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Analysis of Factors Influencing Mayo Adhesive Probability Score in Partial Nephrectomy

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: To retrospectively explore the factors influencing Mayo Adhesive Probability (MAP) score in the setting of partial nephrectomy.

Material/Methods: Data of 93 consecutive patients who underwent laparoscopic and open partial nephrectomy from September 2015 to June 2016 were collected and analyzed retrospectively. Preoperative radiological elements were independently assessed by 2 readers. Ordinal logistic regression analyses were performed to evaluate radiological and clinicopathologic influencing factors of MAP score.

Results: On univariate analysis, MAP score was associated with male sex, older age, higher body mass index (BMI), history of hypertension and diabetes mellitus, and perirenal fat thickness (posterolateral, lateral, anterior, anterolateral, and medial). On multivariate analysis, only posterolateral perirenal fat thickness (odds ratio [OR]=0.88 [0.82–0.95], p=0.001), medial perirenal fat thickness (OR=0.90 [0.83–0.98], p=0.01), and history of diabetes mellitus (OR=5.42 [1.74–16.86], p=0.004) remained statistically significant. Tumor type (malignant *vs.* benign) was not statistically different. In patients with renal cell carcinoma (RCC), there was no difference in tumor stage or grade.

Conclusions: MAP score is significantly correlated with some preoperative factors such as posterolateral and medial perirenal fat thickness and diabetes mellitus. A new radioclinical scoring system including these patient-specific factors may become a better predictive tool than MAP score alone.

MeSH Keywords: **Carcinoma, Renal Cell • Nephrectomy • Urology**

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Background

With the continuous improvement of surgical techniques, partial nephrectomy (PN) is currently applied to patients with clinical stage T1a and T1b (maximum diameter ≤7 cm) renal masses [1]. PN is also internationally recommended for those with solitary kidney, contralateral renal insufficiency, or bilateral renal cell carcinoma. However, the risk of perioperative complications is high, especially when tumor complexity exists. Traditional scoring systems such as the RENAL score and PADUA prediction score are used to predict the complexity of PN [2,3]. However, these scoring systems which focus only on the renal morphometry do not consider the patient-specific factors, one of which is adherent perinephric fat (APF). APF refers to the inflammatory adhesion between perirenal fat and renal parenchyma, which has been shown to be correlated with surgical difficulty and postoperative outcomes [4–7].

Davidiuk et al. developed an imaging-based scoring system called the Mayo Adhesive Probability (MAP) score, which is a quantitative indicator of APF used to predict the difficulty of PN. Preliminary studies have shown that the MAP scoring system is simple, objective, and feasible [8–10].

In the present study, we sought to explore the influencing factors of MAP score itself on PN by analyzing patient and tumor characteristics. To the best of our knowledge, this is the first study of influencing factors of the MAP score.

Material and Methods

Patient population

This study was approved by the Ethics Committee of Peking University First Hospital. A total of 97 consecutive patients underwent partial nephrectomy in the Urology Department, Peking University First Hospital between September 2015 and June 2016. All patients underwent contrast-enhanced CT scanning preoperatively in or outside our hospital. In this study, we only included those who underwent CT scanning (Philips Brilliance 64 CT Scanner, Amsterdam, the Netherlands) in our hospital, then 4 patients were consequently excluded. Finally, 93 patients were enrolled and their radiological and clinicopathologic data were retrospectively reviewed.

Radiological evaluation

All images were processed using Carestream Vue PACS (Carestream, Rochester, NY). With blinding of the readers to patients' APF status, preoperative CT images were assessed by 2 senior radiologists with similar seniority. All data were measured at the level of the renal vein as described by

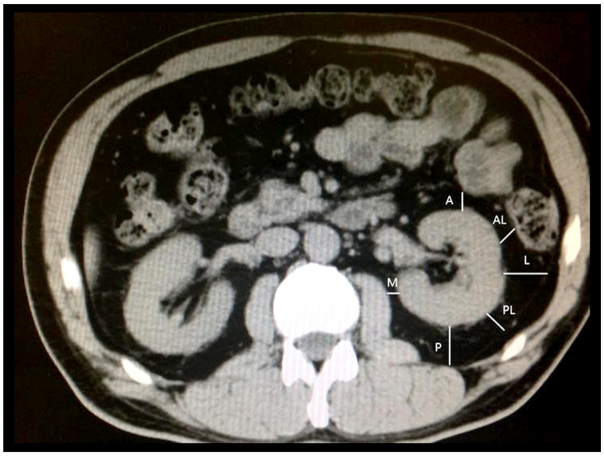

Figure 1. Measurement of perinephric fat at the level of the renal vein. A – anterior perirenal fat thickness; M – medial perirenal fat thickness; L – lateral perirenal fat thickness; AL – anterolateral perirenal fat thickness; PL – posterolateral perirenal fat thickness.

