[a]				0.357
Junior	5 (17.2)	6 (14.6)	0 (0)	
Middle	11 (37.9)	15 (36.6)	8 (53.3)	
Senior	13 (44.9)	20 (48.8)	7 (46.7)	
Resection range[b]				0.025[c]
Standard excision	28 (96.6)	33 (80.5)	11 (73.3)	
Expanded excision	1 (3.4)	8 (19.5)	4 (26.7)	
Layers				0.206
One	8 (27.6)	3 (7.3)	3 (20)	
Two	21 (72.4)	38 (92.7)	12 (80)	
WIT (min)	17.34±6.56	19.83±6.81	18.33±3.96	0.266
Operative time (min)	163.28±38.51	152.07±32.56	148±26.24	0.267
Decrease of eGFR (%)	8.55 (1.91-18.42)	12.2 (6.2-27.85)	7.84 (3.1-34.07)	0.182
Decrease of Hb[d] (%)	10.07 (6.55-14.49)	11.64 (7.57-14.91)	15.5 (9.92-17.78)	0.038[e]
Increase of Cr (%)	18.18 (3.2-30.48)	18.97 (9.82-33.98)	22.06 (7.08-44.8)	0.440
Length of stay (day)	7.16±2.1	7.06±1.63	6.56±1.33	0.679
Time to extubation (day)	4.57±1.88	4.52±1.06	5.17±0.75	0.212
Complication[f]				0.474
No	13 (44.8)	14 (34.1)	4 (26.7)	
Grade I	14 (48.4)	21 (51.2)	9 (60)	
Grade II	1 (3.4)	6 (14.6)	2 (13.3)	
Grade III	1 (3.4)	0	0	
Pathology				0.241
Malignant tumor	24 (82.8)	26 (63.4)	9 (60)	
Benign tumor	4 (13.8)	13 (31.7)	4 (26.7)	
Else	1 (3.4)	2 (4.9)	2 (13.3)	
Extravasation				0.002[g]
No (one day)	19 (65.5)	26 (63.4)	2 (13.3)	
Yes (over one day)	10 (34.5)	15 (36.6)	13 (86.7)	
LOE	1 (1-2)	1 (1-2.5)	2 (2-3)	0.006[h]

Abbreviations: GUIs, grades of US images; RPN, robotic partial nephrectomy; LPN, laparoscopic partial nephrectomy; WIT, warm ischemia time; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; Cr, creatinine; LOE, length of extravasation. Notes: Numbers are n (%) or mean ± standard deviation (SD) or median (Interquartile range); [a]seniority of surgeon, junior, <3 years of experience of RPN, middle, 3-5 years, senior, >5 years; [b]resection range, standard excision included strategic sharp dissection through normal parenchyma and removing a 5 mm rim of healthy tissue along with the tumor, expanded excision included a >5 mm rim of normal parenchyma adjacent to the tumor; [c]Mann-Whitney U test; [d]decrease of Hb (%) meant the decrease of Hb on the first day after surgery, and it is the same with the change of eGFR and Cr. [e]Kruskal-Wallis test, post hoc multiple comparisons showed statistical difference between grade 1 and 3 group (*P*=0.033); [f]Clavien-Dindo classification system; [g]Chi-square test. [h]Kruskal-Wallis test, post hoc multiple comparisons showed a statistical difference between grade 1 and 3 group (*P*=0.005), grade 2 and 3 group (P=0.025).

intraoperative variables, the resection range was the only factor associated with the UIG (**Table 2**, U=300, P=0.025). Compared to standard excision, expanded excision contributed to

