

Factors Predicting Adhesion between Renal Capsule and Perinephric Adipose Tissue in Partial Nephrectomy

Yasuyuki Kobayashi*, Hiroaki Kurahashi, Yuko Matsumoto, Koichiro Wada, Katsumi Sasaki, Motoo Araki, Shin Ebara, Toyohiko Watanabe, and Yasutomo Nasu

*Department of Urology, Okayama University Graduate School of Medicine,
Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan*

In minimally invasive partial nephrectomy (MIPN), it is important to preoperatively predict the degree of difficulty of tumor resection. When severe adhesions occur between the renal capsule and perinephric adipose tissue, detachment can be difficult. Preoperative prediction of adhesion is thought to be useful in the selection of surgical procedure. Subjects were 63 patients of a single surgeon who had received MIPN between April 2008 and August 2013 at Okayama University Hospital. Of these patients, this study followed 47 in whom the presence or absence of adhesions between the renal capsule and perinephric adipose tissue was confirmed using intraoperative videos. Data collected included: sex, BMI, CT finding (presence of fibroids in perinephric adipose tissue), comorbidities and lifestyle. Adhesion was observed in 7 patients (14.9%). The mean operative time was 291.6min in the adhesion group, and 226.3min in the group without. The increased time in the adhesions group was significant ($p < 0.05$). Predictive factors were a positive CT finding for fibroid structure and comorbidity of hypertension ($p < 0.05$). In MIPN, difficulty of surgery can be affected by the presence of adhesion of the perinephric adipose tissue. Predicting such adhesion from preoperative CT is thus important.

Key words: renal cell carcinoma, partial nephrectomy, renal capsule, adhesion

Laparoscopic surgery has become more prevalent in recent years, and minimally invasive partial nephrectomy (MIPN) has become widely used for small renal cell carcinoma. Purely laparoscopic partial nephrectomy (LPN) has a lower degree of freedom of forceps movement compared with robot-assisted laparoscopic partial nephrectomy (RALPN). Thus, LPN is technically more difficult and tends to have a longer warm ischemic time [1–3]. Consequently, LPN is a procedure that creates stress for surgeons. For successful LPN, proper patient selection is necessary

based on the surgeon's skills, and there have been efforts to preoperatively predict the difficulty of tumor resection. In recent years, there has been wide use of the preoperative aspects and dimensions used for anatomic (PADUA) classification and Renal nephrometry scores based on the criteria of tumor localization [3–11]. Some patients have strong adhesions of the renal capsule to the perinephric adipose tissue regardless of tumor localization. In such patients, it is difficult to detach the adipose tissue from the renal capsule. Consequently, it is difficult to create an appropriate environment for tumor resection, includ-

Received May 28, 2015; accepted November 12, 2015.

*Corresponding author. Phone: +81-86-235-7287; Fax: +81-86-231-3986
E-mail: kobayasu@md.okayama-u.ac.jp (Y. Kobayashi)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

ing tumor identification, determination of resection line, and mobilization of the kidney. The presence of the adhesions affects the quality of the laparoscopic surgery, where forceps manipulation is more limited than in laparotomy. If the presence of the adhesions could be predicted from preoperative factors, such information would be useful in the selection of surgical procedure. The incidence of adhesion is empirically thought to be high in patients with a high BMI or a large amount of perinephric adipose tissue. However, patients with a large amount of fat do not necessarily have adhesions.

Materials and Methods

Sixty-three Japanese patients at Okayama University Hospital had undergone MIPN from the same surgeon for renal carcinoma between April 2008 and August 2013. Intraoperative video recordings were retrospectively analyzed. In 47 of these patients, the presence or absence of adhesion could be confirmed between the renal capsule and perinephric adipose tissue; these 47 were thus selected as the subjects of this study (42 patients with LPN and 5 patients with RALPN). Table 1 lists the characteristics of patients. In all patients, the diagnosis of renal carcinoma was made based on preoperative CT images. Adhesions between the renal capsule and perinephric adipose tissue were defined as being present if the following 3 criteria were satisfied based on intraoperative video recordings: (1) the renal capsule and perinephric adipose tissue were strongly adhered to each other; (2) the perinephric adipose tissue could not be detached en bloc (but in pieces and torn) due to adhesions; and (3) adhesions were observed throughout the area of detachment and not only in some parts of the perinephric areas.

