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Factors Associated with Peritumoral Adhesions during Nephrectomy after Renal Mass Biopsy

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Abstract

Objectives: To analyze factors associated with peritumoral adhesions (PTAs) during nephrectomy performed after Renal Mass Biopsy (RMB).

Methods: From January 2009 to September 2013, 80 patients underwent Radical Nephrectomy (RN) or Partial Nephrectomy (PN) following RMB for renal masses that were ambiguous for malignancy on preoperative computed tomography imaging. Patients whose final pathology revealed urothelial carcinoma were excluded. PTAs were prospectively categorized as grade I (from no to moderate) and II (severe) by the operating surgeon immediately after surgery. Multivariate logistic regression analysis was performed to analyze factors associated with PTA.

Results: Among the 80 patients, 60 (75%) were diagnosed as renal cell carcinoma (RCC) and 20 (25%) as benign tumors. The benign tumors included 10 (12.5%) angiomyolipomas, 5 (6.3%) oncocytomas, and 5 (6.3%) leiomyomas. Patients with grade II PTAs had a higher estimated blood loss. There was no conversion to RN in 30 patients treated by PN for RCC; however, of the 20 patients with benign tumors, 10 (50.0%) underwent unplanned conversion to RN. Among the 10 patients who underwent PN for benign tumors, 5 (50.0%) experienced postoperative pseudoaneurysms. Multivariate analysis revealed a younger age (p=0.039), higher Body Mass Index (BMI) (p=0.013), benign pathology (p=0.001), and more numbers of biopsy cores (p=0.045) as independent predictors for grade II PTAs.

Conclusions: Compared to patients with RCC, younger patients with benign renal tumors were more likely to have severe PTAs during nephrectomy following RMB, especially those with a high BMI. Therefore, surgical treatment should be carefully planned for these patients.

Keywords: Biopsy; Needle; Nephrectomy; Tissue adhesions

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Introduction

Thin-slice renal Computed Tomography (CT) remains the single most important radiographic tool for delineating the nature of a renal mass. However, in 10-20% of solid renal masses, CT findings are indeterminate, and pathological ambiguity intensifies, especially for small renal masses [1,2]. To predict the nature of these pathologically ambiguous masses, a Renal Mass Biopsy (RMB) can be performed to identify candidates for extirpative treatment.

Historically, RMB has been reserved for a limited number of indications, such as clinical findings suggestive of renal abscess, lymphoma, or metastatic carcinoma to the kidney [3]. Furthermore, RMB has been primarily reserved for patients with disseminated metastases or unresectable masses because of concerns of false-negatives, complications, and risk of tract seeding. However, contemporary series have shown that RMB is indeed a safe and accurate diagnostic technique, with a 94% overall accuracy and a minor complication rate of less than 5% (with subclinical bleeding being the most common complication) [4]. In accordance with evidence that it is a safe procedure with minimal complications, the role of RMB has expanded, and more nephrectomies are now being performed following RMB [5,6]. However, the presence of unexpected peritumoral adhesions (PTAs) during nephrectomy after RMB is a comorbid condition that has not been accounted for in contemporary studies, although PTAs are known to be a potential risk factor for perioperative morbidity.

Adhesions commonly occur following invasive procedures and pose a tremendous burden on the subsequent surgical therapy. In prostate cancer, several reports have noted the relationship between prostate biopsy and radical prostatectomy [7-12]. However, there is a paucity of literature

Table 1: Patients' characteristics according to the severity of peritumoral adhesions.

	Adhesion degree				p
	Grade I (n=65)		Grade II (n=15)		
Age (yr)	56.0	(46.5-66.5)	45.0	(28.0-57.0)	*0.001*
Sex					*1.000*
Male	20	(30.8%)	4	(26.7%)	
Female	45	(69.2%)	11	(73.3%)	
Body mass index (kg/m²)	23.9	(21.9-24.5)	24.9	(23.2-29.2)	*0.015*
Tumor size (cm)	3.6	(3.0-5.1)	2.6	(2.2-10.2)	*0.346*
RENAL nephrometry score	9.0	(5.0-10.0)	8.0	(5.0-9.0)	*0.512*
Biopsy core number	3.0	(2.0-4.0)	3.0	(2.0-4.0)	*0.615*
Interval between biopsy and nephrectomy (days)	22.0	(15.5-127.0)	22.0	(10.0-40.0)	*0.148*
Tumor pathology					
Renal cell carcinoma	55	(84.5%)	5	(33.3%)	*<0.001*
Benign	10	(15.4%)	10	(66.7%)	
Angiomyolipoma	5	(7.7%)	5	(33.3%)	
Oncocytoma	0	(0%)	5	(33.3%)	
Leiomyoma	5	(7.7%)	0	(0%)	
Operative modality					*0.001*
Laparoscopic	30	(46.2%)	0	(0%)	
Open	35	(53.8%)	15	(100.0%)	
Nephrectomy type					*0.252*
Partial nephrectomy	30	(46.2%)	10	(66.7%)	
Radical nephrectomy	35	(53.8%)	5	(33.3%)	