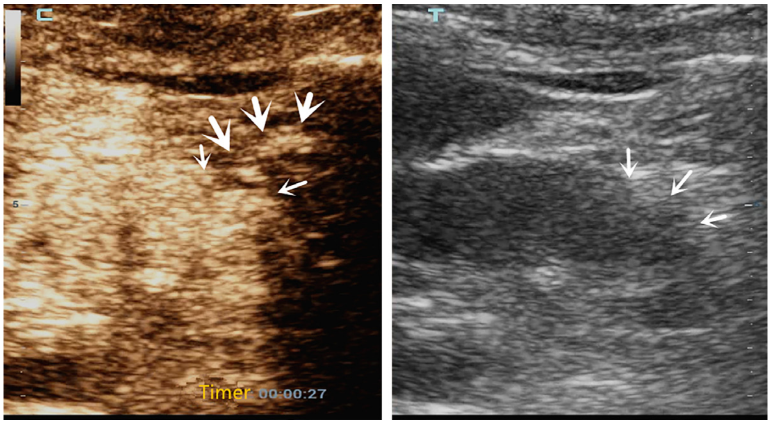

Figure 5. Contrast-enhanced ultrasound (CEUS) images of a band-like spot of contrast agent extravasation. A 67-year-old woman with a 3.0×2.8 cm solid tumor underwent a robotic partial nephrectomy. CEUS demonstrated a band-like spot of contrast agent extravasation (thick arrows) from the wound surface, which was classified as grade 1 (fine arrows), in the cortical phase on postoperative day 1.

a higher UIG (Spearman correlation rho=0.244, P=0.025, Mantel-Haenszel χ^2=4.836, P=0.028).

Multivariable analysis of factors related to the UIGs

In the multivariable ordinal logistic model of preoperative and intraoperative variables, adjusted odds ratios (aORs) were calculated after adjustment for age, sex, and side. The only factors that remained significant were the N component of the R.E.N.A.L. nephrometry score and the resection range (**Table 3**). Patients with N scores of 3 points had a 9.4-fold greater likelihood of having a higher UIG than those with N scores of 1 point (P<0.001). Patients with N scores of 2 points (aOR=12.95, P<0.001) had an increased likelihood of having a higher UIG compared to those with N scores of 1 point. Expanded excision, in contrast to standard excision, was directly related to a higher UIG (aOR=12.14, P=0.001).

Analysis of the association of UIGs with post-operative factors

The Kruskal-Wallis test showed that the UIG was associated with a decrease in hemoglobin (Hb) (%) on postoperative day 1 (P=0.038), and a significant difference was found between the grade 1 and grade 3 groups (P=0.033) according to a post hoc multiple comparisons test. A higher UIG resulted in a greater decrease in Hb (%) on postoperative day 1 (Spearman correlation rho=0.255, P=0.019). The Chi-square test showed that the UIG was related to extravasation (χ^2=13, P=0.002). CEUS imaging identified extravasation (longer than 1 day) in 44.7% (38/85) of patients. The incidence of extravasation increased with grade; 35.5% of grade 1 patients (10/29), 36.6% of grade 2 patients (15/41), and 86.7% of grade 3 patients (13/15) exhibited extravasation (Spearman correlation rho=0.247, P=0.022), and a high grade prolonged the LOE (**Table 2**).

The complication rates increased with the UIG but without statistical significance (**Table 2**, P=0.474). Chi-square test analysis indicated a higher incidence of complications in patients with than in those without extravasation (**Table 4**, P=0.003). A stratified analysis further showed that this difference existed only in patients with a UIG of 1 (**Table 4**), which showed that the LOE might be an individual factor for predicting complications in grade 1 patients.

Discussion

Minimally-invasieve partial nephrectomy (MIPN) has gained wide acceptance as a surgical method for removing renal mass while also preserving renal functional units in patients with T1-stage renal cancer [2]. In addition, a shorter hospital stay and faster return to normal physical activity are well-documented advantages of MIPN over open surgery [17, 18]. Nevertheless, estimation of surgical wound healing still depends on the opinions of doctors, which are derived from experience. Renal wound instability can increase the risk of postoperative hemorrhage, thereby affecting the healing process. Many clinical factors are related to wound healing, but no direct imaging evidence of wound healing has been obtained. To our knowledge, this is the only study to evaluate renal wounds after PN using US imaging.

