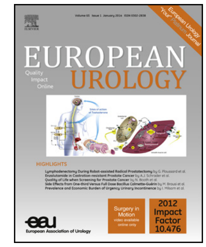
EUROPEAN UROLOGY 66 (2014) 1165–1171

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology

Kidney Cancer

Mayo Adhesive Probability Score: An Accurate Image-based Scoring System to Predict Adherent Perinephric Fat in Partial Nephrectomy

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Article info

Article history:
Accepted August 21, 2014

Keywords:
Renal cell carcinoma
Renal morphometry
Robotic partial nephrectomy
Robotic surgery

Abstract

Background: Image-based renal morphometry scoring systems are used to predict the potential difficulty of partial nephrectomy (PN), but they are centered entirely on tumor-specific factors and neglect other patient-specific factors that may complicate the technical aspects of PN. Adherent perinephric fat (APF) is one such factor known to make PN difficult.
Objective: To develop an accurate image-based nephrometry scoring system to predict the presence of APF encountered during robot-assisted partial nephrectomy (RAPN).
Design, setting, and participants: We prospectively analyzed 100 consecutive RAPNs performed by one surgeon and defined APF as the need for subcapsular renal dissection to isolate the renal tumor for RAPN.
Outcome measurements and statistical analysis: The scoring algorithm to predict the presence of APF was developed with a multivariable logistic regression model using a forward selection approach with a focus on improvement in the area under the receiver operating characteristic curve.
Results and limitations: Thirty patients (30%; 95% confidence interval, 21–40) had APF. Single-variable analysis noted an increased likelihood of APF in male patients ($p < 0.001$), higher body mass index ($p = 0.003$), greater posterior perinephric fat thickness ($p < 0.001$), greater lateral perinephric fat thickness ($p < 0.001$), and those with perirenal fat stranding ($p < 0.001$). Two of these variables, posterior perinephric fat thickness and stranding, were most highly predictive of APF in multivariable analysis and were therefore used to create a risk score, termed *Mayo Adhesive Probability* (MAP) and ranging from 0 to 5, to predict the presence of APF. We observed APF in 6% of patients with a MAP score of 0, 16% with a score of 1, 31% with a score of 2, 73% with a score of 3–4, and 100% of patients with a score of 5.
Conclusions: MAP score accurately predicts the presence of APF in patients undergoing RAPN. Prospective validation of the MAP score is required.
Patient summary: The Mayo Adhesive Probability score that we we developed is an accurate system that predicts whether or not adherent perinephric, or "sticky," fat is present around the kidney that would make partial nephrectomy difficult.

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http://dx.doi.org/10.1016/j.eururo.2014.08.054
0302-2838/

1. Introduction

The American Urological Association and European Association of Urology guidelines currently recommend nephron-sparing surgery as a standard of care for patients with suspected renal cell carcinoma (RCC) <4 cm in size whenever feasible [1–3]. Surgeons use renal morphometry scoring systems such as the RENAL nephrometry score, PADUA prediction score, and centrality index (C-index) to quantify relevant anatomic findings that can predict the complexity of partial nephrectomy (PN) and the likelihood for complications [4–6]. In doing so, these algorithms inform the potential complexity of the procedure and thereby assist in appropriate patient management and selection for PN [4–6]. Although these image-based scoring systems help predict the potential difficulty of PN and standardize PN terminology, they are centered entirely on tumor-specific factors and neglect other patient-specific factors that may complicate the technical aspects of PN.

One non–tumor-related factor that can complicate PN is the presence of so-called sticky fat, or adherent perinephric fat (APF), which can limit mobilization of the kidney and isolation of the renal tumor. Although obesity and increased visceral fat have been linked to increased surgical difficulty and postoperative complications in both radical nephrectomy and PN, there have been limited efforts to determine whether visceral fat can be used to predict the presence of APF [7]. In reply to a recent study in which the authors examined the association of increased abdominal fat (IAF) and perioperative complications, editorials from two experienced partial nephrectomists pointed out the missed opportunity to assess the correlation between increased visceral fat and APF. The authors of the editorials went a step further by citing the specific need to elucidate factors that could help surgeons better predict APF as a way to supplement current systems of preoperative risk assessment for PN [7]. A scoring system that could accurately and reliably predict the presence of APF in a preoperative setting would provide a welcomed adjunct to the RENAL, PADUA, and C-index nephrometry scoring systems, enhancing the predictability of surgical complexity for PN and thereby better informing patient selection and improving outcomes. To address this identified need, we introduce a simple image-based scoring system, called *Mayo Adhesive Probability* (MAP), that is highly predictive of intraoperative APF encountered during robot-assisted partial nephrectomy (RAPN).