Data are presented as number (%) or median (interquartile range)

regarding the incidence and the severity of PTAs following RMB and their impact on the subsequent renal surgery. Indeed, PTAs may lead to significant surgical morbidity, especially in the setting of Partial Nephrectomy (PN). To the best of our knowledge, our study represents the first to analyze the factors associated with PTAs in patients who have undergone RMB prior to nephrectomy.

Methods

Patients

We retrospectively reviewed a prospective database of 80 patients who underwent Radical Nephrectomy (RN) or PN between January 2009 and September 2013 following RMB for renal masses that were ambiguous for malignancy on preoperative CT imaging. Patients whose final pathology revealed urothelial carcinoma were excluded from the study because of disparities in the approach and extent of the surgical field compared to nephrectomy. Patients with previous intra-abdominal or renal surgery or known intra-abdominal or urinary tract infection were excluded.

Ultrasonography-guided percutaneous RMB was performed by a single uro-radiologist using an 18-gauge core biopsy needle according to the previously reported method [13]. The number of RMB cores was determined by the uro-radiologist, depending on the size and location of the tumor.

Patients diagnosed with Renal Cell Carcinoma (RCC) according to the results of the RMB underwent RN or PN by either open or laparoscopic methods, based on the discretion of the surgeon (YDC, WSH). For patients diagnosed with benign tumors by RMB, in whom surgery was indicated for persistent pain, hematuria, or patients' desire, PN via an open or laparoscopic approach was recommended.

Clinicopathological data were collected, including the patients' age, Body Mass Index (BMI), and sex, and the surgical pathology. Data regarding the number of biopsy cores and the time interval between RMB and surgery were also collected. Postoperative complications were classified according to the Clavien-Dindo surgical complications classification [14]. The study was carried out in lieu of a formal ethics committee, followed by the principles of the Helsinki Declaration.

CT data interpretation

Preoperative CT images obtained using a 64-slice detector (Sensation 64, Siemens, Erlangen, Germany) were retrospectively reviewed by a single uro-radiologist who was blinded to the surgical and pathological outcomes. The tumors were classified according to the RENAL nephrometry score based on axial and coronal reconstructed images [15].

Classification of adhesions

PTAs were prospectively identified and graded by each surgeon immediately after surgery. The surgeon was blinded to any confirmatory pathological results. The degree of PTA was classified according to the scoring system of Evans, et al. [16]. This system uses the following criteria: 0=no adhesions, 1=filmy adhesions separating spontaneously, 2=firm adhesions separated by traction, and 3=dense adhesions requiring sharp dissection. For statistical analysis, degrees 0 to 2 were classified as grade I, and degree 3 as grade II.

Statistical analysis

Baseline characteristics of patients and tumors were compared according to the severity of PTA using descriptive statistics. The

Table 2: Perioperative outcomes according to the severity of peritumoral adhesions.

	Adhesion degree				*p*
	Grade I (n = 65)		Grade II (n = 15)		
Estimated blood loss (mL)	140.0	(100-200)	500.0	(150-800)	*<0.001*
Operative time (min)	162.0	(113-186)	124.0	(107-184)	*0.162*
Conversion to radical nephrectomy*	5	(50.0%)	5	(50.0%)	*1.0*
Complications, no. (%)§	0	(0%)	5	(7.7%)	*0.578*

Data are presented as number (%) or median (IQR)
*For patients with benign tumors, in whom partial nephrectomy was planned.
§ IIIa complication; postoperative pseudoaneurysms

Table 3: Univariate and multivariate regression analyses of prognostic factors of grade II peritumoral adhesions.

