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ORIGINAL ARTICLE

The Relationship Between Preoperative Inflammatory Indexes and Adherent Perinephric Fat in Laparoscopic Partial Nephrectomy

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Abstract

Background/Aim: Partial nephrectomy (PN) is favoured for cT1a renal tumours. However, factors like adherent perinephric fat (APF), linked to prolonged operation time due to chronic inflammation are often overlooked. The objective of this study was to assess the relationship between the composite inflammatory index and APF in patients with renal cell carcinoma (RCC) prior to laparoscopic partial nephrectomy (LPN).

Methods: The retrospective analysis included 189 LPN patients from April 2015 to June 2021, categorised by APF presence. Demographic, laboratory and radiological data assessed composite inflammatory index and Mayo adhesion probability (MAP) scores. Chi-Square and Mann-Whitney U-test analysed categorical and continuous variables. Area under curve (AUC) measured parameter discrimination. Logistic regression identified APF predictive factors.

Results: APF was present in 90 patients (47.6 %). The APF-positive group had significantly higher C-reactive protein (CRP) levels and longer operation times ($p = 0.016$ and $p = 0.001$, respectively). Elevated MAP scores and systemic inflammatory index (SII) values were also observed in the APF-positive group ($p = 0.002$ and $p = 0.001$, respectively). Receiver operating characteristic (ROC) analysis determined SII's cut-off at 600 (sensitivity: 60.0 %, specificity: 60.6 %, AUC: 0.640, $p = 0.001$), MAP score at 2.5 (sensitivity: 67.8 %, specificity: 64.5 %, AUC: 0.640, $p < 0.001$) and operation time at 122.5 min (sensitivity: 74.4 %, specificity: 67.7 %, AUC: 0.807, $p < 0.001$).

Conclusion: Presented results indicate that SII is linked to APF in patients undergoing LPN and may serve as an independent predictor of APF positivity.

Key words: Tissue adhesions; Intra-abdominal fat; Nephrectomy; Laparoscopy; Carcinoma, renal cell.

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Introduction

Partial nephrectomy (PN) is favoured for cT1a renal tumours, with open partial nephrectomy (OPN), laparoscopic partial nephrectomy (LPN) and robotic partial nephrectomy (RPN) as common approaches.[1] Preoperative assessment is crucial for risk stratification and outcomes prediction, often using radiological scoring systems like R.E.N.A.L. nephrometry and PADUA scores.[2-3] However, factors like adherent perinephric fat (APF), linked to prolonged operation time due to

chronic inflammation are often overlooked.[4] APF complicates kidney mobilisation and tumour delineation, potentially causing bleeding.[5]

Mayo adhesion probability (MAP) score assesses APF in RPN, focusing on perinephric fat characteristics.[4] Additionally, inflammatory markers are believed to play a role in tumour development and prognosis. In recent years, inflammatory markers have been utilised to evaluate the inflammatory response.[6-8]

Presented study sought to examine how APF correlates with composite inflammatory indices in patients undergoing LPN.

Methods

In retrospective analysis, 189 individuals diagnosed with cT1a renal cell carcinoma (RCC) who had undergone LPN at Clinic from April 2015 to June 2021 were enrolled. Prior to commencement, study protocol received approval from the Institutional Ethics Committee (approval No: 2024/01/12/012). All LPN procedures were conducted by three seasoned urologists, each with over seven years of experience. Based on surgical records, patients were divided into two groups: APF and non-APF.

Radiological evaluations were independently conducted by two radiologists using contrast-enhanced abdominal CT or T1-weighted MRI. In cases of scoring discrepancies between the two radiologists, a consensus was reached through joint evaluation. Patients with preoperative acute urinary tract infections, lung infections, inflammatory allergic diseases, haematological diseases, insufficient data, positive lymph nodes, distant organ metastasis and non-RCC pathologies were excluded from the study.

Various preoperative demographic, laboratory, radiological and pathological factors across cohort were examined. These encompassed age, gender, body mass index (BMI), comorbidities, complete blood count (CBC), C-reactive protein (CRP), creatinine levels, presence or absence APF, tumour size, final tumour pathology, R.E.N.A.L. score, MAP score, systemic immune inflammation index (SII), systemic inflammation response index (SIRI), prognostic nutritional index (PNI), blood loss and operation duration. The MAP score is determined by the thickness of preoperative posterior perinephric fat and perinephric fat stranding. SII was computed by multiplying the platelet count (10^9/L) by the neutrophil count (10^9/L) and then dividing by the lymphocyte count (10^9/L). Similarly, SIRI was calculated by multiplying the monocyte count (10^9/L) by the neutrophil count (10^9/L) and then dividing by the lymphocyte count (10^9/L). PNI was derived by multiplying the serum albumin level (g/dL) by 10 and adding 0.005 times the lymphocyte count (mm^3).

