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ORIGINAL ARTICLE

Roughness of the renal tumor surface could predict the surgical difficulty of robot-assisted partial nephrectomy

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Abstract

Introduction: Preoperative prediction of surgical difficulty of partial nephrectomy (PN) is essential to minimize the perioperative complications and to achieve a good surgical outcome. Recently, various scoring systems have been used to evaluate the difficulty of PN including R.E.N.A.L (Radius, Exophytic/Endophytic, Nearness, Anterior/Posterior, Location) nephrometry score. There were no scoring systems evaluating the roughness of the renal tumor surface and we hypothesized that the roughness of the renal tumor surface might affect the surgical difficulty of robot-assisted partial nephrectomy (RAPN). This study aimed to evaluate the impact of roughness of the renal tumor surface on the surgical outcome of RAPN.

Methods: Overall, 161 patients underwent RAPN performed by the same surgeon between May 2016 and April 2019. We divided those tumors into two groups, like "roughness positive (tumor with roughness of tumor surface)" and "roughness negative (tumor without roughness of tumor surface)" according to the roughness of the endophytic region on preoperative computed tomography images. Clinical and pathological outcomes were compared between the two groups.

Results: Eighty-five and 78 tumors were identified roughness negative and positive, respectively. Cases with roughness positive showed a significantly longer operative time, console time, and ischemia time and had greater blood loss than those with roughness negative. Significant and independent predictors of ischemia time and estimated glomerular filtration rate (eGFR) decrease were roughness of tumor surface, tumor size (not for eGFR decrease), and *N* score of the R.E.N.A.L nephrometry score.

Conclusion: Roughness of renal tumor surface was significantly and positively associated with ischemia time and the eGFR decrease rate.

KEYWORDS

nephrometry score, renal tumor surface, robot assisted partial nephrectomy, roughness

1 | INTRODUCTION

Partial or radical nephrectomy is currently the standard treatment option for patients with localized renal cell carcinoma (RCC). A systematic review showed that partial nephrectomy (PN) and radical nephrectomy for T1a RCC helped patients achieve equivalent cancer-specific survival[1] and PN resulted in less overall and noncancer mortality than radical nephrectomy.[2]

Preoperative prediction of surgical difficulty of PN is essential to perform the surgery safely and reliably to avoid unnecessary perioperative complications and achieve a good surgical outcome. Recently, various scoring systems have been used to evaluate the difficulty of PN, in particular, the R.E.N.A.L (Radius, Exophytic/Endophytic, Nearness, Anterior/Posterior, Location) nephrometry score has been thoroughly validated and employed in clinical practice internationally.[3] This score is based on five anatomical features of renal tumors. Of the five components, four are scored on a 1-, 2-, or 3-point scale, with the fifth indicating the anterior or posterior location of the mass relative to the coronal plane of the kidney. In recent years, robotic surgery has been adapted to PN, and a systematic review and meta-analysis showed that robot-assisted partial nephrectomy (RAPN) is associated with more favorable results in terms of the conversion rate to open or radical surgery, ischemia time, change in the estimated glomerular filtration rate, and a shorter length of hospital stay than laparoscopic partial nephrectomy.[4]

An irregular shape of the renal tumor surface is found to be challenging in ensuring the absence of positive surgical margins so that tumor resection lines are wider than usual. Tumors without capsules also need additional management, as they easily migrate or lead to unintended incision of the tumor. However, the R.E.N.A.L nephrometry score could not evaluate the difficulty of PN for these tumors.

We hypothesized that the roughness of the renal tumor surface might affect the surgical difficulty of RAPN. To address our hypothesis, we evaluated the impact of roughness of renal tumor surface on surgical outcome of RAPN.