2. Materials and methods

2.1. Robot-assisted partial nephrectomy

RAPN was performed by one fellowship-trained robotic surgeon using a well-described standard three robotic arm and one camera port technique [8]. An assistant 12-mm port was placed in the supraumbilical midline, and a 5-mm assistant port was placed in the midline below the xiphoid. The renal hilum was completely dissected in all patients and clamped with bulldog clamps when necessary for resection. The Gerota fat was dissected from the kidney to expose the tumor, and intraoperative ultrasound was utilized to identify tumor margins and tumor volume. Tumor excision was performed athermally, and collecting system closure was completed when necessary with absorbable suture. Renorrhaphy was completed with the well-described sliding-clip technique [9].

2.2. Data collection

Following institutional review board approval, 100 consecutive patients who underwent RAPN by one experienced surgeon were analyzed. Data were collected regarding patient characteristics (age, body mass index [BMI], sex, preoperative creatinine, preoperative glomerular filtration rate, history of hypertension, history of cardiovascular disease, history of diabetes, history of smoking), tumor information (renal mass size, RENAL score, tumor type, posterior perinephric fat thickness, lateral perinephric fat thickness, stranding), and operative factors (presence of APF requiring subcapsular dissection). APF was defined by one surgeon intraoperatively for all 100 cases as perirenal fat within the Gerota fascia requiring subcapsular dissection for exposure of the renal parenchyma and renal tumor.

2.3. Tumor characteristics

For preoperative tumor characteristics, imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) closest to the date of intervention was analyzed. RENAL [4] scores were completed by two reviewers.

2.4. Perirenal fat characteristics

From the images (CT or T1-weighted MRI), perinephric fat thickness was measured at the level of the renal vein as similarly described by Eisner et al., with blinding of the reviewer to APF status [10]. Laterally, the perinephric fat was measured from the renal capsule to the sidewall in parallel to the renal vein; posterior fat was measured as a direct line posteriorly from the renal capsule to the posterior abdominal wall (Fig. 1).

Perinephric stranding, defined as a linear area of soft tissue attenuation in the perinephric space, was noted, if present, for each kidney on CT or MRI and graded according to severity. Stranding was

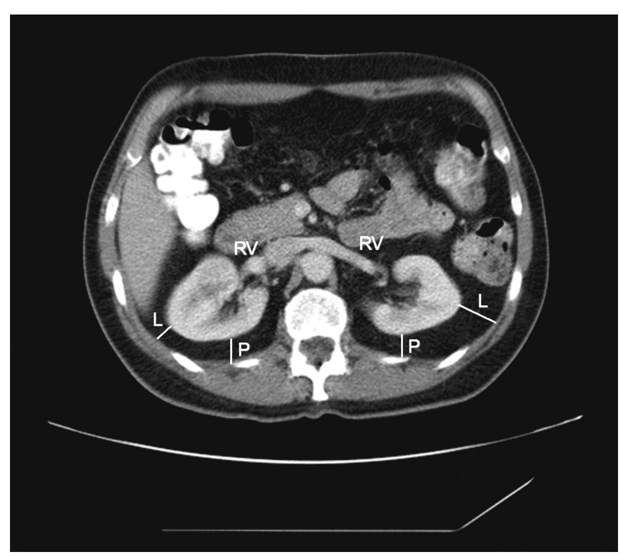

Fig. 1 – Method of determining perinephric fat measurements at the level of the renal vein.
P = posterior (modality used in Mayo Adhesive Probability score), L = lateral, RV = renal vein.