Statistical analysis

Data analysis employed Statistical Package for Social Sciences for Windows (SPSS), v. 29.0, incorporating descriptive statistics, Chi-square test, Mann-Whitney U-test, logistic regression and receiver operating characteristic (ROC) analysis. Demographic characteristics were compared between APF groups. Chi-square and Mann-Whitney U-test assessed relationships with APF for categorical and continuous variables. Cut-off values determined significant parameters for APF prediction. AUC measured discriminatory ability, while multivariate logistic regression modelled APF probability. Data were from distinct individuals, with significance set at $p < 0.05$.

Results

The mean age of the 189 patients in the study was 55.92 years, with 66.7 % being male. Ninety patients (47.6 %) were found to be APF (Table 1 and 2). In the APF group, a statistically significant difference in CRP values was found compared to the non-APF group (1.72 ± 0.80 mg/dL vs 1.42 ± 3.10 mg/dL, respectively), ($p = 0.016$). Significant differences were observed in operation time (143.61 ± 28.76 min vs 112.63 ± 16.27 min, $p = 0.001$), MAP scores (3.06 ± 1.29 vs 2.42 ± 1.30, $p = 0.002$) and average SII values (1283.76 ± 1283.40 vs 719.04 ± 772.43, $p = 0.001$) between the APF and non-APF groups (Table 3).

Table 1: Patients' demographics

Parameters	N (%)
Gender	
Female	63 (33.3)
Male	126 (66.7)
Diabetes mellitus	
No	136 (72.0)
Yes	53 (28.0)
Smoking	
No	112 (59.3)
Yes	77 (40.7)
Hypertension	
No	119 (63.0)
Yes	70 (37.0)
Adherent perinephric fat	
No	99 (53.4)
Yes	90 (47.6)
Localisation	
Left	89 (47.1)
Right	100 (52.9)
Clear cell pathology	
Yes	169 (89.4)
No	20 (10.6)
Renal score	
4-6	61 (32.3)
7-9	79 (41.8)
10-12	49 (25.9)
Surgical margin positivity	
No	173 (91.5)
Yes	16 (8.5)
Distance	
< 1 cm	26 (13.8)
1.1-1.9 cm	83 (43.9)
> 1.9 cm	80 (42.3)
Stranding	
No stranding	68 (36.0)
Mild stranding	87 (46.0)
Severe stranding	34 (18.0)

Table 2: Patients' demographics according to adherent perinephric fat (APF) groups

Parameters	APF (n = 90)	Non-APF (n = 99)	P-value
Age (Mean, SD)	55.69 (9.43)	56.12 (9.69)	[a]0.877
BMI (Mean, SD)	26.96 (2.76)	26.78 (3.10)	[a]0.592
Gender (n, %)			
Female	28 (14.8)	35 (18.5)	[b]0.537
Male	62 (32.8)	64 (33.9)	
Diabetes mellitus (n, %)			
No	65 (34.4)	71 (37.6)	[b]0.938
Yes	25 (13.2)	28 (14.8)	
Smoking (n, %)			
No	53 (28.0)	59 (32.2)	[b]0.921
Yes	37 (19.6)	40 (21.2)	
Hypertension (n, %)			
No	57 (30.2)	62 (32.8)	[b]0.920
Yes	33 (17.5)	37 (19.6)	
Localisation (n, %)			
Left	42 (22.2)	47 (24.9)	b0.911
Right	48 (25.4)	52 (27.5)	
Clear cell pathology (n, %)			
Yes	81 (42.9)	88 (46.6)	[b]0.804
No	9 (4.8)	11 (5.8)	
Renal score (n, %)			
4-6	29 (15.3)	32 (16.9)	
7-9	35 (18.5)	44 (23.3)	[b]0.628
10-12	26 (13.8)	23 (12.2)	
Surgical margin positivity (n, %)			
No	81 (42.9)	92 (48.7)	[b]0.470
Yes	9 (4.8)	7 (3.7)	
Distance (n, %)			
< 1 cm	11 (5.8)	15 (7.9)	
1.1-1.9	40 (21.2)	43 (22.8)	[b]0.841
> 1.9	39 (20.6)	41 (21.7)	