2 | MATERIALS AND METHODS

2.1 | Patients

One hundred and sixty-one patients with suspected RCC cT1a-bN0M0, who were admitted to our hospital, Yokohama City University Hospital—a territorial high-volume center for the treatment of RCC and with surgeons capable of performing RAPN even in highly complicated cases—between May 2016 and April 2019, underwent RAPN performed by the same surgeon. All patients underwent preoperative CTor MRI. According to our hospital's criteria for selecting the surgical method for RCC, the main indication for RAPN (both retroperitoneal and transperitoneal approaches) is RCC cT1N0M0. The choice of approach is based on the tumor location. The retroperitoneal approach was chosen for tumors located on the posterior or lateral side of the kidney, while the transperitoneal approach was chosen for all other tumors. In our institution, all pathological examinations were conducted and final diagnoses were determined by expert pathologists (more than 10 years of experience) on the basis of the valid WHO classification at the time of diagnosis.

2.1.1 | Roughness of the renal tumor surface

We divided renal tumors into two groups according to the roughness of the endophytic region on preoperative contrast-enhanced CT or MRI (in case of patients not eligible for contrast-enhanced CT) images as below (Figure 1). We used both axial and coronal views of images without any autonomic decision-making imaging tools. In this study, one urologist (T.T.) judged the roughness of tumor surface only with his eye, since we aimed to develop new parameters easy for physicians to score in clinics without any specific imaging calculation modalities.

Roughness positive: Renal tumor with roughness of tumor surface showing irregular (not round) shape of endophytic region with/without a tumor capsule. Roughness negative: Renal tumor without roughness of tumor surface showing round shape of endophytic region with a clear tumor capsule.

2.2 | Surgical techniques

All procedures were performed using the da Vinci Surgical System.[5] RAPN was performed using four da Vinci arms and one or two assistant ports. Basically, we clamped the main renal arteries as per the arterial clamping technique. In cases where the tumor was near the hilum of the kidney, we clamped the renal vein. We used an ultrasound probe to determine the excision margins. Tumor excision was performed with scissors, and thick vessels encountered during resection were coagulated using a sealing device. Enucleation was not adopted, and partial nephrectomy with a small margin was used as the regular resection method. In places where the tumor was in contact with the renal sinus, an excision line close to enucleation was selected. After tumor resection, an inner running suture was placed to close large vessels and a collecting system at the tumor base using 3-0 verb sutures. Renal parenchymal suturing

