



Validation of the Mayo Adhesive Probability score as a predictor of adherent perinephric fat and outcomes in open partial nephrectomy

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Background: Adherent perinephric fat (APF) contributes to surgical complexity and can be associated with adverse perioperative outcomes for partial nephrectomy (PN). The Mayo Adhesive Probability (MAP) score accurately predicts the presence of APF during robotic-assisted partial nephrectomy (RAPN). Our primary aim is to validate MAP score as a predictor of APF in open partial nephrectomy (OPNx).

Methods: We reviewed 105 consecutive OPNx (100 patients) performed by a single surgeon with intraoperative determination of APF. We evaluated the ability of the MAP score to discriminate between those with APF and those without APF by estimating the area under the receiver operating characteristic curve (AUROCC). The association of perioperative outcomes with APF was evaluated as well.

Results: Forty-three patients [49%; 95% confidence interval (CI), 39–59%] had intraoperative identification of APF. The MAP score had excellent ability to predict APF in OPNx (AUROCC, 0.82; 95% CI, 0.74–0.92). APF was observed in 6% of patients with a MAP score of 0-1, 27% with score 2, 52% with score 3, 75% with score 4, and 90% with score 5. The presence of APF was associated with longer operative times ($P=0.004$) and higher estimated blood loss (EBL) ($P=0.003$). Although not statistically significant, our study did suggest that APF may be associated with postoperative complications and prolonged length of stay (LOS) (>3 days).

Conclusions: MAP score accurately predicts the presence of APF in patients undergoing OPNx. APF is associated with longer operative time and higher blood loss in OPNx.

Keywords: Mayo Adhesive Probability (MAP) score; open partial nephrectomy (OPNx); RENAL score; adherent perinephric fat (APF); renal cell carcinoma

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Introduction

The Mayo Adhesive Probability (MAP) score is an accurate image-based nephrometry scoring system to predict the presence of APF during robotic assisted partial nephrectomy (RAPN) (1). Nephron sparing surgery has evolved into the preferred management for small renal masses given

the benefits of renal function preservation. Surgical outcomes may be associated with tumor characteristics and the expertise of the surgeon (2). In order to predict the complexity of partial nephrectomy (PN) and the likelihood of complications, surgeons use renal nephrometry scoring systems such as RENAL nephrometry score, PADUA

prediction score, and centrally index (C-index) to quantify the relevant renal tumor findings and the likelihood of complications (3). These scoring systems center on tumor-specific factors and may neglect other patient-specific factors such as increased subcutaneous, intra-abdominal, visceral, and adherent perinephric fat (APF) that may also complicate the technical aspects of PN (1,2,4). The MAP score is an accurate image-based nephrometry scoring system to predict the presence of APF during RAPN. We hypothesize an association between MAP score and the presence of intraoperative APF in patients undergoing Open Partial Nephrectomy (OPNx). We elected to evaluate the ability of the MAP score to predict APF in patients who underwent OPNx. We also evaluated the association of APF with peri-operative outcomes of OPNx. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/tau-20-926>).

Methods

Open partial nephrectomy

OPNx was performed by a single fellowship trained surgeon at one institution via subcostal incision. The kidney was fully mobilized in each case to ensure safe hilar access and identification of the ureter. The perinephric fat was dissected to the renal capsule to allow adequate exposure of the renal tumor. An ultrasound probe was utilized to mark out the margins of the tumor prior to excision. The hilum was controlled using bulldog clamps and the tumor was excised. Disruptions in the collecting system were closed with a running absorbable suture and renorrhaphy was performed using the sliding-clip technique prior to removal of hilar clamp (5). Warm ischemia time (WIT) is defined as the time of renal artery clamp placement until clamp removal from the renal vein. There were no alterations in technique over the study period.

Calculation of MAP score

A single independent reviewer evaluated the preoperative imaging (CT or T1-weighted MRI) for each patient undergoing OPNx. The MAP score was calculated for each patient utilizing the measurement of posterior renal fat thickness and the measure of severity of perinephric stranding (1). Perinephric fat thickness was measured at the level of the renal vein as a direct line from the level

of the renal capsule to the posterior abdominal wall in centimeters (<1 cm =0 points, 1.1–1.9 cm =1 point, >2.0 cm =2 points) (1).

Perinephric stranding was identified as soft tissue attenuation in the fat surrounding the kidney and graded according to severity if present (0= no stranding, 2= thin mild stranding, 3= diffuse stranding) (1). The 2 scores were combined to give a MAP score of 0-5.

Identification of APF

APF was identified by the surgeon and defined as the requirement of subcapsular dissection for full exposure of the renal tumor (1).

