

# Visceral fat is associated with high-grade complications in patients undergoing minimally invasive partial nephrectomy for small renal masses

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## Abstract

**Introduction:** Minimally invasive partial nephrectomy is standard of care treatment for small renal masses.

**Objective:** We evaluated the relationship between subcutaneous and visceral obesity with high-grade postoperative 30-day complications in patients undergoing minimally invasive partial nephrectomy.

**Methods:** We retrospectively identified 98 patients at our institution from 2014 to 2017 who underwent laparoscopic or robotic-assisted partial nephrectomy due to suspected renal cell carcinoma. Patients were stratified based on presence or absence of high-grade (Clavien  $\geq$  IIIa) 30-day postoperative complications. Means were compared with the independent *t* test and proportions with chi-square analysis. Multivariate logistic regression was performed to determine independent predictors of high-grade 30-day complications.

**Results:** Mean nephrometry score was 6.7 with 21 (21.4%) patients having hilar tumors. Mean estimation of blood loss was 207 mL, mean operating time was 223 min, and mean warm ischemia time was 23 min. The majority of patients had clear renal cell carcinoma ( $n=83$ , 84.7%) and pT1a disease ( $n=76$ , 77.6%) with negative margins ( $n=89$ , 90.8%) on pathology. There were 5 (5.1%) patients who experienced a high-grade postoperative 30-day complication. Mean visceral fat index was an independent predictor of high-grade 30-day complications (odds ratio: 1.02; 95% confidence interval: 1.002–1.03;  $p=0.027$ ).

**Conclusions:** Visceral obesity should be considered as a prognostic indicator of outcomes in patients undergoing surgical treatment for a small renal mass.

**Keywords:** Complications; Minimally invasive surgery; Partial nephrectomy; Renal mass; Subcutaneous fat; Visceral fat

## 1. Introduction

Partial nephrectomy, utilizing the laparoscopic or robotic-assisted approach, has become the standard of care when managing small, operable renal masses that are suspicious for renal cell carcinoma (RCC).<sup>[1]</sup> Partial nephrectomy preserves renal function while maintaining similar oncological control compared to radical nephrectomy.<sup>[2]</sup> Minimally invasive approaches to partial nephrectomy cannot only improve healing time but have also been shown to have similar oncological efficacy as open surgery.<sup>[3–5]</sup>

Adipose tissue, or fat, is often assessed through the body mass index (BMI), which provides an incomplete picture of fat distribution. More specific measurements of fat distribution may

be valuable in predicting complications after minimally invasive partial nephrectomy. Subcutaneous, visceral, and perinephric fat are 3 common tissue measurements that have been previously utilized for investigation in these procedures.<sup>[6]</sup> Subcutaneous fat refers to the adipose tissue between the skin and anterior abdominal wall fascia, visceral fat includes fat surrounding organs inside the abdominal cavity, and perinephric fat is strictly the adipose tissue encasing the kidneys within Gerota's fascia.<sup>[7]</sup>

The literature is inconclusive on whether and what type of fat distribution is predictive of short-term outcomes after minimally invasive partial nephrectomy. Some articles report no association between fat distribution and surgical outcomes after laparoscopic or robotic-assisted partial nephrectomy,<sup>[6,8]</sup> while others have demonstrated direct correlations between obesity and surgical complications, though the significance of these results vary.<sup>[7,9–11]</sup> In this study, we sought to determine an association between these 3 different types of fat distribution measurements and 30-day postoperative surgical outcomes after minimally invasive partial nephrectomy for small renal masses.

## 2. Materials and methods

All study subjects have given their written informed consent to participate in compliance with the guidelines for human studies. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki, and our

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study protocol was approved by the Texas Tech University Health Sciences Center committee on human research.