Davidiuk et al. [8]. As similarly described by Eisner et al. [11], some radiological elements which were not involved in MAP score were also collected. The posterior perirenal fat thickness (P), anterior perirenal fat thickness (A), medial perirenal fat thickness (M), lateral perirenal fat thickness (L), anterolateral perirenal fat thickness (AL), and posterolateral perirenal fat thickness (PL) on the same side of the tumor were measured (Figure 1).

Here, we define the posterior perirenal fat thickness as the length of a direct line posteriorly from the renal capsule to the posterior abdominal wall, with its reverse line intersecting with the point of the end of the renal vein. Posterolateral perirenal fat thickness was measured from the renal capsule to the lateral abdominal wall on the projected line from the renal vein. Similarly, the other 4 measurements (anterior, medial, lateral, and anterolateral) were defined as the distance from the kidney to nearest viscera or muscle.

Each corresponding result was averaged and the evaluation of MAP score was calculated as described by Davidiuk et al. [8].

Statistical analyses

For continuous variables, the sample median (minimum and maximum) is listed. Categorical variables were reported as proportions with number of patients (percentage). Ordinal logistic regression analyses (if feasible) were used to compare both continuous and categorical variables. For dependent variables, MAP score=0 was taken as reference, and link function was Logit. If $p<0.05$ in the test of parallel lines in ordinal logistic regression, multiple logistic regression analyses were applied. All reported p-values are 2-sided and statistical significance

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Table 1. Patient (n=93) clinicopathologic and radiological characteristics.

Variables	Summary (n=93)	
Age (yr)	54	(19–77)
Age <55 yr	47	(50.5%)
Age ≥55 yr	46	(49.5%)
Gender		
Male	61	(65.6)
Female	32	(34.4)
Body mass index (BMI, kg/m^2)	25.1	(15.6–33.9)
BMI <25	44	(47.3%)
25≤ BMI ≤30	40	(43.0%)
BMI >30	9	(9.7%)
Hypertension		
Yes	44	(47.3%)
No	49	(52.7%)
Diabetes		
Yes	16	(17.2%)
No	77	(82.8%)
Coronary heart disease		
Yes	6	(6.5%)
No	87	(93.5%)
Side of the tumor		
Left	49	(52.7%)
Right	44	(47.3%)
Tumor size (cm)	2.5	(0.7–13.0)
Tumor type		
Renal cell carcinoma	78	(83.9%)
Benign tumor	15	(16.1%)
Tumor stage(n=78)		
1a	70	(89.7%)
1b	8	(10.3%)
Tumor grade(n=73)		
G1	49	(67.1%)
G2 and G3	24	(32.9%)
Perirenal fat thickness(mm)		
Posterior	15.1	(0–39.6)
Posterolateral	17.0	(0–46.5)
Lateral	16.1	(0–53.7)
Anterior	8.6	(0–39.1)
Anterolateral	10.4	(0–32.7)
Medial	7.3	(0–31.2)
Stranding score		
0	61	(65.6%)
2	19	(20.4%)
3	13	(14.0%)
MAP score		
0	23	(24.7%)
1	29	(31.2%)
2	12	(12.9%)
3	12	(12.9%)
4	13	(14.0%)
5	4	(4.3%)

Continuous variables are listed as the sample median (minimum and maximum) and categorical variables as number of patients (percentage). Tumor stage was only available for renal cell carcinoma patients. Tumor grade was unavailable for 20 patients, including those with benign tumor and some rare types of renal cell carcinoma.

was set at <0.05. All statistical analyses were conducted with SPSS version 20.0 (IBM Corp, Armonk, NY).