Data collection

All procedures performed in this study were in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Mayo Clinic Hospital, (registration ID#20-008079). Because of the retrospective nature of the research, the requirement for informed consent was waived. We included 100 consecutive patients who underwent OPNx at our institution over an 11-year period. Five patients had two OPNx during the study period, however only the first case was used in our analyses. We excluded 13 procedures where the presence or absence of intraoperative APF was not recorded.

We additionally collected data on preoperative patient characteristics [age, sex, body mass index (BMI), hemoglobin, creatinine, estimated glomerular filtration rate (eGFR), hypertension, cardiovascular disease, diabetes and smoking status], tumor characteristics [tumor size, type of renal mass (renal cell carcinoma or benign), and RENAL score (6), posterior perinephric fat, and stranding]. For tumor characteristics, CT scan or MRI less than 3 months old from the date of intervention were analyzed. RENAL scores were completed by two reviewers. Surgical outcomes including estimated blood loss (EBL), warm ischemia time (WIT), total operative time, length of stay (LOS), prolonged LOS defined as more than 3 days, post-operative complications as graded by the Clavien-Dindo Classification (7), hemoglobin at postoperative day (POD) 1, and creatinine at POD 1 were evaluated. Margin, ischemia, and complication (MIC) (8) scoring was used and defined as negative surgical margins, WIT <20 minutes, and no postoperative complications grade III or higher (2).

Table 1 Patient demographics and surgical outcomes

Variable	All (N=87)
Demographics and clinical characteristics	
Age, years	66 [42, 57, 70, 80]
Male sex	61 (70%)
Body mass index, kg/m ²	30.7 (16.7, 26.2, 34.2, 42.2)
MAP score	
0	10 (11%)
1	7 (8%)
2	15 (17%)
3	21 (24%)
4	24 (28%)
5	10 (11%)
Surgical outcomes	
Intraoperative complications	10 (11%)
Length of stay, days	4 [3, 4, 5, 20]
Total operative time, min	176 [90, 147, 201, 342]
Postoperative complication, No (%)	
Grade I	20 (23%)
Grade II	19 (22%)
Grade III	1 (1%)
Grade IV	4 (5%)
Grade V	1 (1%)

Data are given as number (percentage) or median (minimum, 25th percentile, 75th percentile, maximum). MAP, Mayo adhesive probability.

Statistical analysis

We assessed the ability of MAP score to discriminate between the presence and absence of APF in patients undergoing OPNx by estimating the area under the receiving operating characteristic curve (AUROCC) and corresponding 95% confidence interval (CI). To illustrate the ability of MAP score to predict APF, we plotted the observed proportion of patients who had APF along with exact binomial 95% CI according to MAP score. We additionally performed several supplemental analyses replicating those done by Davidiuk *et al.* [2014] and

Davidiuk [2015] that are explained in the results (1,2). SAS statistical software (version 9.4M5, SAS Institute Inc., Cary, NC, USA) was used for statistical analysis and graphics.

Results

Patient characteristics

Our study included a cohort of 87 consecutive patients who underwent OPNx with intraoperative evaluation of APF. *Table 1* outlines the patient demographics and surgical outcomes of the cohort. In our cohort, 6 patients (7%) had major complications (Grade III–V). Grade III complications included an infection requiring drainage. Grade IV complications included hyperkalemia, anuria, acute respiratory failure and encephalopathy. The grade V complication was a death secondary to cerebellar stroke. Median preoperative creatinine was 1.1 mg/dL (IQR, 0.9–1.3 mg/dL) and median preoperative hemoglobin was 13.6 mg/dL (IQR, 12.8–14.7 mg/dL). Nineteen patients had diabetes (22%), 63 (72%) had hypertension, and 14 (16%) had cardiovascular disease. Median primary tumor size was 4.0 cm (IQR, 3.0–6.0 cm). The majority of tumors (82%) were renal cell carcinoma; the remaining tumors (19%) were benign histology.

Validation of MAP score as a predictor of APF in OPNx (Primary Aim)

APF was identified intraoperatively in 49% (43/87) of patients (95% CI, 39–59%). APF was observed in 6% of patients with a MAP score of 0–1, 27% with a score of 2, 52% with a score of 3, 75% with a score of 4, and 90% with a score of 5 (*Table 2, Figure 1*). The MAP score was an excellent predictor of APF in OPNx (AUROCC, 0.82; 95% CI, 0.74–0.92; $P < 0.001$).