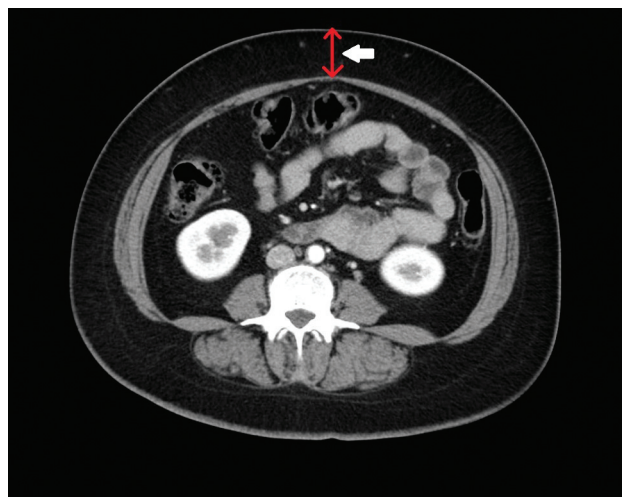
### 2.1. Data collection

After institutional review board approval (TTUHSC IRB#: L18-140), we retrospectively identified 98 patients who underwent laparoscopic (LAPN) or robotic-assisted partial nephrectomy (RAPN) for a renal mass due to suspected RCC at our institution (Texas Tech University Health Sciences Center) between January 2014 and December 2017 with curative intent. Pathology was confirmed by central histopathological review of the renal mass specimen. We excluded patients with urothelial carcinoma of the kidney, patients with clinically suspected metastatic disease to the kidney or metastatic RCC (confirmed through pathology or radiographic imaging), patients who received prior surgery (including partial nephrectomy) or ablative therapy (including cryotherapy or radiofrequency ablation) for their suspected renal mass, as well as patients who received prior systemic therapy (including tyrosine kinase inhibitors) or radiation therapy to the kidney for treatment.

Sociodemographics including age, gender, race, BMI, and comorbidity indicators (Charlson Comorbidity Index) were collected and abstracted from the initial urology clinic visit. Additional accompanying clinical conditions were identified and collected separately including the presence or absence of diabetes (defined as treatment with oral medications or insulin-dependent diabetes and/or a hemoglobin A1c > 6.5), chronic kidney disease (defined as an estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m<sup>2</sup>), and a history of tobacco abuse on initial presentation to the Urology clinic. American Society of Anesthesiologists score was assessed at time of LAPN or RAPN by the covering anesthetist. Preoperative creatinine (Cr) levels and eGFR values were abstracted and recorded based on the most recent serum levels prior to surgery, while postoperative values were measured at 3 months after surgery. Postoperative change in eGFR was subsequently calculated by subtracting postoperative serum levels measured at 3 months after LAPN or RAPN from preoperative measurements.

Subcutaneous fat thickness was measured manually with an electronic ruler on computed tomography (CT) scan imaging from the skin to the fascia of the anterior abdominal wall (ie, anterior rectus fascia) measured in centimeters (cm) (Fig. 1). Subcutaneous fat index consisted of the entire circumferential area of subcutaneous adipose tissue (in cm<sup>2</sup>) from the skin to the muscle layer of the abdominal cavity (Fig. 2A). Visceral fat index was defined as the area of all adipose tissue within the abdominal wall musculature and abdominal cavity measured in cm<sup>2</sup> (Fig. 2B). Finally, perinephric fat thickness was measured manually with an electronic ruler on CT scan imaging as an average of the distance from the lateral and posterior abdominal wall to the level of the renal capsule measured in cm (Fig. 3). All imaging measurements were made at the L3–4 level (kidney level) on an axial slice CT scan with thickness of 3 mm with patients in the supine position.