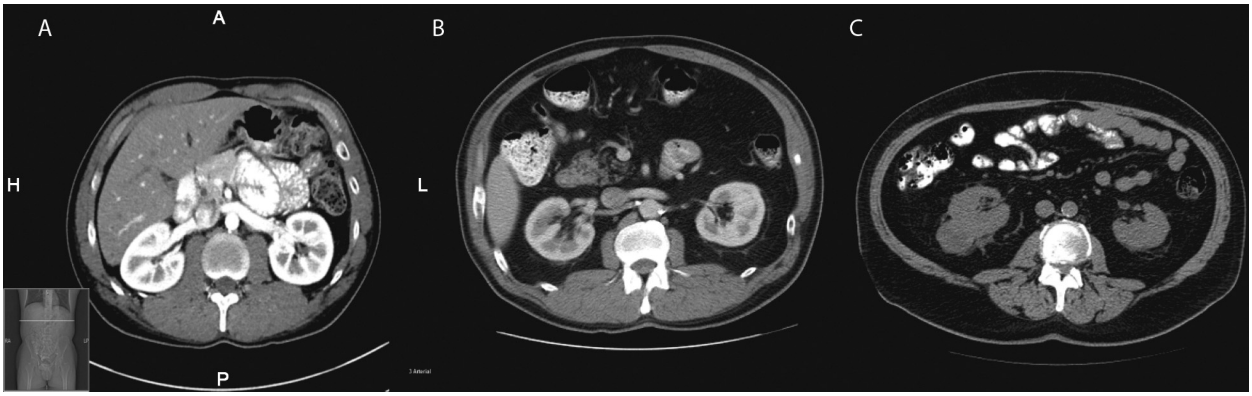

Fig. 2 – Grading of perinephric stranding. (A) None: 0 points. The fat around the kidney demonstrates no stranding. On this computed tomography image, the tissue surrounding the kidney is completely black. (B) Mild/moderate (type 1): 2 points. The fat around the kidney has some image-dense stranding present but no thick bars of inflammation. (C) Severe stranding (type 2): 3 points. Image shows severe stranding around the kidney with thick image-dense bars of inflammation.

graded as 0 (no stranding; Fig. 2A), type 1 (thin rimlike mild stranding; Fig. 2B), or type 2 (diffuse, thick-banded severe stranding; Fig. 2C), as previously used and described in the literature on perinephric stranding by Kim et al. [11].

2.5. Statistical analysis and development of the Mayo Adhesive Probability score

The proportion of patients who had APF was estimated along with a 95% confidence interval (CI). Associations of patient and tumor characteristics with the presence of APF during RAPN were evaluated using logistic regression models, where odds ratios and 95% CIs were estimated. For easier interpretation of results in association analysis, continuous variables were categorized based on approximate sample tertiles (age, preoperative creatinine, size of renal mass, posterior perinephric fat thickness, and lateral perinephric fat thickness) or predefined cut-offs of interest (BMI and RENAL nephrometry score). We adjusted for multiple testing using the Holm step-down method [12]. To create a scoring algorithm that classifies patients according to the likelihood of the presence of APF, a multivariable logistic regression model was developed using a forward selection approach, with a focus on improvement in the area under the receiver operating characteristic curve (AUC). All analyses were performed using SAS v.9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

Table 1 summarizes the baseline characteristics of the cohort. Of the 100 patients who had PN, 30 (30%; 95% CI, 21–40) had APF. The median age was 63 yr (interquartile range [IQR]: 54–68 yr), the median BMI was 28.9 kg/m^2 (IQR: 25.8–32.7 kg/m^2), and most patients were men (62%). A total of 79% of tumors were RCC (no positive surgical margins). Patients with APF were noted to have longer operative times than those without APF (median: 223 min vs 199 min; $p = 0.026$).