Associations of preoperative patient and tumor characteristics with APF in OPNx

Table 3 demonstrates a supplemental analysis evaluating associations of preoperative patient and tumor characteristics with the presence of APF during OPNx. In single variable logistic regression analysis, there was a significantly increased likelihood of APF with male sex (70% *vs.* 0%; $P < 0.001$), history of hypertension (59% *vs.* 25%; $P = 0.007$), greater posterior perinephric fat thickness

Table 2 Predicted *vs.* observed APF according to MAP score in open partial nephrectomy patients

MAP score	No. of patients	Predicted APF, (95% CI)	Observed APF
0	10	4% (1% to 17%)	1 (10%)
1	7	11% (4% to 28%)	0 (0%)
2	15	27% (14% to 43%)	4 (27%)
3	21	51% (39% to 64%)	11 (52%)
4	24	75% (60% to 86%)	18 (75%)
5	10	90% (75% to 96%)	9 (90%)

The predicted % of patients with APF was estimated from a logistic regression model with the simplified risk score as the only predictor variable. APF, adherent perinephric fat; MAP, Mayo Adhesive Probability.

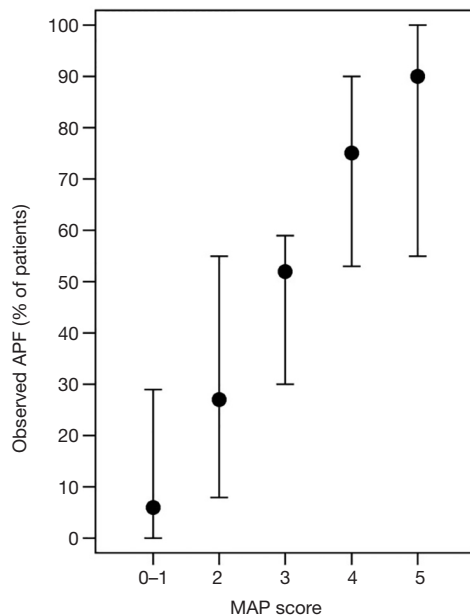


Figure 1 Observed proportion (%) of open partial nephrectomy patients with APF according to MAP score. Circles represent the observed percentage of patients with APF in our cohort based on the MAP score. Vertical bars represent the 95% confidence interval. The seven patients with a MAP score of 1 were combined with the 10 patients with a MAP score of 0. APF, adherent perinephric fat; MAP, Mayo Adhesive Probability.

(<1.0 cm, 12%; 1.0–1.9 cm, 43%; ≥ 2 cm, 70%; $P < 0.001$), in patients with type 1 or 2 stranding (none, 15%; type 1, 60%; type 2, 79%; $P < 0.001$), and in patients with a high MAP score (MAP score 0–3: 30%, MAP score 4–5: 79%; $P < 0.001$) after adjustment for multiple testing (Holm method, $P \leq 0.005$ was considered statistically significant).

Perioperative outcomes in OPNx

Median total operative time for all patients was 176 minutes (IQR, 147–201 minutes). Median EBL was 600 mL (IQR, 500–1,000 mL). Comparisons of perioperative outcomes according to the presence of APF are displayed in *Table 4*. Patients with APF compared to those without APF were shown to have longer operative times (median, 193 *vs.* 170 minutes; $P = 0.004$) and higher EBL (median, 800 *vs.* 600 mL; $P = 0.003$). These remained statistically significant after applying Bonferroni adjustment for multiple comparisons ($P \leq 0.0045$). Although not statistically significant, our study did suggest that the presence of APF may be associated with postoperative complications (63% *vs.* 41%; $P = 0.054$) and length of hospital stay > 3 days (91% *vs.* 73%; $P = 0.051$). There were no other notable associations between the presence of APF and perioperative outcomes (all, $P \geq 0.077$). We additionally explored associations of the same perioperative outcomes with BMI and RENAL score. Our study did not find any notable associations of perioperative outcomes with BMI (all $P \geq 0.084$). However, our study did find evidence of an association of higher RENAL score with both longer WIT ($P = 0.011$) and higher incidence of postoperative complications ($P < 0.001$), but only the association of RENAL score with postoperative complications remained statistically significant after adjustment for multiple comparisons. Although not statistically significant, our data did suggest that a higher RENAL score may be associated with length of hospital stay longer than 3 days ($P = 0.056$). There were no other notable associations between RENAL score and perioperative outcomes (all $P \geq 0.13$).