The following factors were examined regarding their association with the presence or absence of adhesion between the renal capsule and perinephric

adipose tissue: sex, BMI (less than 25 kg/m² vs. 25 kg/m² or more), tumor size (less than 2 cm vs. 2 cm or more), CT finding (presence or absence of fibroid structure in perinephric adipose tissue), comorbidities (with or without treatment for hypertension and diabetes), and lifestyle (with or without a history of smoking and alcohol intake). A “fibroid structure in the perinephric adipose tissue (FSPA) on CT” was defined as a structure that, on plain CT, appeared membranous in the perinephric adipose tissue (fat between the Gerota’s fascia and renal capsule) of the affected kidney (Fig. 1). Statistical analysis was performed using JMP 10, and the level of significance was set at 0.05. The Okayama University Hospital Institutional review board and an ethics committee review board study approved this study (No. 862).

Results

Five patients (10.6%) had FSPA on CT. Meanwhile, 12 patients (25.5%) had hypertension, 10 patients (21.3%) had diabetes, 23 patients (48.9%) had a history of smoking, and 24 patients (51.1%) had a history of alcohol intake (Table 2). The mean operative time was 236.0 min (SD: 78.7 min), and the mean ischemic time was 25.9 min (SD: 10.9 min). Mean blood loss was 115.3 ml (SD: 142.5 ml). There were 7 patients (14.9%) with adhesions between the renal capsule and perinephric adipose tissue. Mean operative time was 193.6 and 262.4 min for tumors of less than 2 cm and those of 2 cm or more, respectively ($p < 0.05$); mean time was 291.6 and 226.3 min for patients with adhesion and those without ($p < 0.05$); and 275.4 and 222.5 min for patients with comorbidity (hypertension) and those without ($p < 0.05$). The factors that significantly prolonged operative time were tumor size of 2 cm or more, the presence of adhesion, and hypertension. Sex and BMI did not affect operative time (Table 2). Blood loss was not affected by any factor. The mean ischemic time was 19.5 and 29.1 min

Table 1 Patient characteristics

	Age (years old)	Sex	Body mass index (kg/m ²)	Tumor size (cm)	Renal nephrometry score
Median	62	Male: 37	23.5	2.2	6
(range)	(34–79)	Female: 10	(19.4–30.9)	(0.9–5.1)	(4–10)

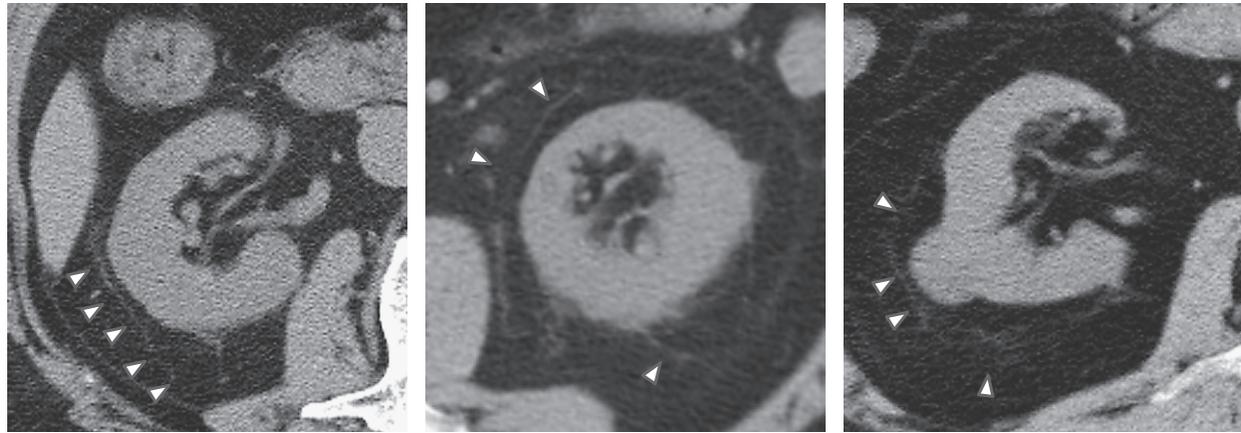


Fig. 1 Definition of fibroid structure in perinephric adipose tissue on CT: membrane-like fibrous structure in fat between the renal capsule and Gerota's fascia. The structure is indicated by the arrow. Δ FSPA on CT: fibroid structure in the perinephric adipose tissue.