Variables	Univariate analysis			Multivariate analysis		
	OR	(95% CI)	*p*	OR	(95% CI)	*p*
Age	0.923	(0.877-0.972)	*0.002*	0.872	(0.765-0.993)	*0.039*
Body mass index	1.252	(1.039-1.508)	*0.018*	3.629	(1.317-9.998)	*0.013*
RENAL nephrometry score	0.924	(0.730-1.168)	*0.507*	0.565	(0.224-1.426)	*0.227*
Tumor histology			*<0.001*			*0.001*
Benign	1	(reference)		1	(reference)	
Malignant	0.091	(0.026-0.323)		0.001	(0-0.156)	
Number of biopsy cores	0.864	(0.492-1.518)	*0.611*	4.884	(1.035-23.042)	*0.045*
Interval between biopsy and nephrectomy	0.984	(0.962-1.005)	*0.137*	1.003	(0.993-1.012)	*0.568*

OR: Odds Ratio; CI: Confidence Interval

Mann-Whitney U-test and the Fisher's exact test were used to compare continuous and categorical variables, respectively. Univariate and multivariate logistic regression analysis was performed to analyze the factors predicting grade II PTA: age, BMI, RENAL nephrometry score, number of biopsy cores, time interval between biopsy and nephrectomy, and tumor pathology (which was dichotomized as benign or malignant). All tests were two-sided, with statistical significance set at p <0.05. The statistical analyses were performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA).

Results

Among the 80 patients, 60 (75%) were diagnosed with RCC and 20 (25%) were diagnosed with benign tumors. The benign tumors including the following: 10 (50.0%) angiomyolipoma (AML), 5 (25.0%) oncocytoma, and 5 (25.0%) leiomyoma. Patients' characteristics according to the severity of PTA are presented in Table 1. Patients with grade II adhesions were younger (p=0.001) and had a higher BMI (p=0.015) than those with grade I adhesions. All patients with grade II adhesions underwent open surgery (p=0.001). However, patients with grade I and II adhesions had similar tumor size (p=0.346), RENAL nephrometry scores (p=0.512), and time interval since RMB (p=0.148). Patients diagnosed with RCC underwent nephrectomy according to the surgeon's discretion (RN, 30 patients; PN, 30 patients), among which 5 (8.3%) patients exhibited grade II adhesions. Patients with RCCs had less severe adhesions than those with benign tumors, especially oncocytomas or AMLs (p <0.001).

Perioperative outcomes according to the severity of PTAs are presented in Table 2. The presence of grade II adhesions was associated with higher Estimated Blood Loss (EBL) (p <0.001); however, the operative time was comparable for those with grade I and II PTAs, possibly due to a higher rate of open surgery performed for patients who had grade II PTAs. In patients treated by PN for RCC, none required conversion to RN. By contrast, among the 20 patients with benign tumors diagnosed by RMB in whom PN was planned for persistent pain, hematuria, or patients' desire, 10 (50.0%) underwent unplanned conversion to RN. The conversion to RN rates of patients with benign tumors did not differ between the grade I and II PTA groups. All five patients with grade I PTAs who required conversion to RN underwent surgery via a laparoscopic approach. Conversion to RN was required for the five patients with grade II PTAs, even though all patients underwent surgery via an open approach. Although there were no grade IV and V Clavien-Dindo complications in any patients, 5 of the 10 patients who underwent PN for benign tumors experienced grade IIIa complications; postoperative pseudo aneurysms.

When we analyzed the factors predicting grade II PTAs during nephrectomy after RMB (Table 3), younger age (p=0.002), higher BMI (p=0.018), and benign pathology (p <0.001) were significant predictors for grade II adhesions on univariate analysis. Younger age (p=0.039), higher BMI (p=0.001), benign pathology (p <0.001), and more numbers of biopsy cores were significant predictors on multivariate analysis.

Discussion

An adhesion occurs when two tissues that normally move freely past each other are attached via a fibrous bridge [17]. Although the exact mechanism that shifts the normal healing process after renal injury to PTA formation remains unclear, the fibrinolytic system, extracellular matrix deposition and remodeling, and inflammation are generally accepted interrelated processes that are involved in the subsequent transition of persistent fibrinoid adhesions to permanent fibrous tissue [18,19]. The presence of adhesions during surgery due to previous violation of the tissue, such as during needle biopsy, may result in a longer operative time and increased complications, both immediately and for up to 10 years [20]. Therefore, predicting their presence and degree may considerably aid urological surgeons in selecting the appropriate surgical plane and modality, and in counseling patients about the potential risks of surgery.