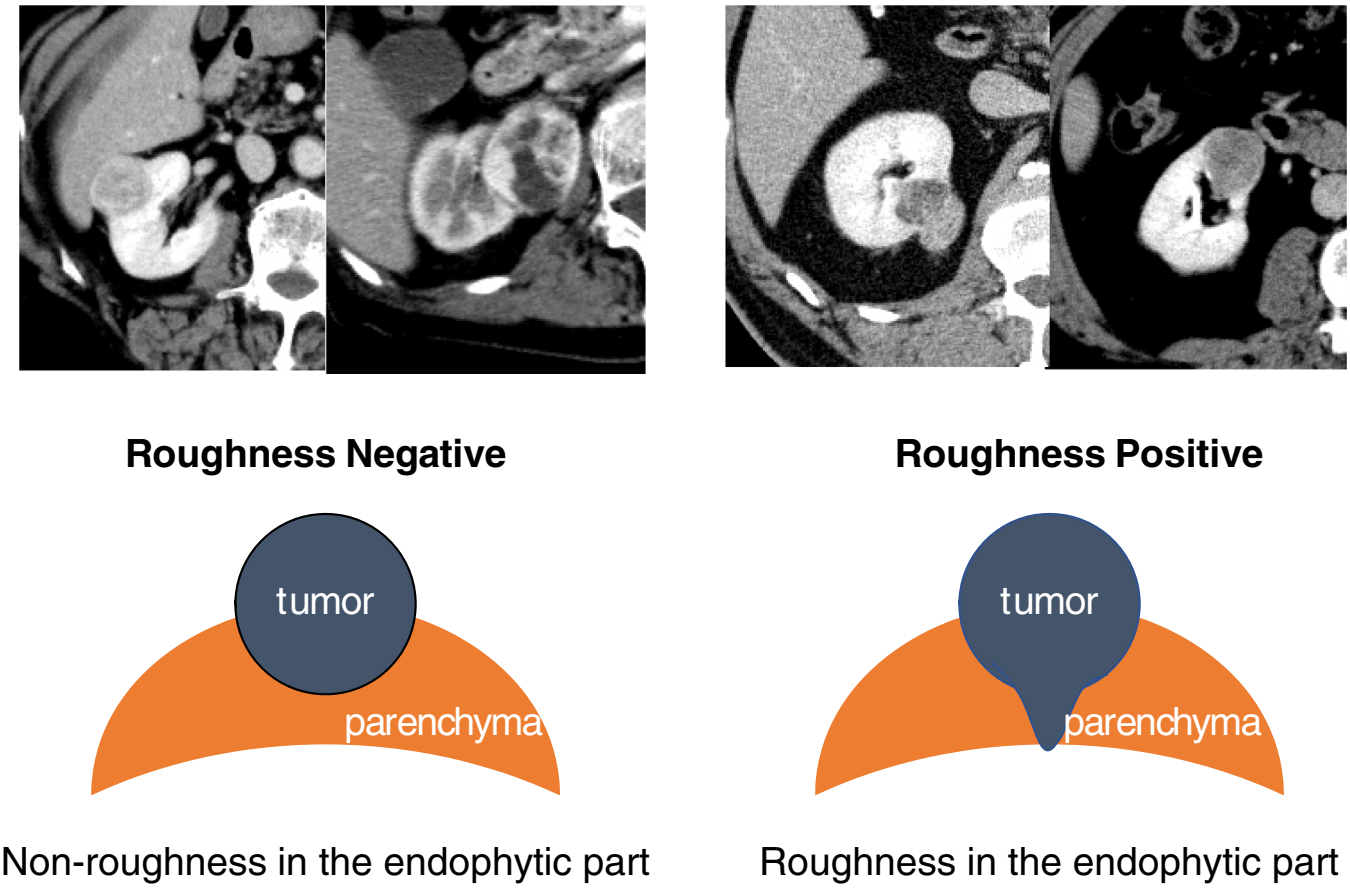

FIGURE 1 Example of roughness negative and roughness positive

was performed using 0-verb sutures. An early unclamping technique was adopted depending on individual cases, such as the case that the ischemia time became long or a need to confirm bleeding.

2.3 | Clinical parameters

The clinical factors analyzed in this study included the roughness to tumor surface, sex, operative time, maximum tumor diameter, robotic approach (retroperitoneal or transperitoneal), R.E.N.A.L nephrometry score, blood loss, weight of the specimen, and postoperative pathological findings including the histologic subtypes. The roughness to tumor surface, R.E.N.A.L nephrometry score, and tumor diameter were measured by a urologist using preoperative CT scans.

2.4 | Interobserver reliability of the decision for roughness status of renal tumor surface

Three urologists scored the same 30 images of the renal tumor in a blinded manner, even without knowing any perioperative outcomes, and evaluated the reproducibility of decision-making for roughness status.

2.5 | Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences, v. 23 (SPSS, IBM, Armonk, NY, USA.). Single-factor analysis of variance and the Kruskal–Wallis test were used to assess the difference in patient characteristics, perioperative outcomes, and pathological outcomes between the two groups with roughness positive and negative. Logistic regression analysis was used as the multivariate analysis to identify the independent factors of surgical difficulty; $p < 0.05$ was considered significant.

3 | RESULTS

Among the 161 patients who participated in the study, the median age was 67 years, 71% were men, and the average tumor size was 29 mm; 123 of 163 cases (78.3%)

were of pT1a and the remaining 38 (21.7%) were of pT1b and pT3a.