*[a]Mann-Whitney U-test; [b]Chi-square analysis; *p < 0.05; BMI: Body mass index; SD: standard deviation;*

Table 3: Patients' radiological and laboratory parameters according to adherent perinephric fat (APF) groups

Parameters	APF (n = 90)	Non-APF (n = 99)	P-value
CRP (Mean, SD)	1.72 ± 0.80	1.42 ± 3.10	**0.016***
Creatinine (Mean, SD)	0.99 ± 0.24	0.96 ± 0.22	0.573
Tumour size (Mean, SD)	3.44 ± 0.41	3.38 ± 0.56	0.585
Blood loss (Mean, SD)	65.72 ± 16.46	62.02 ± 17.56	0.153
Operation time (Mean, SD)	143.61 ± 28.76	112.63 ± 16.27	**0.001***
MAP score	3.06 ± 1.29	2.42 ± 1.30	**0.002***
Albumin (Mean, SD)	3.74 ± 0.69	3.73 ± 0.68	0.960
SII (Mean, SD)	1283.76 ± 1283.40	719.04 ± 772.43	**0.001***
SIRI (Mean, SD)	1.47 ± 1.37	1.25 ± 1.33	0.649
PNI (Mean, SD)	37.40 ± 6.95	37.33 ± 6.81	0.975

*Mann-Whitney U Test; *p < 0.05, CRP: C-reactive protein; MAP: Mayo adhesion probability score; SII: systemic immune inflammation index; SIRI: systemic inflammation response index; PNI: prognostic nutritional index; SD: standard deviation;*

Table 4: Multivariable binary logistic regression analysis for adherent perinephric fat (APF)

Parameters	95 % CI	Odds ratio	P-value
CRP	0.718	0.343-1.503	0.379
Operation time	0.933	0.903-0.963	0.001*
MAP score	0.884	0.581-1.345	0.565
SII	1.000	0.998-1.001	0.477

**p < 0.05; CI: confidence interval; CRP: C-reactive protein; MAP score: Mayo adhesion probability score; SII: systemic immune inflammation index;*

Table 5: The receiver operating characteristic (ROC) analysis for positive prognostic factors associated with adherent perinephric fat (APF) in renal cell carcinoma

Parameters	Cut-off value	Sensitivity (%)	Specificity (%)	AUC (95 % CI)	P-value
Tumour size	3.45	0.667	0.404	0.477 (0.394-0.561)	0.592
SII	600.00	0.600	0.606	0.640 (0.560-0.720)	0.001*
SIRI	0.80	0.533	0.505	0.519 (0.434-0.604)	0.657
PNI	37.00	0.533	0.455	0.501 (0.419-0.584)	0.975
MAP score	2.50	0.678	0.645	0.640 (0.562-0.719)	0.000*
Operation time	122.50	0.744	0.677	0.807 (0.747-0.867)	0.000*

**ROC analysis, p < 0.05, CI: confidence interval; SII: systemic immune inflammation index; SIRI: systemic inflammation response index; PNI: prognostic nutritional index; MAP score: Mayo adhesion probability score;*

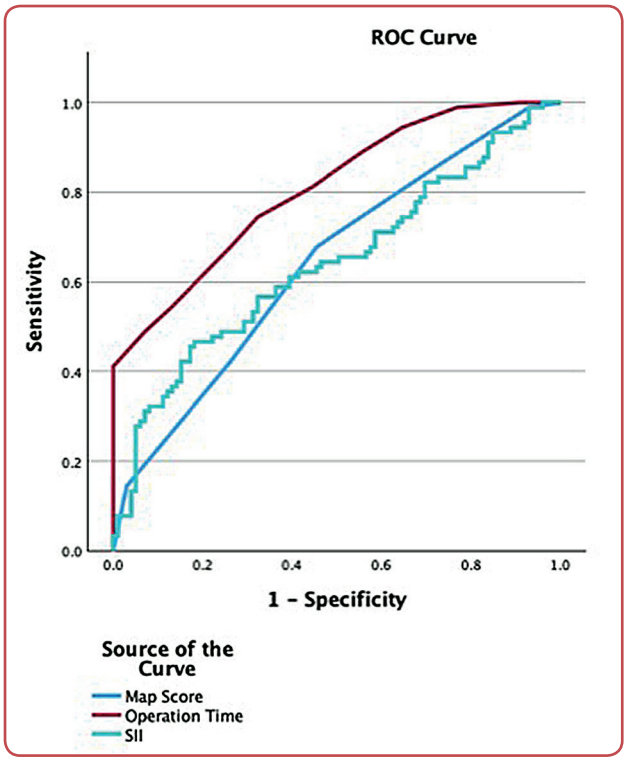

Figure 1: The receiver operating characteristic (ROC) curves for Mayo adhesion probability (MAP) score, systemic inflammatory index (SII) and operation time

No significant differences were found in SIRI and PNI between the groups (p = 0.649 and p = 0.975, respectively). Multivariate logistic regression analysis (Table 4) revealed a significant effect of operation time on APF (OR: 0.930, 95 % CI: 0.899-0.961, p = 0.001).