Table 2 Perioperative outcomes and factors

	No Pts. (%)	Operative time Mean \pm SD (min)	<i>P</i>	Estimated blood loss Mean \pm SD (ml)	<i>P</i>	Warm ischemic time Mean \pm SD (min)	<i>P</i>
Sex							
Male	37 (78.7)	243.6 \pm 12.9	0.21	116.5 \pm 23.7	0.92	25.6 \pm 1.74	0.81
Female	10 (21.2)	208.0 \pm 24.7		111.0 \pm 45.6		24.7 \pm 3.36	
Body mass index							
Less than 25kg/m ²	30 (63.8)	222.2 \pm 14.1	0.11	105.3 \pm 26.2	0.53	24.9 \pm 1.93	0.63
25 kg/m ² or greater	17 (36.2)	260.5 \pm 18.7		132.9 \pm 34.8		26.4 \pm 2.57	
Tumor size							
Less than 2cm	18 (38.3)	193.6 \pm 16.9	<0.05	81.7 \pm 33.4	0.21	19.5 \pm 2.2	<0.05
2cm or greater	29 (61.7)	262.4 \pm 13.3		136.2 \pm 26.3		29.1 \pm 1.76	
Presence of adhesion							
Yes	7 (14.9)	291.6 \pm 28.7	<0.05	78.6 \pm 54.1	0.47	25.9 \pm 4.0	0.91
No	40 (85.1)	226.3 \pm 12.0		121.8 \pm 22.6		25.4 \pm 1.68	
Hypertension							
Yes	12 (25.5)	275.4 \pm 21.9	<0.05	106.7 \pm 41.5	0.81	28.8 \pm 3.0	0.20
No	35 (74.5)	222.5 \pm 12.9		118.3 \pm 24.3		24.3 \pm 20.7	
Diabetes mellitus							
Yes	10 (21.3)	249.7 \pm 25.1	0.54	107.0 \pm 45.5	0.83	27.2 \pm 3.3	0.55
No	37 (78.7)	232.4 \pm 13.0		117.6 \pm 23.7		24.9 \pm 1.74	
Smoking							
Yes	23 (48.9)	231.8 \pm 16.6	0.72	109.1 \pm 48.7	0.77	25.7 \pm 2.2	0.82
No	24 (51.1)	240.1 \pm 16.2		121.3 \pm 62.1		25.1 \pm 2.2	
Alcohol intake							
Yes	24 (51.1)	242.7 \pm 16.2	0.56	105.4 \pm 29.3	0.63	28.8 \pm 2.0	<0.05
No	23 (48.9)	229.1 \pm 16.5		125.7 \pm 30.0		21.9 \pm 2.1	

t-test

for tumors of less than 2cm and tumors of 2cm or more, respectively ($p < 0.05$), and 28.8 and 21.9min for patients with a history of alcohol intake and those without ($p < 0.05$).

When we examined the relationship between the factors and the presence of adhesion, there were a significantly higher number of patients with adhesions in the group with a positive CT finding (presence of fibroid structure in perinephric adipose tissue) ($p < 0.05$), as well as in the group with comorbidity (hypertension) ($p < 0.05$). However, there was no relationship between the presence of adhesion and sex, BMI, tumor size, diabetes, history of smoking, or history of alcohol intake (Table 3). The sensitivity and specificity was 71.4% (5/7) and 100% (40/40), respectively, for diagnosis of the presence of adhesion based on a positive CT finding (presence of fibroid

structure in perinephric adipose tissue).

Discussion

Tumor localization and various patient factors have been reported as features that affect the perioperative outcome of partial nephrectomy. Forceps manipulation is limited in MIPN, and it is very important to preoperatively examine these factors in order to assess the degree of surgical difficulty. In recent years, PADUA scores and RENAL nephrometry scores have been used widely for assessment of surgical difficulty based on tumor localization, and their usefulness has been reported [3–11].

In clinical settings, the use of BMI has been prevalent as an obesity index, and BMI has been reported to be a patient factor that affects the periop-

Table 3 Examination of presence of adhesion between the renal capsule and perinephric adipose tissue by factor

Factor	No Pts.	Presence of adhesion No Pts.	<i>P</i> value
Sex			
Male	37	7	0.13
Female	10	0	
Body mass index			
Less than 25kg/m ²	30	3	0.21
25kg/m ² or more	17	4	
Tumor size			
Less than 2cm	18	2	0.56
2cm or more	29	5	
FSPA* on CT			
Yes	5	5	<0.05
No	42	2	
Hypertension			
Yes	12	5	<0.05
No	35	2	
Diabetes mellitus			
Yes	10	3	0.13
No	37	4	
Smoking			
Yes	23	4	0.63
No	24	3	
Alcohol intake			
Yes	24	5	0.24
No	23	2	