Table 2 shows an evaluation of associations of patient characteristics with the presence of APF. After adjusting for multiple testing ($p \leq 0.005$ was considered significant), in single-variable analysis there was a significantly increased likelihood of APF in patients who were male (44% vs 8%; $p < 0.001$), patients who had a higher BMI (BMI <25: 5%; BMI 25–30: 30%; BMI >30: 43%; $p = 0.003$), patients who had a greater posterior perinephric fat thickness (<1.0 cm: 5%; 1.0–1.9 cm: 23%; ≥2.0 cm: 66%; $p < 0.001$), patients who had a greater lateral perinephric fat thickness (<1.5 cm: 5%; 1.5–2.4 cm: 30%; ≥2.5 cm: 64%; $p < 0.001$), and patients who had type 1 or type 2 stranding (no stranding: 14%, type 1: 80%, type 2: 92%; $p < 0.001$).

Due to the limited number of patients who experienced APF and the relatively strong correlations between most of the previously mentioned five factors, the use of multivariable analysis attempting to identify independent associations with APF was challenging [13]. Given that our goal was to create a score that effectively predicts which patients have the highest likelihood of APF, a forward selection approach was utilized with a focus on the estimated AUC of the given logistic regression model. Of the five variables significantly associated with the presence of APF in single-variable analysis, several had very good predictive ability on their own, the most effective of which was posterior perinephric fat thickness with an AUC of 0.83. When retaining posterior perinephric fat thickness in the model and including each of the other four variables one at a time, the model with the highest AUC included posterior perinephric fat thickness and stranding (AUC: 0.89). When retaining both posterior perinephric fat thickness and stranding in the model and including each of the remaining three variables one at a time, there was no noticeable increase in estimated AUC (all AUCs between 0.90 and 0.91). When retaining both stranding and posterior perinephric fat thickness in the model and including each of the variables nominally associated with APF in single-variable analysis (preoperative creatinine, cardiovascular disease, history of smoking), estimated AUC did not increase noticeably (all AUCs between 0.90 and 0.91). Therefore, we included two variables, posterior perinephric fat thickness and stranding, in our risk score.

The risk score, which we refer to as the MAP score, was created based on posterior perinephric fat thickness and

Table 1 – Patient and tumor characteristics

Variable	Summary $n = 100$
Sticky fat	
No	70 (70)
Yes	30 (30)
Age, yr	63 (54–68)
<60	39 (39)
60–65	26 (26)
>65	35 (35)
Sex	
Female	38 (38)
Male	62 (62)
Body mass index, kg/m^2	28.9 (25.8–32.7)
<25	21 (21)
25–30	37 (37)
>30	42 (42)
Preoperative creatinine, mg/dl	0.9 (0.8–1.1)
≤0.8	39 (39)
0.9–1.0	31 (31)
>1.0	30 (30)
Preoperative eGFR <60 ml/min	
No	83 (83)
Yes	17 (17)
Hypertension	
No	38 (38)
Yes	62 (62)
Cardiovascular disease	
No	71 (71)
Yes	29 (29)
Diabetes	
No	77 (77)
Yes	23 (23)
History of smoking	
No	65 (65)
Yes	35 (35)
Size of renal mass, cm	2.5 (2.0–4.0)
≤2.0	32 (32)
2.1–3.5	41 (41)
>3.5	27 (27)
RENAL nephrectomy score (%)	
4–6	38 (38)
7–9	49 (49)
10–12	13 (13)
Tumor type	
Benign tumor	21 (21)
Renal cell carcinoma	79 (79)
Posterior distance, cm	1.3 (0.8–2.3)
<1.0	37 (39)
1.0–1.9	22 (23)
≥2.0	35 (37)
Stranding	
None	71 (76)
Type 1	10 (11)
Type 2	13 (14)

eGFR = estimated glomerular filtration rate.
Data are shown as number (percentage). For continuous variables, the sample median (first quartile, third quartile) is given. We also present the number and percentage of patients in the different categories that were utilized for creation of a risk score. Posterior distance and stranding were unavailable for six patients.

stranding as follows. The odds ratio estimates from the multivariable logistic regression model including both posterior perinephric fat thickness and stranding were used to create an individual score for each different level of these two variables; these logistic regression results and variable-specific scores are displayed in Table 3. The individual scores for posterior perinephric fat thickness and stranding were then summed to create the MAP score that ranges from 0 to 5. As shown in Table 4, the proportion of patients with APF for each level of the MAP score was as follows: 0 ($n = 36$), 6%; 1 ($n = 19$), 16%; 2 ($n = 16$), 31%; 3–4 ($n = 11$), 73%; 5 ($n = 12$), 100%.