Eighty-five and 78 tumors were divided into "roughness negative" and "roughness positive," respectively. Table 1 shows a comparison of patient characteristics between roughness positive and negative. Patients with tumors with roughness positive had larger tumor diameters and higher R.E.N.A.L nephrometry scores than those with tumors with roughness negative ($p < 0.001$). Table 2 shows the perioperative outcomes divided by roughness of renal tumor surface. Patients with tumors with roughness positive had longer operative times ($p = 0.040$), console times ($p = 0.030$), and ischemia times ($p < 0.001$) and greater blood loss ($p = 0.010$) than those with tumors with roughness negative. However, there was no significant difference in intraoperative transfusion and complications between the two groups. The eGFR reduction rate 1 mo after surgery was significantly higher for patients with tumors with roughness positive ($p = 0.009$) than those with roughness negative. Table 3 shows the pathological outcomes with respect to roughness of the tumor surface. There was no significant difference in the rate of positive surgical margin, pathological stage, or histological type between each of the groups.

In multivariate analysis, the significant and independent predictors of ischemia time during surgery were the roughness of tumor surface ($p = 0.008$), tumor size ($p < 0.001$), and N ($p = 0.03$) scores of the R.E.N.A.L nephrometry score. Meanwhile, the significant and independent predictors of eGFR decrease rates at 1 mo after surgery were the roughness of tumor surface ($p = 0.023$) and N ($p = 0.02$) scores of the R.E.N.A.L nephrometry score. (Table 4). Additionally, the roughness of tumor surface was the independent predictor of ischemia time and eGFR decrease rate even for tumors larger than 3 cm (Table 5). However, only the tumor size ($p < 0.001$) was an independent predictor of both the total operation time and console time of RAPN (data not shown). The assessment of reproducibility for judging of the roughness of renal tumor surface among three urologists showed the concordance rate was 77.8%.

TABLE 1 Patients' characteristics in tumors with roughness negative and positive

	Roughness negative83 patients85 tumors	Roughness positive78 patients78 tumors	*p* value
Age, years	65	65	0.88
Sex			0.87
Female	23 (27.7%)	23 (29.5%)	
Male	60 (72.3%)	55 (70.5%)	
BMI	24.7	24.9	0.65
Laterality			0.58
Left	39 (45.9%)	40 (51.3%)	
Right	46 (54.1%)	38 (48.7%)	
Clinical tumor size, mm	22	35	<0.001
Approach			0.79
Retroperitoneal	39 (47.0%)	34 (51.6%)	
Transperitoneal	44 (53.0%)	44 (48.4%)	
Preoperative eGFR, ml/min	68.5	65.7	0.38
R.E.N.A.L score	7	8	<0.001
Observation period, mo	7.9	6.6	0.52

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate.

TABLE 2 Surgical outcome in tumors with roughness negative and positive

	Roughness negative	Roughness positive	*p* value
Operative time, min	166	181	0.04
Console time, min	103	123	0.03
Ischemia time, min	16.5	23.2	<0.001
Blood loss, ml	20.5	73.4	0.01
Intraoperative transfusion	1 For nephrogenic anemia	2 For nephrogenic anemia	0.55
Complication	2 1: Postoperative hemorrhage Grade II 1: Chylorrhea GradeII	2 2: Postoperative hemorrhage Grade I	0.98
eGFR decrease rate, %	6.7	12.7	0.009

Abbreviation: eGFR, estimated glomerular filtration rate.

TABLE 3 Pathological findings of tumors with roughness negative and positive

	Roughness negative	Roughness positive	*p* value
Surgical margin			0.60
R0	76 (89.4%)	71 (91.0%)	
R1	2 (2.4%)	3 (3.8%)	
Difficult to evaluate	2 (2.4%)	2 (2.6%)	
No description	5 (5.9%)	2 (2.6%)	
Pseudocapsule			0.69
(+)	55 (64.7%)	57 (73.1%)	
(−)	14 (16.5%)	17 (21.8)	
No description	16 (18.8%)	4 (5.1%)	
Pathological stage			0.008
pT1a	66 (93.0%)	57 (73.1%)	
pT1b	3 (4.2%)	15 (19.2%)	
pT3a	2 (2.8%)	3 (3.8%)	
Histological type			0.007
Malignancy	71 (83.5%)	75 (96.2%)	
Clear	58	62	
Papillary	3	4	
Chromophobe	3	5	
Others	7	4	
Benign	14 (16.5%)	3 (3.8%)	