FSPA: fibroid structure in the perinephric adipose tissue

Fisher exact test

erative outcome of MIPN. However, BMI was not found to be an important factor affecting perioperative outcome in our study. This might have been because median BMI in our study (23.5 kg/m^2) was lower than in other reports. Eaton *et al.* [12] examined 125 patients who had undergone LPN. They reported that there was a significant relationship between EBL (estimated blood loss) and increased BMI, but that no significant differences were observed with regard to operative time, transfusion rate, complication, or surgical margin status. Isac *et al.* [13] examined the perioperative outcome of robotic partial nephrectomy. They categorized patients based on BMI, and reported a significant association between increased BMI and higher EBL. Increased BMI was also associated with longer operation duration. Kiziloz *et al.* [14] examined 283 patients who had undergone robotic partial nephrectomy. They found that there was a statistically significant difference in EBL, operative time, and length of stay between patients with normal weight and overweight. One cannot rule out BMI as a useful factor in preoperatively predicting the difficulty of partial nephrectomy. However, in reality, there are often patients for whom surgical difficulty is not directly related to BMI. That is, intraoperative manipulation is not difficult even in some patients with high BMI if patients with severely high BMI levels are excluded. In addition, intraoperative manipulation is difficult in some patients without high BMI. Gorin *et al.* [15] reported that BMI has not been uniformly shown to be associated with complications of MIPN. They focused their study on intra-abdominal fat (IAF), outer-abdominal fat (OAF), and BMI, and reported that IAF was independently associated with the risk of complications following minimally invasive partial nephrectomy. Macleod *et al.* [16] examined 53 patients who had undergone RAPN and reported that perinephric fat thickness was associated with increased EBL and operative time during RAPN, independent of BMI and nephrometry.

In partial nephrectomy, a special process is necessary that is different from radical nephrectomy. This process involves detachment and removal of perinephric adipose tissue from the renal capsule as a preliminary step before tumor identification and resection. Thus, the finding that perinephric fat thickness affects perioperative outcome is thought to be consistent with the importance of this process. When removing peri-

nephric fat tissue, the amount of such fat tissue can become problematic. In addition, the presence of severe adhesion between the renal capsule and perinephric fat tissue is a very important factor. In LPN where forceps manipulation is limited, identification of tumor location is difficult in patients with severe adhesions. There is also a risk of injury to the renal and tumor capsules. Thus, this process creates stress for surgeons.

In our study, it was speculated these were the reasons why patients with adhesions had a significantly longer operative time. The method that uses preoperative plain CT to determine the presence or absence of fibroid structure in perinephric fat tissue is a very simple method. When the presence of a fibroid structure was determined by this method, it predicted the presence of adhesion at high sensitivity (71.4%) and specificity (100%). If the presence of adhesion can be predicted preoperatively using this method, then the information can be combined with tumor location to select the appropriate surgical procedure. For example, a surgeon can select laparoscopic partial nephrectomy instead of the laparoscopic procedure, or select RAPN with more freedom of forceps manipulation instead of LPN.

What is the fibroid structure in the perinephric adipose tissue on CT? In obese patients, immunocompetent cells, mainly macrophages, infiltrate obese adipose tissue. Dysregulation of adipocytokine production occurs, dysfunction of adipose tissue is induced, and inflammation of adipose tissue develops [17, 18]. This inflammation is considered chronic non-infectious inflammation that occurs without pathogen infection and results in hypersecretion of various inflammatory cytokines. In this study, patients with hypertension tended to have adhesion between the renal capsule and perinephric adipose tissue. Considering that obesity can cause hypertension, we think that this result is reasonable. When a fibroid structure in the perinephric adipose tissue is detected on CT scans, it is speculated to be the product of such chronic inflammation. Thus, patients with these fibroid structures are thought to be more likely to have adhesions due to chronic inflammation of the perinephric adipose tissue and renal capsule.

One limitation of our study was the subjective evaluation regarding the presence of fibroid structures on CT and the presence of adhesions. If the

severity of the fibroid structure and adhesions could be quantified by numbers or stratified, they would be better indices. Another limitation was that the study was a retrospective examination. Further studies are necessary, including prospective examinations and studies involving other institutions. In conclusion, removal of perinephric adipose tissue is a special process in partial nephrectomy. Adhesion between the renal capsule and perinephric adipose tissue is an important factor that affects the difficulty of this process. It is important to preoperatively predict the presence of such adhesion so that the degree of surgical difficulty can be predicted and an appropriate surgical procedure selected. In our study, we reported a simple method using plain CT to determine the presence of fibroid structure in perinephric adipose tissue, and thereby predict the presence of adhesion between the renal capsule and perinephric adipose tissue. The method predicted the presence of adhesion at high sensitivity (71.4%) and specificity (100%).