Renal wounds after surgery have a similar morphological and physiopathologic status to that

Table 3. Multivariable ordinal logistic regression analysis of the associations of factors with ultrasound image grades

Value	B	SE	Wald	*P* value	aOR (95% CI)
Threshold Grade =1[a]	-0.388	1.164	0.111	0.739	0.68 (0.07-6.64)
Grade =2[b]	2.349	1.161	4.093	0.043	10.47 (1.08-101.87)
N=3	2.24	0.64	12.247	<0.001	9.4 (2.68-32.96)
N=2	2.561	0.649	15.589	<0.001	12.95 (3.63-46.18)
N=1	0[c]				Reference
Expanded excision	2.496	0.722	11.963	0.001	12.14 (2.95-49.95)
Standard excision	0[c]				Reference
Right	0.307	0.453	0.458	0.499	1.36 (0.56-3.3)
Left	0[c]				Reference
Male	-0.328	0.451	0.526	0.468	0.72 (0.3-1.75)
Female	0[c]				Reference
Age	-0.3	0.019	2.529	0.112	0.97 (0.94-1.01)

Abbreviations: GUIs, grades of US images; B, regression coefficient B; SE, standard error; Wald: Wald value; ORaj: odds ratios adjusted; 95% CI, confidence interval of 95%. Notes: Adjusted variables are N component, resection range, gender, side and age; [a]grade 1 vs grade 2 and grade 3; [b]grade 1 and grade 2 vs grade 3; [c]this parameter is set to zero because it is redundant.

Table 4. Stratified analysis of the association of the length of extravasation with complications

GUIs	LOE (day)	Complication		Total	*P* value
		No	Yes		
Grade 1	=1	13 (68.4)	6 (31.6)	19	0.021
	>1	2 (20)	8 (80)	10	
Grade 2	=1	10 (38.5)	16 (61.5)	26	0.512
	>1	4 (26.7)	11 (73.3)	15	
Grade 3	=1	2 (100)	0 (0)	2	0.057
	>1	2 (15.4)	11 (84.6)	13	
Total	=1	25 (53.2)	22 (46.8)	47	0.003
	>1	8 (21.1)	30 (78.9)	38	

Abbreviations: GUIs, grades of US images; LOE, length of extravasation. Notes: Numbers are expressed as n (%).

of mild renal trauma [19]; however, surgical wounds are much more stable because of suture ligation. The present guidelines and classifications consider renal trauma according to the hemodynamic status and anatomic grading of the injury, which mainly involves laceration of the capsule and parenchyma [20]. Therefore, we evaluated the severity of renal wounds by grading the capsule and parenchyma based on conventional US images. Some normal renal units surrounding the tumor are resected during PN, leading to increased wound instability and different degrees of morphologic changes in the kidney. Therefore, we added morphologic changes to the grading scale as supplementary information for severity. Our grading system mainly considered the anatomic features of the wound and showed a close correlation with factors that affect wound healing.

Regarding the preoperative and intraoperative variables, the N component of the R.E.N.A.L. score and the resection range were significant factors related to the UIG. The N component can objectively reflect the depth of the tumor before surgery. Standard excision included strategic sharp dissection through normal parenchyma and removal of a 5-mm rim of healthy tissue along with the tumor. In recent years, laparoscopic aspiration for angiomyolipoma and tumor enucleation have been applied to increase nephron preservation, which may contribute to the recovery of renal function after PN [21, 22]. However, in our study, expanded excision was performed on some patients with N scores of 3 points to guarantee negative surgical margins, which was subject to the personal discretion of the surgeon. This classification system based on US images was feasible, objective, and repeatable for evaluation of the range and severity of kidney wounds, which were affected both objectively by the preoperative tumor depth and subjectively by the intraoperative resection range. Moreover, a higher UIG resulted in a greater decrease in Hb (%) on the first day after surgery, a higher extravasation rate, and a longer LOE, which indicated a longer healing time [23].