Receiver operating characteristic (ROC) analysis (Table 5) identified cut-off values for SII (600), MAP score (2.5) and operation time (122.5 min) with corresponding sensitivities and specificities. The AUC values were 0.640 (SII and MAP score) and 0.807 (operation time) (p < 0.001). ROC curves are depicted in Figure 1.

Discussion

The study aimed to explore APF's relationship with composite inflammatory markers in RCC patients undergoing LPN. Results identified CRP, operation time, SII value and MAP score as significant predictors of APF positivity. LPN has become the preferred method for treating small renal tumours due to technological advancements.[9] Factors like tumour location, size, vascular structure and patient-related factors, along with APF presence, can complicate kidney mobilisation and tumour exposure, potentially leading to surgical complications and prolonged operation times.[10]

Kawamura et al investigated the impact of APF on complications in patients undergoing PN in a study with 231 Asian patients and found a significant increase in blood loss.[11] Macleod et al showed that the adhesiveness and thickness of perinephric fat could affect increased operation time and blood loss, making the surgery more

complex in their study of 53 patients undergoing RPN.[12] In presented study, although blood loss did not significantly differ in the APF group, operation times were notably prolonged. These results suggest that preoperative evaluation of APF may be important for patient selection and more accurate planning in the preoperative period.

The mechanism of APF formation remains unclear but is believed to involve fibrosis, autoimmunity or inflammatory reactions.[13] While this study found a significant association between CRP elevation and APF positivity, this may be a natural consequence of inflammation rather than clinically significant. Recent studies have explored composite inflammatory markers, including neutrophil, lymphocyte and monocyte levels, to detect APF. Neutrophils, originating from the bone marrow, play a key role in phagocytosis and bacterial killing, potentially influenced by cytokines in the tumour microenvironment. This increase can lead to a decrease in lymphocytes and a reduction in immune function. Monocytes gather around the tumour, supporting the inflammatory response and tumour growth.[14] Inflammation cytokines increase platelet counts and promote tumour proliferation. Increased neutrophils, platelets and monocytes indicate worsening inflammation, while decreased lymphocytes suggest reduced anti-tumour immunity.

Composite inflammatory indexes can reflect immunity and inflammation more comprehensively.[15] SII, a novel inflammation index based on neutrophil, platelet and lymphocyte counts, has been linked to poor prognosis in various cancers.[16-18] Ma et al found SII predictive of APF in LPN patients, echoing study's findings.[19] The mechanism may involve chronic systemic inflammation triggering tissue adhesion, leading to APF formation characterised by dense foci on CT imaging.[20, 21] Despite the MAP score's high sensitivity and specificity, presented study suggests SII's simplicity, objectivity and cost-effectiveness make it a favourable choice for APF prediction. Feng et al demonstrated that SII is associated with postoperative infectious complications following colorectal cancer surgery.[22] Presented study did not examine the relationship between postoperative complications and composite inflammatory markers, but in the future, authors plan to evaluate the effects of APF SII and other inflammatory indexes on postoperative complications.

Presented study has several limitations. Firstly, although patients with inflammatory conditions and those that could affect inflammatory markers were excluded from the study, the retrospective nature of the study means that there was a possibility of including other conditions that could affect inflammatory markers. Secondly, there is no established standard cut-off value for SII and other inflammatory markers in the literature. Thirdly, only patients undergoing LPN were included. The results for OPN and RPN is unknown. Fourthly, single-centre study with a small sample size underscores the need for larger, multicentre prospective studies for conclusive findings in the future.

Conclusion

This study demonstrated that the SII is associated with APF in patients diagnosed with RCC and may serve as an independent predictor. Its ease of calculation, objectivity and low cost make it a preferable tool for preoperative detection of APF. This can assist surgeons in evaluating surgical risks and making more accurate preoperative plans.

Ethics

The study was approved by the Ethical Committee of the University of Health Sciences, Bagcilar Training and Research Hospital, approval number: 2024/01/12/012, dated 12 January 2024.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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