References

1. Benway BM, Bhayani SB, Rogers CG, Dulabon LM, Patel MN, Lipkin M, Wang AJ and Stifelman MD: Robot assisted partial nephrectomy versus laparoscopic partial nephrectomy for renal tumors: a multi-institutional analysis of perioperative outcomes. *J Urol* (2009) 182: 866–872.
2. Thompson RH, Lane BR, Lohse CM, Leibovich BC, Fergany A, Frank I, Gill IS, Blute ML and Campbell SC: Every Minute Counts When the Renal Hilum Is Clamped During Partial Nephrectomy. *Eur Urol* (2010) 58: 340–345.
3. Liu ZW, Olweny EO, Yin G, Faddegon S, Tan YK, Han WK and Cadeddu JA: Prediction of perioperative outcomes following minimally invasive partial nephrectomy: role of the R.E.N.A.L nephrometry score. *World J Urol* (2013) 31: 1183–1189.
4. Kruck S, Anastasiadis AG, Walcher U, Stenzl A and Herrmann TR: Laparoscopic partial nephrectomy: risk stratification according to patient and tumor characteristics. *World J Urol* (2012) 30: 639–664.
5. Hew MN, Baseskioglu B, Barwari K, Axwijk PH, Can C, Horenblas S, Bex A, Rosette JJ and Pes MP: Critical appraisal of the PADUA classification and assessment of the R.E.N.A.L. nephrometry score in patients undergoing partial nephrectomy. *J Urol* (2011) 186: 42–46.
6. Zhang ZY, Tang Q, Li XS, Zhang Q, Mayer WA, Wu JY, Yang XD, Zhang XC, Wang XY and Zhou LQ: Clinical analysis of the PADUA and the RENAL scoring systems for renal neoplasms: a retrospective study of 245 patients undergoing laparoscopic partial nephrectomy. *Int J Urol* (2014) 21: 40–44.
7. Satasivam P, Sengupta S, Rajarubendra N, Chia PH, Munshey A and Bolton D: Renal lesions with low R.E.N.A.L nephrometry score are associated with more indolent renal cell carcinomas (RCCs) or benign histology: findings in an Australian cohort. *BJU international* (2012) 109 Suppl 3: 44–47.
8. Simhan J, Smaldone MC, Tsai KJ, Canter DJ, Li T, Kutikov A, Viterbo R, Chen DY, Greenberg RE and Uzzo RG: Objective measures of renal mass anatomic complexity predict rates of major complications following partial nephrectomy. *Eur Urol* (2011) 60: 724–730.
9. Hayn MH, Schwaab T, Underwood W and Kim HL: RENAL nephrometry score predicts surgical outcomes of laparoscopic partial nephrectomy. *BJU international* (2011) 108: 876–881.
10. Stroup SP, Palazzi K, Kopp RP, Mehrazin R, Santomauro M, Cohen SA, Patterson AL, L'Esperance JO and Derweesh IH: RENAL nephrometry score is associated with operative approach for partial nephrectomy and urine leak. *Urology* (2012) 80: 151–156.
11. Mullins JK, Kaouk JH, Bhayani S, Rogers CG, Stifelman MD, Pierorazio PM, Tanagho YS, Hillyer SP, Kaczmarek BF, Chiu Y and Allaf ME: Tumor complexity predicts malignant disease for small renal masses. *J Urol* (2012) 188: 2072–2076.
12. Eaton SH, Thirumavalaven N, Katz MH, Babayan RK and Wang DS: Effect of body mass index on perioperative outcomes for laparoscopic partial nephrectomy. *J Endourol* (2011) 25: 1447–1450.
13. Isac WE, Autorino R, Hillyer SP, Hernandez AV, Stein RJ and Kaouk JH: The impact of body mass index on surgical outcomes of robotic partial nephrectomy. *BJU international* (2012) 110: E997–E1002.
14. Kiziloz H, Dorin R, Finnegan KT, Shichman S and Meraney A: The impact of body mass index on perioperative outcomes in robot-assisted laparoscopic partial nephrectomy. *J Endourol* (2013) 27: 1000–1007.
15. Gorin MA, Mullins JK, Pierorazio PM, Jayram G and Allaf ME: Increased intra-abdominal fat predicts perioperative complications following minimally invasive partial nephrectomy. *Urology* (2013) 81: 1225–1230.
16. Macleod LC, Hsi RS, Gore JL, Wright JL and Harper JD: Perinephric Fat Thickness Is an Independent Predictor of Operative Complexity During Robot-Assisted Partial Nephrectomy. *J Endourol* (2014) 28: 587–591.
17. Hotamisligil GS: Inflammation and metabolic disorders. *Nature* (2006) 444: 860–867.
18. Suganami T and Ogawa Y: Adipose tissue macrophages: their role in adipose tissue remodeling. *J Leuko Biol* (2010) 88: 33–39.