CEUS can obtain findings not accessible by conventional US imaging, such as tissue hypoperfusion, nonperfusion, hyperemia, and contrast extravasation. Many studies have reported that CEUS can detect active bleeding in abdominal trauma [10, 11]. Moreover, contrast extravasation from the injury site of the kidney has been observed in animal experiments [24]. Closure of the renal remnant during surgery, often called renorrhaphy, is a critical step to avoid bleeding complications [6]. Therefore, a spring-like extravasation representing active hemorrhage might seem unlikely in our cases. However, low-velocity extravasation was detected as a drip or as band-like isoechoic spots bubbling up through the capsule during the cortical to medullary phase, which resulted from incomplete closure of the microvasculature after PN. Although we did not have sufficient clinical or physiopathologic evidence to conclude that these features represented mild active bleeding, we consider them to indicate inferior wound closure because patients with a high UIG had higher extravasation rates (more than 1 day) and a longer LOE. The presence of extravasation resulted in a higher complication rate according to our findings. This trend matched the UIG, especially for grades 2 and 3. However, for grade 1 patients, whom we expected to have a good prognosis of the wound, those with extravasation also had higher complication rates. This might indicate that slight morphologic changes do not necessarily indicate better wound closure. Therefore, extravasation might be an individual factor in wound healing.

Nevertheless, contrast extravasation still needs to be verified as a repeatable method for examining postoperative patients because extravasation is much less obvious than that in organic trauma as described in the literature. During dynamic scanning, mild extravasation can easily be ignored or confused with low perfusion of the surrounding tissue. Therefore, this factor was not added to the UIG but was regarded as a complementary sign of insufficient wound closure in our study.

There are some limitations to our study. Postoperative subcutaneous emphysema could impede the implementation of CEUS. Additionally, US image acquisition and interpretation are subject to the examiner, and the small sample size of our study may increase the probability of type II errors. Further animal experiments and histologic verification are needed to determine whether the UIG is associated with the range and severity of renal wounds after surgery. Furthermore, other imaging examinations, such as CT, could be performed in the early postoperative stage to compare the sensitivity and specificity of renal wound evaluation with that of the US in follow-up studies.

Conclusions

The tumor depth and resection range were related to the UIG. Conventional US and CEUS were feasible and repeatable methods that reflect the morphologic changes in renal wounds after MIPN and may be useful to evaluate their severity.

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Written informed consent was obtained from the participants.

Disclosure of conflict of interest

None.

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References

[1] Capitanio U, Bensalah K, Bex A, Boorjian SA, Bray F, Coleman J, Gore JL, Sun M, Wood C and

Russo P. Epidemiology of renal cell carcinoma. Eur Urol 2019; 75: 74-84.

[2] Ljungberg B, Albiges L, Abu-Ghanem Y, Bedke J, Capitanio U, Dabestani S, Fernández-Pello S, Giles RH, Hofmann F, Hora M, Klatte T, Kuusk T, Lam TB, Marconi L, Powles T, Tahbaz R, Volpe A and Bex A. European Association of Urology guidelines on renal cell carcinoma: the 2022 update. Eur Urol 2022; 82: 399-410.

[3] Ghani KR, Sukumar S, Sammon JD, Rogers CG, Trinh QD and Menon M. Practice patterns and outcomes of open and minimally invasive partial nephrectomy since the introduction of robotic partial nephrectomy: results from the nationwide inpatient sample. J Urol 2014; 191: 907-912.

[4] Castilho TML, Lemos GC, Cha JD, Colombo JR, Claros OR, Lemos MB and Carneiro A. Transition from open partial nephrectomy directly to robotic surgery: experience of a single surgeon to achieve “TRIFECTA”. Int Braz J Urol 2020; 46: 814-821.

[5] Ficarra V, Rossanese M, Gnech M, Novara G and Mottrie A. Outcomes and limitations of laparoscopic and robotic partial nephrectomy. Curr Opin Urol 2014; 24: 441-447.

[6] Zhao PT, Richstone L and Kavoussi LR. Laparoscopic partial nephrectomy. Int J Surg 2016; 36: 548-553.

[7] Zanghi J, Boyer J, Martinez C, Patel A, Petit C, Siegert J and Nguyen T. Tensile force exerted by suture during renorrhaphy using current techniques. J Robot Surg 2020; 14: 383-386.

[8] Bertolo R, Campi R, Klatte T, Kriegmair MC, Mir MC, Ouzaid I, Salagierski M, Bhayani S, Gill I, Kaouk J and Capitanio U; Young Academic Urologists (YAU) Kidney Cancer working group of the European Urological Association (EAU). Suture techniques during laparoscopic and robot-assisted partial nephrectomy: a systematic review and quantitative synthesis of peri-operative outcomes. BJU Int 2019; 123: 923-946.