To determine tumor complexity during surgical resection with partial nephrectomy, the R.E.N.A.L nephrometry standardized scoring system was utilized for quantitating renal tumor size, location, and depth based on (R)adius (tumor size as maximal diameter in cm), (E)xophytic/endophytic properties of the tumor, (N)earness of tumor deepest portion to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor and the (L)ocation relative to the polar lines.<sup>[12]</sup> The suffix h (hilar) was assigned to tumors that abut the main renal artery or vein. Mean percent

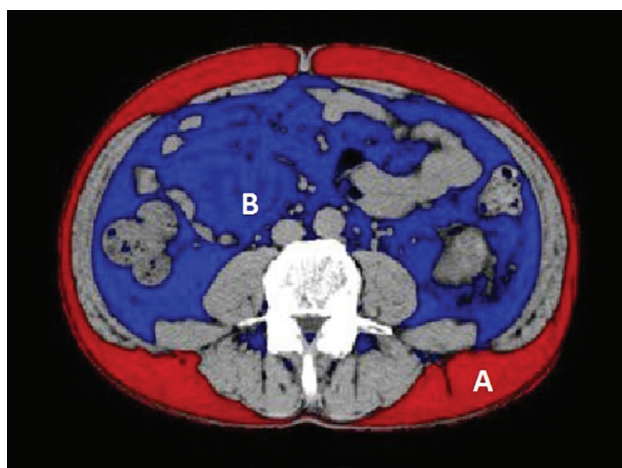


**Figure 1.** Measurement technique of subcutaneous fat thickness on axial computed tomography scan image.

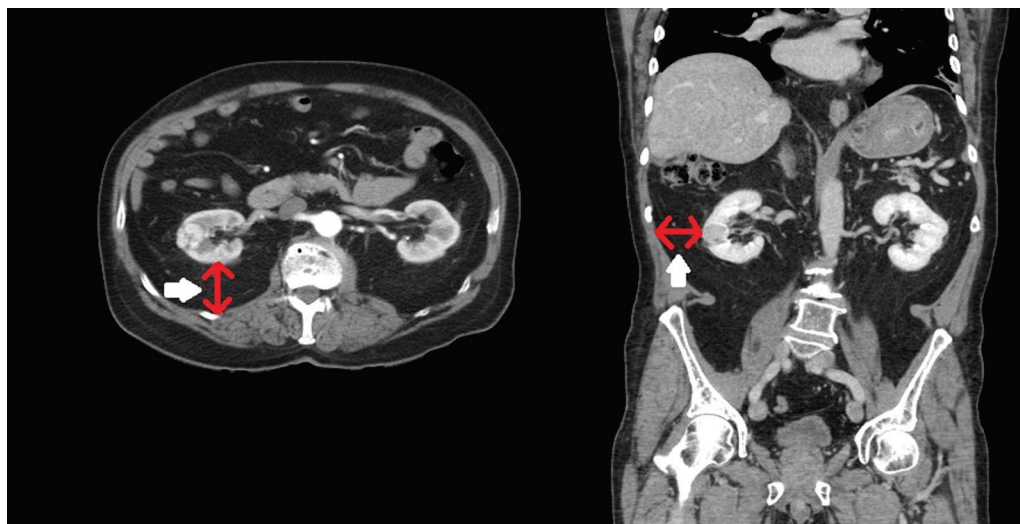
tumor to kidney diameter was also measured by dividing the tumor size at the maximal diameter by the kidney size at the maximal diameter.

### 2.2. Clinical management and follow-up

Partial nephrectomy was performed robotically or laparoscopically with warm ischemia using bulldog clamps for hilar clamping of the renal artery and/or renal vein. Need for clamping of the renal artery and/or renal vein was based on intraoperative assessment by the surgeon. The surgical approach to partial nephrectomy (transperitoneal vs. retroperitoneal) was also dependent on surgeon comfort. Ultrasound-guided demarcation of the renal mass prior to partial nephrectomy was based on the exophytic or endophytic nature of the tumor and surgeon decision-making. A concurrent lymphadenectomy or hilar lymph node dissection was not routinely performed during partial nephrectomy. A 2-layer renorrhaphy was typically performed after partial nephrectomy.



**Figure 2.** Measurement technique of subcutaneous fat index (A-red) and visceral fat index (B-blue) on axial CT scan image.