For prostate cancer, essentially all prostatectomies are performed after a confirmative prostate biopsy. Therefore, numerous reports exist regarding the effect of preoperative prostate biopsies on perioperative outcomes [7-12]. However, preoperative RMB has only recently increased in frequency, as a consequence of the exponential increase in the incidence of small renal masses, recognition of the heterogeneity of the biological aggressiveness of renal masses, and awareness of the improved accuracy and safety profile of RMB [2,4,6]. There have heretofore been no reports regarding PTAs and perioperative outcomes of nephrectomy after RMB. In our study, we sought to evaluate the preoperative factors predicting PTA during nephrectomy after RMB using our prospective database of 80 consecutive patients who underwent RN or PN after RMB for renal masses that were ambiguous for malignancy.

As predicted, patients with grade II PTAs had a higher EBL. These patients were also expected to have longer operative times; however, all underwent open surgery, unlike those patients with grade I PTAs whose surgery was performed via either the open or laparoscopic approach. This observation may account for the comparable operative times between the grade I and II PTA groups. Moreover, there was no difference in the rate of conversion to RN for benign tumors between the two groups. Therefore, considering that patients with grade II PTAs were performed by the open approach, we presume that a subset of patients with grade I PTAs may have avoided conversion to RN if a laparoscopic approach had not been performed.

In contrast to our expectations, the RENAL nephrometry score, and time interval from biopsy were not significant predictors for grade II PTAs. Rather, patients with grade II adhesions were younger and had a higher BMI than those with grade I adhesions. Moreover, malignant tumors were associated with less severe adhesions than benign tumors, especially oncocytomas and AMLs. On multivariate analysis, a younger age, higher BMI, the presence of benign tumors, and more numbers of biopsy cores were significant predictors for grade II PTAs. Considering that hemorrhage and extension into perirenal fat may occur in up to one third of renal oncocytomas [21], and that AML is the most common renal tumor associated with spontaneous peritumoral hemorrhage [22], it can be assumed that PTAs may intensify with RMB by worsening of peritumoral hemorrhage. To date, the explanation for the correlation between young age, high BMI and PTA is less clear. However, it has been reported that adhesion formation is a normal part of wound healing, with a number of factors then differentiating between resolution and pathological adhesion formation and should be considered as highly cellular, vascularized and dynamic structures under the influence of complex signalling pathways.(new references 1, 2 add) And it is known that the perirenal fat can be firmly attached to the kidney in patients with metabolic syndrome (new reference 3 add) like our result that BMI was found to be a significant independent predictor of the severity of adhesions. Therefore, younger patients with high BMI may have rapid wound healing, but pathological adhesion formation compared to older patients with normal BMI. Moreover, it is possible that a narrower surgical field in patients with higher BMI may have increased the difficulty of surgery and thereby influenced the surgeon's subjective assessment of PTA severity.

We acknowledge several limitations to our findings. First, our data were retrospectively collected from surgery performed by two surgeons, thus the results are prone to selection bias. Second, although the adhesion scores were evaluated by surgeons blinded to the pathological results, adhesion scoring systems are prone to subjectivity and inter-observer variation. Moreover, the final results may differ depending on the types of adhesion scoring system and the surgical approach used. To ensure consistency in the assessment and avoid bias, it would have been better to have one single surgeon assess and grade the severity of adhesions on video-recorded procedures. Third, as mentioned earlier, there can be correlation between firm perirenal fat attachment and metabolic syndrome. Therefore, although the information on the concomitant presence of hypertension and diabetes mellitus should be also accounted for in the analysis, unfortunately, our prospective database did not include these in formations.

Our study showed that PTAs following RMB in patients diagnosed with RCC were generally not severe, irrespective of the patient or tumor characteristics. By contrast, younger patients diagnosed with oncocytoma or AML were frequently noted to have severe PTAs, especially those patients with a high BMI. Therefore, surgical treatment should be carefully planned in patients with benign mass characteristics who undergo nephrectomy after RMB.