[9] Miele V, Piccolo CL, Galluzzo M, Ianniello S, Sessa B and Trinci M. Contrast-enhanced ultrasound (CEUS) in blunt abdominal trauma. Br J Radiol 2016; 89: 20150823.

[10] Trinci M, Piccolo CL, Ferrari R, Galluzzo M, Ianniello S and Miele V. Contrast-enhanced ultrasound (CEUS) in pediatric blunt abdominal trauma. J Ultrasound 2019; 22: 27-40.

[11] Feng C, Wang L, Huang S, Wang L, Zhou X, Cui X, Chen L, Lv F and Li T. Application of contrast-enhanced real-time 3-dimensional ultrasound in solid abdominal organ trauma. J Ultrasound Med 2020; 39: 869-874.

[12] Lv F, Tang J, Luo Y, Li Z, Meng X, Zhu Z and Li T. Contrast-enhanced ultrasound imaging of active bleeding associated with hepatic and splenic trauma. Radiol Med 2011; 116: 1076-1082.

[13] Rosenblatt GS and Fuchs GJ. A comparison of running suture versus figure-8 sutures as the initial step in achieving hemostasis during laparoscopic partial nephrectomy. J Endourol 2010; 24: 421-424.

[14] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC and Vandenbroucke JP; STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007; 147: 573-577.

[15] Dagenais J, Maurice MJ, Mouracade P, Kara O, Malkoc E and Kaouk JH. Excisional precision matters: understanding the Influence of excisional volume loss on renal function after partial nephrectomy. Eur Urol 2017; 72: 168-170.

[16] Hennessey DB, Wei G, Moon D, Kinnear N, Bolton DM, Lawrentschuk N and Chan YK. Strategies for success: a multi-institutional study on robot-assisted partial nephrectomy for complex renal lesions. BJU Int 2018; 121 Suppl 3: 40-47.

[17] Chang KD, Abdel Raheem A, Kim KH, Oh CK, Park SY, Kim YS, Ham WS, Han WK, Choi YD, Chung BH and Rha KH. Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years’ follow-up. BJU Int 2018; 122: 618-626.

[18] Choi JE, You JH, Kim DK, Rha KH and Lee SH. Comparison of perioperative outcomes between robotic and laparoscopic partial nephrectomy: a systematic review and meta-analysis. Eur Urol 2015; 67: 891-901.

[19] Huber J, Pahernik S, Hallscheidt P, Sommer CM, Hatiboglu G, Haferkamp A and Hohenfellner M. Risk factors and clinical management of haemorrhage after open nephron-sparing surgery. BJU Int 2010; 106: 1488-1493

[20] Kozar RA, Crandall M, Shanmuganathan K, Zarzaur BL, Coburn M, Cribari C, Kaups K, Schuster K and Tominaga GT; AAST Patient Assessment Committee. Organ injury scaling 2018 update: spleen, liver, and kidney. J Trauma Acute Care Surg 2018; 85: 1119-1122.

[21] Xu B, Zhang Q and Jin J. Laparoscopic aspiration for central renal angiomyolipoma: a novel technique based on single-center initial experience. Urology 2013; 81: 313-318.

[22] Blackwell RH, Li B, Kozel Z, Zhang Z, Zhao J, Dong W, Capodice SE, Barton G, Shah A, Wetterlin JJ, Quek ML, Campbell SC and Gupta GN. Functional implications of renal tumor enucleation relative to standard partial nephrectomy. Urology 2017; 99: 162-168.

[23] Niu D, Li L, Du H, Shi H, Zhou J, Tai S, Xu H, Chen W, Yang C and Liang C. Application of contrast-enhanced ultrasonography (CEUS) in the assessment of kidney wound recovery after nephron-sparing surgery. Cancer Manag Res 2021; 13: 3925-3934.

[24] Xu RX, Li YK, Li T, Wang SS, Yuan GZ, Zhou QF, Zheng HR and Yan F. Real-time 3-dimensional contrast-enhanced ultrasound in detecting hemorrhage of blunt renal trauma. Am J Emerg Med 2013; 31: 1427-1431.