Results

Patients' characteristics

Patients' radiological and clinicopathologic characteristics are summarized in Table 1. The median age was 54 years, and the median BMI was 25.1 kg/m^2. Most patients were men (65.6%). A total of 6 patients underwent open partial nephrectomy, and the other 87 cases underwent laparoscopic PN. For postoperative pathologic data, tumor stage was only available for renal cell carcinoma patients; tumor grade was unavailable for 20 patients, including 15 patients with benign tumor (14 angioleiomyolipoma and 1 neurilemmoma) and 5 patients with chromophobe renal cell carcinoma. RCC comprised 83.9% of the total tumors (without positive surgical margins). Tumor

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Table 2. Associations of patients' characteristics with MAP score.

Variables	MAP score 0	1	2	3	4	5	*p* Value
Age (yr)	49 (19–71)	49 (28–73)	59 (29–67)	62.5 (37–77)	54 (42–74)	62.5 (51–72)	**0.001**
Gender							**<0.001**
Male	8 (34.8%)	20 (69.0%)	9 (75.0%)	9 (75.0%)	11 (84.6%)	4 (100.0%)	
Female	15 (65.2%)	9 (31.0%)	3 (25.0%)	3 (25.0%)	2 (15.4%)	0 (0.0%)	
Body mass index (BMI, kg/m^2)	22.5 (17.6–30.5)	25.3 (15.6–31.6)	25.6 (20.7–28.7)	26.3 (22.0–28.6)	26.1 (21.3–33.9)	26.8 (22.0–31.8)	**0.001**
Hypertension							**0.004**
Yes	4 (17.4%)	15 (51.7%)	8 (66.7%)	6 (50.0%)	3 (23.1%)	1 (25.0%)	
No	19 (82.6%)	14 (48.3%)	4 (33.3%)	6 (50.0%)	10 (76.9%)	3 (75.0%)	
Diabetes							**<0.001***
Yes	2 (8.7%)	2 (6.9%)	0 (0.0%)	2 (16.7%)	9 (69.2%)	1 (25.0%)	
No	21 (91.3%)	27 (93.1%)	12 (100.0%)	10 (83.3%)	4 (30.8%)	3 (75.0%)	
Coronary heart disease							0.416
Yes	0 (0.0%)	3 (10.3%)	1 (8.3%)	0 (0.0%)	2 (15.4%)	0 (0.0%)	
No	23 (100.0%)	26 (89.7%)	11 (91.7%)	12 (100.0%)	11 (84.6%)	4 (100.0%)	
Tumor type							0.086
Renal cell carcinoma	17 (73.9%)	24 (82.8%)	11 (91.7%)	10 (83.3%)	12 (92.3%)	4 (100.0%)	
Benign tumor	6 (26.1%)	5 (17.2%)	1 (%8.3)	2 (16.7%)	1 (7.7%)	0 (0.0%)	
Tumor size (cm)	2.5 (1.0–6.2)	2.7 (1.2–5.0)	2.2 (1.4–13.0)	2.3 (0.7–12.5)	2.5 (1.2–4.2)	2.3 (1.7–3.7)	0.864
Side of the tumor							0.576
Left	12 (52.2%)	17 (58.6%)	7 (58.3%)	5 (41.7%)	6 (46.2%)	2 (50.0%)	
Right	11 (47.8%)	12 (41.4%)	5 (41.7%)	7 (58.3%)	7 (53.8%)	2 (50.0%)	
Perirenal fat thickness (mm)							
Posterolateral	7.0 (0–18.7)	17.6 (3.62–35.7)	21.9 (3.7–46.5)	20.1 (9.7–28.6)	19.6 (8.8–24.6)	28.1 (18.1–37.0)	**<0.001***
Lateral	5.6 (0–37.7)	18.2 (0–53.68)	24.7 (3.7–52.1)	16.1 (5.52–28.6)	18.6 (12.9–31.9)	18.0 (5.4–40.1)	**0.002***
Anterior	3.3 (0–23.8)	10.64 (0–21.0)	9.2 (0–37.2)	11.9 (0–31.7)	14.4 (0–39.1)	12.8 (8.0–17.8)	**0.002**
Anterolateral	5.0 (0–29.5)	11.3 (3.2–29.0)	15.1 (0–21.5)	8.7 (0–20.7)	10.9 (2.7–32.7)	20.8 (7.7–30.9)	**0.002***
Medial	3.5 (0–19.8)	9.0 (0–20.0)	7.4 (0–31.2)	8.1 (0–14.3)	9.3 (2.6–22.0)	15.2 (6.5–26.7)	**<0.001**
Tumor stage(n=78)							0.153
1a	14 (82.4%)	21 (87.5%)	10 (90.9%)	10 (100.0%)	11 (91.7%)	4 (100.0%)	
1b	3 (17.6%)	3 (12.5%)	1 (9.1%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	
Tumor grade(n=73)							0.777
G1	8 (66.7%)	16 (66.7%)	8 (72.7%)	7 (70.0%)	9 (75.0%)	1 (25.0%)	
G2 and G3	4 (33.3%)	8 (33.3%)	3 (27.3%)	3 (30.0%)	3 (25.0%)	3 (75.0%)	