**Figure 3.** Measurement technique of perinephric fat thickness on axial CT scan image.

Use of an abdominal Jackson-Pratt drain or ureteral stent postoperatively was surgeon dependent. Length of stay was defined as the time elapsed (in days) from the date of surgery until the date of initial hospital discharge. Complications were captured via retrospective chart review of the patient's postoperative course (ie, progress notes, telephone records, and discharge summaries) and subsequent clinic visits up to 30 days after LAPN or RAPN. The Clavien-Dindo classification was used to categorize 30-day complications with high-grade complications defined as Clavien  $\geq$  IIIa within 30 days of surgery. Finally, National Comprehensive Cancer Network guidelines were used to define pathological tumor stage and Fuhrman grade based on final histopathological review of the submitted renal mass specimen.<sup>[1]</sup>

### 2.3. Statistical analysis

Our primary endpoint was the development of a high-grade complication (defined as Clavien  $\geq$  IIIa) within 30 days after LAPN or RAPN. Secondary endpoints included the incidence of any 30-day complication after surgery, mean postoperative change in eGFR at 3 months, and surgical margin status on final histopathology.

Continuous variables were reported as means and standard deviations (SD), and categorical variables were reported as frequency counts and percentages. We used the independent *t* test to determine any differences in continuous variables and the chi-square test for categorical variables. Multivariate logistic regression analysis was performed using clinically relevant pre-determine variables in addition to our three fat indicators/measurements to evaluate the association of these reported variables with our primary endpoint, and odds ratios (OR) with 95% confidence intervals (CI) were reported.

Statistical analysis was performed with the Statistical Package for the Social Sciences software package (IBM Corporation, Armonk, NY). All tests were 2-sided, with  $p < 0.05$  considered to be statistically significant.

## 3. Results

Patient sociodemographics and clinical characteristics are shown in Table 1. Mean age of our study population was 56.7 years and

mean BMI was 33.0 kg/m<sup>2</sup>. The majority of our patients were non-hispanic white (53.1%), male (52.0%), non-smokers (57.1%), non-diabetic (75.5%), and without chronic kidney disease (81.6%). Mean preoperative Cr was 0.95 mg/dL (eGFR = 82 mL/min/1.73 m<sup>2</sup>). In terms of body morphometrics, mean subcutaneous fat thickness was 2.59 cm, mean perinephric fat thickness was 2.02 cm, and mean visceral fat index was 180 cm<sup>2</sup>.

Patient disease-specific characteristics are shown in Table 2. Mean nephrometry score was 6.7 with 21 (21.4%) patients having hilar tumors. Incidence of anterior (n=35, 35.7%), posterior (n=35, 35.7%), and lateral (n=28, 28.6%) tumors were similar. Mean tumor/kidney diameter was 29%. Mean estimation of blood loss (EBL) during surgery was 207 mL, mean operative time was 223 min, and mean warm ischemia time was 23 min. The majority of patients had clear cell RCC (n=83, 84.7%) and pT1a disease (n=76, 77.6%) with lower Fuhrman grade (I-II) (n=79, 80.6%) and negative surgical margins (n=89, 90.8%). Mean postoperative Cr at 3 months after partial nephrectomy was 0.93 mg/dL with an eGFR of 85 mL/min/1.73 m<sup>2</sup>. Mean postoperative change in eGFR was 10 mL/min/1.73 m<sup>2</sup>.

Mean length of stay after surgery was 2.5 days. One intraoperative complication (a small bowel serosal injury requiring primary repair and closure) was identified. The overall 30-day postoperative complication rate after partial nephrectomy was 20.6% (n=20). There were 10 (10.2%) patients who had a grade I complication within 30 days after LAPN or RAPN, and 5 (5.1%) patients had a grade II complication. There were 5 (5.1%) patients experienced a high-grade postoperative 30-day complication after surgery with one postoperative death and a 30-day mortality rate of 1% after LAPN or RAPN. Patients who experienced high-grade postoperative complications 30 days after LAPN or RAPN were more likely to be male (100% vs. 49.5%,  $p=0.028$ ), have an intraoperative complication (20% vs. 0%,  $p < 0.01$ ), and have a higher mean postoperative Cr level at 3 months after surgery (1.28 vs. 0.91 mg/dL,  $p=0.011$ ).