References

1. Heuer R, Gill IS, Guazzoni G, Kirkali Z, Marberger M, Richie JP, et al. A critical analysis of the actual role of minimally invasive surgery and active surveillance for kidney cancer. Eur Urol. 2010; 57: 223-232.
2. Vasudevan A, Davies RJ, Shannon BA, Cohen RJ. Incidental renal tumours: the frequency of benign lesions and the role of preoperative core biopsy. BJU Int. 2006; 97: 946-949.
3. Sahni VA, Silverman SG. Biopsy of renal masses: when and why. Cancer Imaging. 2009; 6: 44-55.
4. Schmidbauer J, Remzi M, Memarsadeghi M, Haitel A, Klingler HC, Katzenbeisser D, et al. Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol. 2008; 53: 1003-1011.
5. Londoño DC, Wuerstle MC, Thomas AA, Salazar LE, Hsu JW, Danial T, et al. Accuracy and implications of percutaneous renal biopsy in the management of renal masses. Perm J. 2013; 17: 4-7.
6. Ordon M, Landman J. Renal mass biopsy: "just do it". J. Urol. 2013; 190: 1638-1640.
7. Choi H, Ko YH, Kang SG, Park HS, Cheon J, Patel VR. Biopsy related prostate status does not affect on the clinicopathological outcome of robotic assisted laparoscopic radical prostatectomy. Cancer Res Treat. 2009; 41: 205-210.
8. Lee DK, Allareddy V, O'Donnell MA, Williams RD, Konety BR. Does the interval between prostate biopsy and radical prostatectomy affect the immediate postoperative outcome? BJU Int. 2006; 97: 48-50.
9. Martin GL, Nunez RN, Humphreys MD, Martin AD, Ferrigni RG, Andrews PE, et al. Interval from prostate biopsy to robot-assisted radical prostatectomy: effects on perioperative outcomes. BJU Int. 2009; 104: 1734-1737.
10. Kim IS, Na W, Nam JS. Interval from Prostate Biopsy to Robot-Assisted Laparoscopic Radical Prostatectomy (RALP): Effects on Surgical Difficulties. Korean J Urol. 2011; 52: 664-668.
11. Shah JB, McKiernan JM, Elkin EP, Carroll PR, Meng MV. Prostate biopsy patterns in the CaPSURE database: evolution with time and impact on outcome after prostatectomy. J Urol. 2008; 179: 136-140.
12. Eggener SE, Yossepowitch O, Serio AM, Vickers AJ, Scardino PT, Eastham JA. Radical prostatectomy shortly after prostate biopsy does not affect operative difficulty or efficacy. Urology. 2007; 69: 1128-1133.

13. Lee SW, Lee MH, Yang HJ. Experience of ultrasonography-guided percutaneous core biopsy for renal masses. Korean J Urol. 2013; 54: 660-665.

14. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009; 250: 187-196.

15. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009; 182: 844-853.

16. Evans DM, McAree K, Guyton DP, Hawkins N, Stakleff K. Dose dependency and wound healing aspects of the use of tissue plasminogen activator in the prevention of intra-abdominal adhesions. Am J Surg. 1993; 165: 229-232.

17. Ward BC, Panitch A. Abdominal adhesions: current and novel therapies. J. Surg. Res. 2011; 165: 91-111.

18. Pismensky SV, Kalzhanov ZR, Eliseeva MY, Kosmas IP, Mynbaev OA. Severe inflammatory reaction induced by peritoneal trauma is the key driving mechanism of postoperative adhesion formation. BMC Surg. 2011; **14**: 11-30.

19. Tokgöz H, Bektaş S, Hancı V, Erol B, Akduman B, Karakaya K, et al. Postoperative adhesions after application of topical hemostatic agents: outcomes in a rat partial nephrectomy model. Urology. 2011; **78**: 970. 9-14.

20. Hellebrekers BW, Kooistra T. Pathogenesis of postoperative adhesion formation. Br. J. Surg. 2011; **98**: 1503-1516.

21. Perez-Ordonez B, Hamed G, Campbell S, Erlandson RA, Russo P, Gaudin PB, et al. Renal oncocytoma: a clinicopathologic study of 70 cases. Am. J. Surg. Pathol. 1997; **21**: 871-83.

22. Zhang JQ, Fielding JR, Zou KH. Etiology of spontaneous perirenal hemorrhage: a meta-analysis. J. Urol. 2002; **167**: 1593-1596.