MAP – Mayo adhesive probability. Continuous variables are listed as the sample median (minimum and maximum) and categorical variables as number of patients (percentage). Tumor stage was only available for renal cell carcinoma patients. Tumor grade was unavailable for 20 patients, including those with benign tumor and some rare types of renal cell carcinoma. * *P* value was based on multiple logistic regression analyses as ordinal logistic regression analyses were unfeasible.

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Table 3. Multivariable analysis of influencing factors of MAP score.

Variables	*p* Value		OR	95% CI
	Univariate	Multivariate		
Age(yr)	0.001	0.351		
Gender	<0.001	0.315		
Body mass index (BMI, kg/m^2)	0.001	0.225		
Hypertension	0.004	0.547		
Diabetes	<0.001	**0.004**	5.42	1.74–16.86
Tumor type	0.086	0.983		
Perirenal fat thickness(mm)				
Posterolateral	<0.001	**0.001**	0.88	0.82–0.95
Lateral	0.002	0.083		
Anterior	0.002	0.714		
Anterolateral	0.002	0.926		
Medial	<0.001	**0.010**	0.90	0.83–0.98

CI – confidence interval; OR – odds ratio; MAP score – 0 was taken as reference.

stage of most RCC was 1a (89.7%). MAP scores of 81.7% of tumors were from 0 to 3.

Univariate analysis of associations of patients' characteristics with MAP score is shown in Table 2. $P<0.05$ was considered statistically significant. On univariate analysis, MAP score was significantly associated with male sex ($p<0.001$), older age ($p=0.001$), higher body mass index ($p=0.001$), history of hypertension ($p=0.004$) and diabetes mellitus ($p<0.001$), and greater perirenal fat thickness (posterolateral [$p<0.001$], lateral [$p=0.002$], anterior [$p=0.002$], anterolateral [$p=0.002$], and medial [$p<0.001$]). The groups were not significantly comparable for tumor side, size, or type (malignant *vs.* benign). No significant difference was found in tumor stage or grade in RCC.

As displayed in Table 3, variables for which $p<0.1$ in univariate analysis were selected for multivariable analysis. Only posterolateral perirenal fat thickness (odds ratio [OR]=0.88 [0.82–0.95], $p=0.001$), medial perirenal fat thickness (OR=0.90 [0.83–0.98], $p=0.01$), and history of diabetes mellitus (OR=5.42 [1.74–16.86], $p=0.004$) remained statistically associated with MAP score.

Discussion

Partial nephrectomy is currently recommended as a standard treatment for patients with stage T1 renal cell carcinoma in both the American Urological Association and the European Association of Urology guidelines [1,12]. To predict the difficulty of PN, scoring systems focusing on renal morphometry, such as the RENAL score and PADUA prediction score, have been introduced, but these scoring systems do not include the patient-related factors such as adherent perinephric fat. APF can often cause more surgical difficulties in kidney mobilization and separating the renal tumor from renal parenchyma [5]. Chang et al. noted in 2015 that the presence of APF significantly increased the operative time and complexity of kidney mobilization and tumor isolation [13]. Similarly, Khene et al. analyzed the data of 202 patients who underwent robot-assisted partial nephrectomy (RAPN) and noted that the average operative time for patients with APF was 40 min longer, with 2-fold more blood loss and an increased risk of converting the operation into open surgery or radical nephrectomy [14].