TABLE 4 Multivariate analysis of ischemia time (A) and of eGFR decrease rate at 1 mo after surgery (B)

			95% CI	
(A)	**HR**	***p* value**	**Lower**	**Upper**
(Constant)	0.05	<0.001	0.01	0.28
Roughness of tumor surface	3.06	0.008	1.34	6.98
Tumor size (<28 mm/28 mm≤)	6.23	<0.001	2.53	15.4
E score	0.85	0.820	0.19	3.63
N score	6.10	0.030	1.09	34.1
			95% CI	
(B)	**HR**	***p* value**	**Lower**	**Upper**
(Constant)	0.29	0.021	0.10	0.83
Roughness of tumor surface	2.34	0.023	1.12	4.87
Tumor size (<28 mm/28 mm≤)	1.19	0.670	0.52	2.66
E score	1.42	0.590	0.38	5.21
N score	4.39	0.020	1.22	15.8

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

4 | DISCUSSION

An irregular renal tumor surface and tumors with incomplete capsule often need additional attention from the surgeon to avoid tumor incision and positive surgical margin during PN. Our clinical impression was that the shape and texture of the renal tumor surface might contribute to surgical difficulty and the surgical outcome of PN. Various scoring systems, including the R.E.N.A.L nephrometry score, PUDUA classification, C-index scoring system, and contact surface area have been used to predict the surgical complexity and outcomes for renal

TABLE 5 Multivariate analysis of ischemia time for tumors over 3 cm (A) and of eGFR decrease rate for tumors over 3 cm (B)

			95% CI	
(A)	**HR**	***p* value**	**Lower**	**Upper**
(Constant)	0.012	0.042	<0.001	0.852
Roughness of tumor surface	2.36	0.004	1.31	4.24
E score	2.09	0.115	0.83	5.24
N score	1.59	0.524	0.38	6.66
			95% CI	
(B)	**HR**	***p* value**	**Lower**	**Upper**
(Constant)	0.391	0.561	0.016	9.30
Roughness of tumor surface	3.09	0.027	1.14	8.42
E score	0.93	0.874	0.39	2.20
N score	1.34	0.588	0.46	3.89

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

tumors[6–9]; however, none of them score the renal tumor smoothness or the shape. In this study, roughness of renal tumor surface was significantly associated with ischemia time and eGFR decrease rate, indicating that an irregular tumor surface required the surgeon to perform PN more cautiously and, subsequently, more time was required for tumor resection.

However, the roughness of the tumor surface did not influence the total surgical and console time, suggesting that an irregular tumor surface status contributed only to a longer tumor resection time and had less effect on the overall surgical procedure time. Further studies will be needed to confirm that roughness of renal tumor surface can truly predict surgical difficulty. Borgmann et al. demonstrated that the R.E.N.A.L nephrometry score, among the C-index scoring system, PADUA classification, and diameter-axial-polar (DAP), correlated best with trifecta achievement and quantitative perioperative outcomes of nephron-sparing surgery.[10] In this study multivariate analysis showed that roughness of the tumor surface was an independent factor to predict surgical difficulty in a way different from that of R.E.N.A.L nephrometry scoring. We consider that we can predict surgical difficulty more accurately by adding tumor surface information to the R.E.N.A.L nephrometry scoring.