Predictors of postoperative 30-day high-grade complications after partial nephrectomy are shown in Table 3. Mean visceral fat index was an independent predictor of high-grade complications

**Table 1**  
**Patient sociodemographics and clinical characteristics.**

	No high-grade complications (n=93)	High-grade complications (n=5)	Total (n=98)	p
Mean age, y	56.6 ± 13.6	58.6 ± 18.7	56.7 ± 13.8	0.75
Mean BMI, kg/m <sup>2</sup>	33.2 ± 12.5	28.9 ± 9.2	33.0 ± 12.4	0.50
Race, n (%)				0.79
Non-hispanic white	49 (52.7)	3 (60.0)	52 (53.1)	
Hispanic white	36 (38.7)	2 (40.0)	38 (38.8)	
Black	8 (8.6)	0 (0.0)	8 (8.2)	
Gender, n (%)				0.028
Male	46 (49.5)	5 (100.0)	51 (52.0)	
Female	47 (50.5)	0 (0.0)	47 (48.0)	
History of tobacco abuse, n (%)				0.44
None	53 (57.0)	3 (60.0)	56 (57.1)	
Former	19 (20.4)	0 (0.0)	19 (19.4)	
Current	21 (22.6)	2 (40.0)	23 (23.5)	
Prior abdominal surgery, n (%)				0.18
No	46 (49.5)	4 (80.0)	50 (51.0)	
Yes	47 (50.5)	1 (20.0)	48 (49.0)	
ASA score, n (%)				0.34
1–2	36 (38.7)	3 (60.0)	39 (39.8)	
3–4	57 (61.3)	2 (40.0)	59 (60.2)	
CCI, n (%)				0.99
0–3	38 (40.9)	2 (40.0)	40 (40.8)	
4–5	38 (40.9)	2 (40.0)	40 (40.8)	
≥6	17 (18.3)	1 (20.0)	18 (18.4)	
Diabetes, n (%)				0.81
No	70 (75.3)	4 (80.0)	74 (75.5)	
Yes	23 (24.7)	1 (20.0)	24 (24.5)	
CKD, n (%)				0.20
No	77 (82.8)	3 (60.0)	80 (81.6)	
Yes	16 (17.2)	2 (40.0)	18 (18.4)	
Mean preoperative Cr, mg/dL	0.95 ± 0.33	0.93 ± 0.15	0.95 ± 0.33	0.93
Mean preoperative eGFR, mL/min/1.73m <sup>2</sup>	81 ± 25	93 ± 26	82 ± 24	0.42
Mean subcutaneous fat thickness, cm	2.64 ± 1.26	1.54 ± 0.52	2.59 ± 1.25	0.054
Mean subcutaneous fat index, cm <sup>2</sup>	263 ± 149	143 ± 63	257 ± 148	0.079
Mean perinephric fat thickness, cm	1.98 ± 1.27	2.70 ± 2.11	2.02 ± 1.32	0.24
Mean visceral fat index, cm <sup>2</sup>	176 ± 106	242 ± 275	180 ± 118	0.23

ASA = American Society of Anesthesiologists, CCI = comprehensive complication index, CDK = chronic kidney disease.

within 30 days of surgery on multivariate analysis (OR: 1.02; 95% CI: 1.002–1.03;  $p=0.027$ ).