Bylund et al. first sought to explore the factors related to APF, and found that there was a significant correlation between APF and male sex, perirenal fat thickness, and stranding [4], but the study was limited by sample size and the rather subjective evaluation of APF. Davidiuk et al. in 2014 prospectively analyzed 100 patients with RAPN and created the Mayo Adhesive Probability (MAP) scoring system, which helps to predict the presence of APF and therefore the surgical complexity in PN [8]. Chang et al. analyzed the relationship between APF and the patient-specific factors in 43 patients with RAPN, and noted that APF was significantly correlated with type 2 diabetes, perirenal fat stranding, preoperative serum creatinine, medial perirenal fat thickness, and MAP score [13]. By studying the clinical data of 245 patients who underwent minimally invasive partial nephrectomy, Kocher et al. showed that the relationship between APF and age, male sex, posterior perirenal fat thickness, perirenal fat stranding, and the MAP score was statistically significant [7]. Similarly, in a retrospective case-control study involving 86 patients, Martin et al. confirmed that the MAP score was predictive of APF in open PN [9].

The above studies did confirm the ability of MAP score to predict APF. However, the evaluation of APF has always depended on surgeon experience and subjective determination. We noticed that surgeons with different experience had different understanding of adhesion during the operation; therefore, the severity of adhesion may not be objectively reflected merely from the operative notes. Besides, although the MAP score is an easy-to-use scoring system, it does not include all the factors associated with APF. It has been reported that a radioclinical score based on MAP score and other clinical factors was more predictive of APF [10]. Our aim in the present study was to find more objective quantitative factors to optimize the MAP score. To avoid the bias caused by subjective conclusions, we directly analyzed the influencing factors of the more objective MAP score itself. Our study is the first to report the influencing factors of the MAP score. In our study, we found the MAP score was associated with diabetes, posterolateral perirenal fat thickness, and medial perirenal fat thickness in multivariate analysis.

It is worth noting that previous studies have shown that APF was significantly associated with sex [4,5,8], showing that men are more likely to develop perirenal 'sticky fat', which increases surgical difficulty, perhaps due to differences in fat distribution between men and women. Anderson et al. found that the thickness of subcutaneous fat was greater in women than in men, while men have thicker perirenal fat than women [15], which was subsequently confirmed by Eisner et al. [11]. However, in our study, the MAP score was not correlated with sex in multivariate analysis. This may be explained by the interaction between sex and perirenal fat thickness.

Our study confirmed that the MAP score was not associated with BMI. Previous studies have demonstrated that BMI can reflect the individual total fat content (includes visceral fat). Macleod et al. compared the complexity of RAPN with the measurement of perirenal fat thickness and BMI, noting that it was perirenal fat thickness but not BMI that was associated with increased blood loss and operative time [16]. Therefore, compared with BMI, it is more meaningful to focus on the intra-abdominal fat thickness, which may help predict surgical difficulty and serve as a reference for the choice of operation [14].

The association between diabetes mellitus and APF has been previously reported [13], and our study shows the significant association between diabetes mellitus and MAP score, with the odds ratio of 5.42. Visceral fat accumulation is closely related with posterior perinephric fat thickness, and also has a reciprocal causal relationship with the occurrence and development of type 2 diabetes mellitus. An increase in total and visceral fat can cause insulin resistance and a series of inflammatory responses [17,18]. Conversely, insulin resistance can make the distribution of adipose tissue change, and visceral fat increases further [19]. This change may then have an impact on the body's inflammatory response, since visceral fat can produce higher levels of inflammatory markers compared with subcutaneous fat [20]. Thus, type 2 diabetes can increase both the body's visceral fat content and the body's inflammatory response. In addition, the relationship between perirenal fat stranding and APF may also suggest that the inflammatory response plays a role in the development of APF. However, Dariane et al. reported that no inflammatory infiltration was found in perirenal fat [10]. The specific mechanism still needs further study.

Davidiuk et al. has reported the association between posterolateral perirenal fat thickness and APF [8], although the former was not selected to create the MAP score. As for radiological elements not included in the MAP score, our study showed the potential significance of medial perirenal fat thickness, as reported by a previous study [13]. Further study needs to be done to evaluate whether an optimized MAP score including more radiological elements can better predict APF.

There are some limitations in our study. This was a retrospectively study and results need to be further validated by prospective studies. Imaging evaluation was performed by 2 different radiologists, so the MAP score may be biased. Moreover, the sample size needs to be further enlarged. Further efforts should be focused on creating a new radioclinical score and assessing whether it is more predictive of APF.

Conclusions

In conclusion, the MAP score is highly correlated with posterolateral perirenal fat thickness, medial perirenal fat thickness, and history of diabetes mellitus, and may be optimized by these influencing factors. It needs to be further explored whether the MAP score can be improved.

Conflicts of Interest

None.

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