Table 3 Associations with presence of adherent perinephric fat during open partial nephrectomy

Variable	Fraction (%) with APF	OR (95% CI)	P value
Age, year			0.047
<60	11/29 (38%)	1.00 (reference)	
60–65	4/13 (31%)	0.73 (0.18–2.94)	
>65	28/45 (62%)	2.70 (1.03–7.05)	
Sex			<0.001
Female	0/26 (0%)	N/A	
Male	43/61 (70%)	N/A	
Body mass index, kg/m ²			0.08
<25	3/14 (21%)	1.00 (reference)	
25–30	15/25 (60%)	5.50 (1.22–24.81)	
>30	25/48 (52%)	3.99 (0.99–16.11)	
Preoperative creatinine, mg/dL			0.012
≤0.8	4/21 (19%)	1.00 (reference)	
0.9–1.0	12/20 (60%)	6.38 (1.56–26.1)	
>1.0	27/46 (59%)	6.04 (1.75–20.81)	
Preoperative eGFR <60 mL/min/1.73 m ²			0.23
No	26/58 (45%)	1.00 (reference)	
Yes	17/29 (59%)	1.74 (0.71–4.30)	
Hypertension			0.007
No	6/24 (25%)	1.00 (reference)	
Yes	37/63 (59%)	4.27 (1.49–12.22)	
Cardiovascular disease			0.53
No	35/73 (48%)	1.00 (reference)	
Yes	8/14 (57%)	1.45 (0.46–4.59)	
Diabetes			0.067
No	30/68 (44%)	1.00 (reference)	
Yes	13/19 (68%)	2.74 (0.93–8.07)	
History of smoking			0.10
No	15/38 (39%)	1.00 (reference)	
Yes	28/49 (57%)	2.04 (0.86–4.84)	
Renal mass size categories (cm)			0.56
≤2	3/9 (33%)	1.00 (reference)	
2.1–3.5	14/29 (48%)	1.87 (0.39–8.93)	
>3.5	26/49 (53%)	2.26 (0.51–10.08)	

Table 3 (continued)

Table 3 (continued)

Variable	Fraction (%) with APF	OR (95% CI)	P value
RENAL nephrectomy score			0.24
4–6	11/28 (39%)	1.00 (reference)	
7–9	30/53 (57%)	2.02 (0.79–5.12)	
10–12	2/6 (33%)	0.77 (0.12–4.96)	
Tumor type			0.15
Oncocytoma	4/6 (67%)	1.00 (reference)	
Renal cell carcinoma	37/71 (52%)	0.54 (0.09–3.16)	
Other pathology	2/10 (20%)	0.13 (0.01–1.25)	
MAP score tumor kidney			<0.001
0–3	16/53 (30%)	1.00 (reference)	
4–5	27/34 (79%)	8.92 (3.23–24.97)	

The number of patients with APF/number of patients in the category (percentage of patients with APF) is given along with the unadjusted odds ratios (95% confidence intervals) for the association with APF vs. without APF. APF, adherent perinephric fat; OR, odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; MAP, Mayo adhesive probability.

Table 4 Comparison of perioperative outcomes between patients with adherent perinephric fat and patients without adherent perinephric fat during open partial nephrectomy

Variable	Adherent perinephric fat (N=43)	No adherent perinephric fat (N=44)	P value
Operative time (min)	193 [97, 171, 206, 342]	170 [90, 142, 189, 325]	0.004
Warm ischemia time (min)	10 [0, 5, 13, 19], n=42	8 [0, 7, 14, 22], n=42	0.58
Estimated blood loss (mL)	800 [120, 600, 1,200, 2,000]	600 [0, 390, 800, 1,800]	0.003
Any postoperative complication, grade I-V, n (%)	27 (63%)	18 (41%)	0.054
Postoperative complication, grade III-V, n (%)	4 (9%)	2 (5%)	0.43
Change in laboratory measures (preoperative to POD 1)			
Hemoglobin (mg/dL)	-2.9 (-5.5, -3.7, -2.1, -1.1)	-2.8 (-6.6, -3.9, -1.8, 39.8)	0.51
Creatinine (mg/dL)	0.5 (-0.2, 0.2, 0.7, 1.5)	0.3 (-0.2, 0.2, 0.7, 9.3)	0.85
Length of hospital stay (d)	4 [3, 4, 6, 20]	4 [3, 3, 4, 13]	0.077
Length of hospital stay >3 d, n (%)	39 (91%)	32 (73%)	0.051
MIC*, n (%)	37/42 (88%)	39/43 (91%)	0.74

Data are given as the sample median (minimum, 25th percentile, 75th percentile, maximum) or number (percent). P values result from the Wilcoxon rank sum test or the Fisher exact test. Warm ischemia time was not available for 3 patients; the number of patients with available data is given for warm ischemia time and MIC. *, margins, ischemia, and complications is defined as having negative surgical margins, warm ischemia time <20 minutes, and no postoperative complications grade III or higher. P values ≤ 0.0045 were considered statistically significant after applying a Bonferroni adjustment for multiple testing based on 11 tests. MIC, margins, ischemia, and complications; POD, postoperative day.