4. Discussion

APF can be a frustrating surgical variable encountered during PN that can limit mobilization of the kidney and isolation of the kidney tumor, and its removal can often lead to tearing of the renal capsule [14]. Experienced and respected partial nephrectomists have openly commented on the need for a model that predicts the risk of encountering intraoperative APF [7]. Given these difficulties, we aimed to develop a user-friendly scoring system to predict the probability of encountering APF intraoperatively. In our study, we found five such factors associated with APF including male gender, increased BMI, increased posterior and lateral perinephric fat thickness, and perirenal fat stranding. We utilized the two most predictive factors, posterior perinephric fat thickness and stranding, to create a MAP nephrometry score that accurately classifies patients according to the likelihood of the presence of APF intraoperatively.

Both the general surgery and urology literature have noted the difficulty of abdominal surgery on patients with significant visceral obesity. Morris et al. noted in 2010 that IAF, as compared with BMI and outer abdominal fat, better predicted postoperative complications and mortality in abdominal surgery [15]. More specifically, it was discovered that retro-renal visceral fat >2.0 cm was significantly associated with surgical complications after pancreaticoduodenectomy [16]. Anderson et al. noted that operative times for laparoscopic donor nephrectomies are longer in patients with increased posterior renal fat, and this increased renal fat is more often seen in men [17]. These findings have been mirrored in the urology literature as well. IAF, as measured by perirenal fat thickness, was a better predictor than outer abdominal fat or BMI in predicting longer operative times, postoperative complications, and estimated blood loss for patients undergoing PN [7,18,19]. These studies fail to elucidate the reason why surgery in patients with increased IAF is so fraught with complications. It is our belief that hostile APF may complicate surgery on patients with increased visceral fat.

Bylund et al. first sought to elucidate certain characteristics that may be associated with APF encountered intraoperatively during PN [19]. Male sex, stranding, and increased thickness of perinephric fat were all associated with the finding of APF in a cohort of 29 patients. Our study both confirms their findings in a larger cohort and develops a nephrometry scoring system that can easily and accurately predict APF preoperatively. Although the RENAL, PADUA, and C-index nephrometry scoring systems look to classify the difficulty of each individual tumor based on its location, they each fail to account for patient-specific factors such as APF that may complicate an otherwise simple exophytic anterior

Table 2 – Associations with the presence of adherent perinephric fat during partial nephrectomy