#### 4. Discussion

We evaluated 3 easily measured adipose tissue variables (perinephric fat, subcutaneous fat, and visceral fat) as predictors of 30-day high-grade complications after minimally invasive partial nephrectomy. Our findings concluded that the degree of perinephric fat was not associated with a higher complication rate after surgery in our study population ( $p=0.24$ ). In 2 prior studies by Kocher et al.<sup>[13]</sup> and Lee et al.,<sup>[14]</sup> they found that perinephric fat was associated with longer operative times and increased EBL. Another study by Khene et al.<sup>[15]</sup> found that the amount of perinephric fat was associated with a higher risk of conversion to open surgery as well as radical nephrectomy in addition to increased EBL and perioperative blood transfusion rate. A study by Davidiuk et al.,<sup>[16]</sup> however, found that while perinephric fat may be associated with slightly longer operative times during RAPN, it does not affect perioperative outcomes or complication rates, which is further supported by our results. A possible flaw in our study design was using a linear measurement from the posterior edge of the kidney to the wall of the

retroperitoneum for perinephric fat. This measurement technique was chosen because previous research used the same linear measurement.<sup>[10]</sup> Area measurements, on the other hand, were used for both subcutaneous and visceral fat variables, which may have been a higher fidelity metric in detecting an association with our desired outcomes.

In our study, the degree of subcutaneous fat was not a statistically significant predictor of 30-day postoperative outcomes after LAPN or RAPN. Both measurements of subcutaneous fat including the linear distance from the skin to the anterior abdominal wall ( $p=0.054$ ) as well as the area ( $p=0.079$ ) of subcutaneous fat at the level of the kidney were not associated with the 30-day complication rate after surgery. Macleod et al.<sup>[10]</sup> reported no relationship between the degree of abdominal wall fat and operative times or EBL although perinephric fat measurements were independently associated with increased EBL and operative times during surgery. For each 1-mm increase in medial perinephric fat, EBL increased 24 mL and operative time increased 3.3 min in their study. Another study by Raman et al.<sup>[7]</sup> reported that an increased proportion of perinephric to subcutaneous fat increased the risk of complications following RAPN (OR: 1.82,  $p=0.02$ ) as well as operative times, but neither measurement on their own was predictive of these endpoints.

**Table 2**  
**Patient disease-specific characteristics.**

	No high-grade complications (n=93)	High-grade complications (n=5)	Total (n=98)	p
Mean nephrometry score, n	6.6±2.1	7.0±3.3	6.7±2.2	0.72
Tumor location, n (%)				0.30
Anterior	33 (35.5)	2 (20.0)	35 (35.7)	
Posterior	32 (34.4)	3 (60.0)	35 (35.7)	
Lateral	28 (30.1)	0 (0.0)	28 (28.6)	
Hilar location, n (%)				0.30
No	74 (79.6)	3 (60.0)	77 (78.6)	
Yes	19 (20.4)	2 (40.0)	21 (21.4)	
Mean tumor/kidney diameter, n (%)	29 (16)	31 (15)	29 (16)	0.77
Mean operative time, minutes	223±63	209±31	223±62	0.65
Mean EBL, mL	200±206	350±367	207±216	0.13
Mean warm ischemia time, min	23±15	30±4	23±14	0.39
Intraoperative blood transfusion, n (%)				0.52
No	86 (92.5)	5 (100.0)	91 (92.9)	
Yes	7 (7.5)	0 (0.0)	7 (7.1)	
Intraoperative complication, n (%)				<0.01
No	93 (100.0)	4 (80.0)	97 (99.0)	
Yes	0 (0.0)	1 (20.0)	1 (1.0)	
Mean length of stay, d	2.5±2.0	3.2±2.5	2.5±2.0	0.44
Mean postoperative Cr, mg/dL	0.91±0.30	1.28±0.36	0.93±0.32	0.011
Mean postoperative eGFR, mL/min/1.73m <sup>2</sup>	86±26	65±21	85±26	0.095
Mean postoperative change in eGFR, mL/min/1.73m <sup>2</sup>	10±12	24±14	10±12	0.06
Histology, n (%)				0.97
Clear cell RCC	78 (83.9)	5 (100.0)	83 (84.7)	
Papillary RCC	3 (3.2)	0 (0.0)	3 (3.1)	
Chromophobe RCC	2 (2.2)	0 (0.0)	2 (2.0)	
Oncocytic RCC	6 (6.5)	0 (0.0)	6 (6.1)	
Angiomyolipoma	3 (3.2)	0 (0.0)	3 (3.1)	
Oncocytoma	1 (1.1)	0 (0.0)	1 (1.0)	
Pathological T stage, n (%)				0.88
T1a	72 (77.4)	4 (80.0)	76 (77.6)	
T1b	12 (12.9)	1 (20.0)	13 (13.3)	
T2–T3	5 (5.4)	0 (0.0)	5 (5.1)	
Negative for malignancy	4 (4.3)	0 (0.0)	4 (4.1)	
Pathological Fuhrman grade, n (%)				0.53
I–II	74 (79.6)	5 (100.0)	79 (80.6)	
III–IV	15 (16.1)	0 (0.0)	15 (15.3)	
Negative for malignancy	4 (4.3)	0 (0.0)	4 (4.1)	
Surgical margins, n (%)				0.39
Negative	85 (91.4)	4 (80.0)	89 (90.8)	
Positive	8 (8.6)	1 (20.0)	9 (9.2)	