Discussion

Nephron sparing surgery is an alternative treatment for small localized renal masses with variable postoperative outcomes (9). The presence of APF makes kidney dissection difficult which can result in excessive bleeding and decapsulation (2). The presence of APF may contribute to postoperative PN outcomes (4,10). MAP score, an image based score highly predictive of intraoperative APF during RAPN, utilizes posterior fat thickness and perinephric fat stranding as the two most reproductive variables to predict the presence of APF (1). Multiple studies have found that the presence of APF is associated with increased operative time and EBL (10). Among these studies, risk factors such as male sex, age, larger tumor size, perinephric fat stranding, increased BMI, hypertension, diabetes, waist circumference, and MAP score have been identified as predictors of APF (1,4,11-15). As such, we decided to evaluate if there is any association between APF and MAP score in patients undergoing OPNx.

Our study yielded notable findings. First, we found that MAP score is an excellent predictor of APF in OPNx. Furthermore, the presence of APF was associated with an increased operative time and higher EBL. There was evidence of an association of higher RENAL score with both longer WIT and higher postoperative complications. However, only postoperative complications remained statistically significant after adjustment for multiple comparisons.

Regardless of surgical approach, the presence of APF during PN has been estimated to be between 10.6–55.2% (16). APF was detected in 49% of patients in our study. In a previous prospective evaluation of APF in RAPN, we found the rate to be 30% (2). This higher percentage of APF in patients undergoing OPNx could be attributed to the choice to pursue OPNx over RAPN although that is not proven. At the same time, multiple studies have associated an increased prevalence of APF in elderly males (1,4,13-15). Based on our results, we support these findings. Fat distribution among men and women differ, men tend to have more visceral fat than women, and aging also contributes to an increase in the amount of visceral fat (17,18).

Darlane *et al.* conducted a retrospective study of 245 OPNx patients in which they looked for APF predictive factors. In this study, the presence of APF was noted in 40.8% of patients. MAP score was the most predictive factor for APF ($P < 0.001$). They also found that there was a

significant association between the general Clavien-Dindo classification and the presence of APF ($P = 0.05$), but when this classification was rearranged into major and minor complications, this significance was lost ($P = 0.7$) (4). In our cohort, we did find a possible association between APF and postoperative complications; however, it was not statistically significant. Martin *et al.* similarly studied a group of 86 patients who had OPNx, to assess the reproducibility of the MAP score. They found that the incidence of APF in their cohort was 50%. Age and diabetes were significant risk factors for the presence of APF. Moreover, stranding score, lateral fat thickness, posterior fat thickness and MAP score were a significant predictor for the presence of APF. After multivariate analysis, only MAP score and age remained statistically significant (15). Their results differed from our data in that there was no association between diabetes and APF.

Bylund *et al.*, studied the association between clinical and radiological variables with the presence of APF (11). In this study, the presence of APF was determined to be 55.2%. However, this group did not find an association between APF and increased blood loss. They did find an association between high grade tumors and APF (11). We propose that the increase in blood loss could be due to the highly inflammatory state which leads to increased adhesion of the perinephric fat (10). Also, the increased total operative time could be attributed to the difficulty in tumor dissection when encountering APF, rather than the result of surgeon experience. Shumate *et al.*, studied the association of APF in perioperative outcomes of 100 patients undergoing RAPN following elimination of the surgical learning curve. This group found that even after elimination of the learning curve, APF was associated with an increased operative time (19). Further studies should be conducted in order to identify additional factors that aid in the prediction of the presence of intraoperative APF in patients undergoing partial nephrectomy (20).

The strength of this study is the single surgeon nature of the evaluation to eliminate surgical technique variation as a contributor to outcomes. There are important limitations to this study. The study was performed using a cohort of patients undergoing OPNx by a high volume surgeon at a tertiary care hospital and which may limit generalizability to other populations. Additionally, the visualization of APF is subjective and can be limited by the expertise and experience of the surgeon. Thirteen out of 100 patients had no APF recorded. Lastly, our small sample size may limit the power of our conclusions. Therefore, the possibility of a

false negative association might be considered.

Conclusions

MAP score accurately predicts the presence of APF in patients undergoing OPNx. APF appears to be associated with longer operative time and EBL in OPNx.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/tau-20-926>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Mayo Clinic Hospital, (registration ID #20-008079). Because of the retrospective nature of the research, the requirement for informed consent was waived.

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