Variable	Fraction (%) with adherent perinephric fat	Association with presence of adherent perinephric fat	
		OR (95% CI)	*p* value
Age, yr			0.12
<60	8/39 (21)	1.00 (reference)	
60–65	9/26 (35)	2.05 (0.67–6.29)	
>65	13/35 (37)	2.29 (0.81–6.46)	
Sex			<0.001
Female	3/38 (8)	1.00 (reference)	
Male	27/62 (44)	9.00 (2.50–32.42)	
Body mass index, kg/m^2			0.003
<25	1/21 (5)	1.00 (reference)	
25–30	11/37 (30)	8.46 (1.01–71.03)	
>30	18/42 (43)	14.99 (1.84–122.29)	
Preoperative creatinine, mg/dl			0.012
≤0.8	6/39 (15)	1.00 (reference)	
0.9–1.0	11/31 (35)	3.02 (0.97–9.45)	
>1.0	13/30 (43)	4.21 (1.36–13.03)	
Preoperative eGFR <60 ml/min			0.098
No	22/83 (27)	1.00 (reference)	
Yes	8/17 (47)	2.46 (0.85–7.19)	
Hypertension			0.13
No	8/38 (21)	1.00 (reference)	
Yes	22/62 (35)	2.06 (0.81–5.27)	
Cardiovascular disease			0.042
No	17/71 (24)	1.00 (reference)	
Yes	13/29 (45)	2.58 (1.04–6.43)	
Diabetes			0.11
No	20/77 (26)	1.00 (reference)	
Yes	10/23 (43)	2.19 (0.83–5.78)	
History of smoking			0.014
No	14/65 (22)	1.00 (reference)	
Yes	16/35 (46)	3.07 (1.26–7.47)	
Size of renal mass, cm			0.32
≤2.0	8/32 (25)	1.00 (reference)	
2.1–3.5	12/41 (29)	1.24 (0.44–3.53)	
>3.5	10/27 (37)	1.76 (0.58–5.40)	
RENAL nephrectomy score			0.63
4–6	12/38 (32)	1.00 (reference)	
7–9	12/49 (24)	0.70 (0.27–1.81)	
10–12	6/13 (46)	1.86 (0.51–6.73)	
Tumor type			0.15
Benign tumor	9/21 (43)	1.00 (reference)	
Renal cell carcinoma	21/79 (27)	0.48 (0.18–1.31)	
Posterior perinephric fat thickness, cm			<0.001
<1.0	2/37 (5)	1.00 (reference)	
1.0–1.9	5/22 (23)	5.15 (0.90–29.29)	
≥2.0	23/35 (66)	33.53 (6.86–163.86)	
Lateral perinephric fat thickness, cm			<0.001
<1.5	2/38 (5)	1.00 (reference)	
1.5–2.4	7/23 (30)	7.87 (1.47–42.15)	
≥2.5	21/33 (64)	31.49 (6.42–154.50)	
Stranding			<0.001
None	10/71 (14)	1.00 (reference)	
Type 1	8/10 (80)	24.40 (4.51–131.92)	
Type 2	12/13 (92)	73.20 (8.55–626.39)	

CI = confidence interval; eGFR = estimated glomerular filtration rate; OR = odds ratio.
ORs and 95% CIs were estimated from single-variable logistic regression models. Categories for age, body mass index, preoperative creatinine, size of renal mass, posterior perinephric fat thickness, and lateral perinephric fat thickness were chosen based on approximate sample tertiles or predefined cut-offs of interest. The p values ≤ 0.005 were considered as statistically significant after a Holm stepdown adjustment for multiple testing. Posterior perinephric fat thickness, lateral perinephric fat thickness, and stranding were unavailable for six patients.

lower pole renal tumor. The precedent for scoring perinephric stranding is drawn from Kim et al., who utilized noncontrast CT scanning in stone patients undergoing ureteroscopy to analyze its association with intraoperative mucosal edema [11]. They noted stranding to be absent or mild/moderate when some bands were present and severe when thick strands were present (Fig. 2). A stranding score of 2 or 3 in our MAP scoring system may alter the MAP score to a 4 or 5, but there should not be any question about the score if stranding is absent. The measurement of posterior renal

Table 3 – The Mayo Adhesive Probability score algorithm

Variable	Multivariable association with adherent perinephric fat		MAP score
	OR (95% CI)	*p* value	
Posterior perinephric fat thickness, cm		0.003	
<1.0	1.00 (reference)		0
1.0–1.9	4.58 (0.64–32.63)		1
≥2.0	13.25 (2.18–80.67)		2
Stranding		<0.001	
None	1.00 (reference)		0
Type 1	10.95 (1.87–64.11)		2
Type 2	35.71 (3.42–372.88)		3

CI = confidence interval; MAP = Mayo Adhesive Probability; OR = odds ratio.
ORs and 95% CIs result from the final multivariable logistic regression model that was adjusted for both posterior perinephric fat thickness and stranding. Scores for posterior perinephric fat thickness and stranding were given based on the magnitude of ORs. Reference categories were assigned 0 points, the "low" OR of 4.58 was assigned 1 point, the two relatively similar "moderate" ORs of 10.95 and 13.25 were each assigned 2 points, and the "high" OR of 35.71 was assigned 3 points. Scores for the two variables are summed to create a total score, the MAP score, with a possible range of 0 to 5.

distance from the renal capsule to the body wall at the level of the renal vein was established by other investigators in an attempt to quantify the amount of IAF present during abdominal surgery and minimally invasive PN [7,18].