Ficarra et al. reported that surgeons' experience, clinical tumor size, upper collecting system repair, and anatomical tumor characteristics according to the PADUA classification score predicted ischemia time >20 min in multivariate analyses.[11] It was also reported that the total R.E.N.A.L nephrometry score, as well as the *N* and *R* scores, can help predict longer ischemia times during RAPN.[12] Similar to *N* and *R* scores of the R.E.N.A.L nephrometry score and the tumor size, the roughness of the tumor surface was an independent predictor of ischemic time in this study. The roughness tended to be more positive as the tumor was larger. However, the roughness of the tumor surface was an independent factor of ischemia time and resection time even for large tumors (3 cm<), as well as for any size of the tumor. These results suggested that information of tumor surface was useful regardless of tumor size.

Miyake et al. reported that the total R.E.N.A.L nephrometry score was shown to be significantly correlated with changes in eGFR at 1 and 4 weeks after RAPN, but each component of the R.E.N.A.L nephrometry score alone had no significant impact on postoperative changes in eGFR at 1 and 4 weeks after RAPN.[13] However, the roughness of the tumor surface was the significant and independent predictors of eGFR decrease rate at 1 mo after surgery in this study, which might reflect the result that the same parameter was the independent predictor of ischemia time. Furthermore, the residual parenchymal volume also correlates with postoperative eGFR. Ginzburg et al. reported that residual functional parenchymal volume was the predictor of ultimate renal function following PN.[14] When we resected the tumor with an irregularly shaped surface, extensive resection was required to obtain a negative margin. Compared to the tumor with no roughness, the residual parenchymal volume will be lost.

Roughness of tumor surface was not associated with the rate of positive surgical margins, intraoperative transfusion, or complications, indicating that the tumor surface status might not affect the surgical outcome if the surgeon is experienced. However, this study included only a single surgeon who was well experienced in RAPN, having operated on more than 150 patients, and it was quite possible that his extensive surgical skill could avoid positive surgical margins during RAPN for

complicated surfaced tumors after identifying a proper incision line. Previous reports have shown that surgical experience was significantly associated with a shorter ischemia time in RAPN along with the tumor size and R.E.N.A.L nephrometry score.[15] Meanwhile, evaluation of ischemia time of RAPN indicated that the learning curve for RAPN was 30–150 cases.[15,16] Thus, it is possibly not enough for inexperienced surgeons (<30–150 cases of RAPN) to maintain the required surgical quality in RAPN with tumors with an irregular surface.

Reproducibility of R.E.N.A.L nephrometry scoring made by the radiologists and by the urologists were not consistent, especially in terms of the tumor location.[17] Meanwhile, we believed that roughness of the tumor surface was a simple and easy parameter for physicians to determine consistently. In fact, roughness of the tumor surface showed high reproducibility (77.8%) and we believed that it was acceptable compared with those of R.E.N.A.L nephrometry scoring (50%–93.3%).[17,18] However, there is still the necessity to investigate the reproducibility of those scores among multiple observers in the future.

There are some limitations to this study. This study was a retrospective single-center and single-surgeon experience with a relatively small number of patients. We believe that the analysis of a single surgeon's experience avoided surgeons' skill bias and enabled us to focus on the efficacy of smoothness scoring. Another limitation was the short-term analysis. Long-term oncological outcome and kidney functional outcome should be evaluated in future research. Finally, we need to conduct a prospective study evaluating PN performed by multiple surgeons to determine whether it is as accurate and effective as universal nephrometry scoring.

In conclusion, the roughness of the renal tumor surface was significantly and positively associated with ischemia time and a postoperative eGFR degrease rate at 1 mo after RAPN.

CONFLICT OF INTEREST

The authors do not have any conflicts of interest.

AUTHOR CONTRIBUTIONS

Tomoyuki Tatenuma, Hiroki Ito, and Kazuhide Makiyama designed this study. Tomoyuki Tatenuma and Hiroki Ito wrote the article and performed the statistical analyses. Kazuhide Makiyama supervised the study. All authors have read and approved the final article.

ETHICAL CONSIDERATIONS

The Ethics Committee of Yokohama City University Hospital approved this study (B200500010). This study was a retrospective study, and we applied the Opt-out method to obtain consent for this study.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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