This study was designed with the sole purpose of creating an easy-to-calculate scoring system that predicts the likelihood of encountering APF during PN. Therefore, we did not include an analysis of the impact of APF on the outcomes of RAPN. In the only studies thus far examining APF along with operating room variables, APF was shown to predict longer operating room times for PN [14,19]. APF alone may be a surrogate for surgical complexity and may push less experienced partial nephrectomists to select an alternative approach, such as an open PN or an ablation, for treating small renal masses in these particular patients.

We did not merge the MAP with other tumor-based morphometric scoring systems (eg, RENAL, PADUA, C-index) to examine if it will be a useful adjunct to those well-validated scoring systems. It is our opinion that useful morphometric scoring must be intuitive and easy to calculate or it will not be widely used in the urology community. One large benefit of the MAP is that it can be easily calculated simultaneously with the existing tumor-based morphometry scoring systems utilizing the same images. Another large benefit of the MAP is its reliance on only two image-based variables. However, it should be noted that the RENAL, PADUA, and C-index nephrometry scoring systems have all been demonstrated to affect the rate of complications following PN.

The MAP score predicts only the presence of APF, which may not play a role in predicting complications associated with PN. The MAP score was created based on data from a single-surgeon experience of RAPN. It cannot be directly determined in our cohort whether the data presented will be transferable to open or laparoscopic PN; however, it seems likely that preoperative knowledge of hostile APF would be useful to all surgeons attempting surgery on the kidney. It could be argued that the intraoperative classification of APF appears to be subjective; however, it is our opinion that most experienced partial nephrectomists are able to recognize APF, especially when perirenal fat is so adherent that the thin rim of the capsule must be dissected to mobilize the renal parenchyma and tumor for PN. APF was present in 30% of the RAPN in this series. The true incidence of APF encountered during PN is difficult to determine due to limited data, and the only two assessments in the literature of APF encountered during PN note that 53.7% [14] and 55.2% [19] of patients had APF. The true rate of APF encountered during PN will need to be elucidated in larger series.

Although the MAP score appears promising, the sample size (and number of patients with APF) is relatively small, and the score was developed using a data-driven approach, both of which will require the MAP to be validated in a larger patient cohort. As a result, this score is currently being validated in a larger independent group of patients undergoing various types of PN at several national centers.

Table 4 – Proportion of partial nephrectomy patients with adherent perinephric fat according to the Mayo Adhesive Probability score

MAP score	Proportion of patients with adherent perinephric fat	
	Fraction (%)	95% CI
0	2/36 (6)	1–19
1	3/19 (16)	3–40
2	5/16 (31)	11–59
3	2/4 (50)	7–93
4	6/7 (86)	42–100
5	12/12 (100)	74–100

CI = confidence interval; MAP = Mayo Adhesive Probability.
The MAP score was not calculated for six patients due to missing data (posterior perinephric fat thickness and stranding). None of the six patients excluded from the risk score had adherent perinephric fat.

5. Conclusions

The MAP score is an easy-to-calculate image-based nephrometry scoring system that accurately predicts the probability of encountering troublesome APF during RAPN. This promising risk score requires prospective validation in a large patient cohort and with alternative modalities of PN.

Author contributions: David D. Thiel had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Thiel, Davidiuk, Parker.
Acquisition of data: Thiel, Davidiuk, Custer.
Analysis and interpretation of data: Thiel, Thomas, Heckman.
Drafting of the manuscript: Thiel, Davidiuk, Castle, Leibovich.
Critical revision of the manuscript for important intellectual content: Thiel, Parker, Castle, Davidiuk.
Statistical analysis: Thomas, Heckman.
Obtaining funding: None.
Administrative, technical, or material support: Custer.

Supervision: None.
Other (specify): None.

Financial disclosures: David D. Thiel certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: David D. Thiel is a consultant for Cooper Surgical Corporation. The other authors have nothing to disclose.

Funding/Support and role of the sponsor: None.

Acknowledgment statement: The authors thank Victoria L. Jackson for her editorial assistance in the preparation of this paper.

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