**Table 3**  
**Predictors of postoperative 30-day high-grade complications.**

	OR	Multivariate		p
		95% CI		
		Lower	Upper	
Mean ASA score	0.10	0.009	1.19	0.069
Mean CCI	0.45	0.13	1.51	0.19
Mean BMI, kg/m <sup>2</sup>	0.96	0.85	1.09	0.55
Mean subcutaneous fat index, cm <sup>2</sup>	0.98	0.95	1.001	0.061
Mean visceral fat index, cm <sup>2</sup>	1.02	1.002	1.03	<b>0.027</b>
Mean nephrometry score	1.58	0.81	3.07	0.18

ASA = American Society of Anesthesiologists, CCI = comprehensive complication index.  
Bold values are statistically significant variables ( $p < 0.05$ ).

Since the  $p$ -values in our study approached statistical significance, there is the possibility of a type II error with a larger cohort yielding different results. Additionally, changing the measurement location from the level of the kidney to the level of the incisions and/or instrument placement might increase the accuracy of this association.

The only statistically significant predictor of 30-day high-grade complications after LAPN or RAPN in our study was the amount of measured visceral fat (based on area) at the level of the kidney ( $p=0.027$ ), which is surprising given prior literature reporting on its minimal impact on surgical field visibility.<sup>[6]</sup> Ioffe et al.<sup>[6]</sup> found no association between visceral fat and perioperative parameters including EBL, complications, and warm ischemia time after laparoscopic or RAPN. Gorin et al.,<sup>[11]</sup> on the other hand, found that intra-abdominal fat was independently associated with complications following minimally invasive partial nephrectomy in their single-institutional cohort of 195 patients. Finally, a prior study by Lee et al.<sup>[17]</sup> found that visceral fat was actually predictive of better prognosis in patients undergoing nephrectomy for advanced RCC. High visceral fat area (defined as >50 percentile in each sex) was associated with longer cancer-specific survival ( $p=0.01$ ) and overall survival ( $p=0.03$ ) during follow-up. A possible flaw with visceral fat index, however, is the variability of the abdominal structure from person to person secondary to patient organ distribution. Visceral fat is also linked to obesity complications such as type II diabetes and coronary artery disease, while subcutaneous fat is typically not.<sup>[18]</sup> Visceral fat is believed to have the greatest negative effect on metabolic and cardiovascular health when compared to other adipose tissue measurements such as subcutaneous fat or perinephric fat. Larger amounts of visceral fat correlate with health complications such as type II diabetes, hypertension, and heart disease. Visceral fat, therefore, may be a good predictor of high-grade 30-day complications after LAPN or RAPN not secondary to its impact on surgical field visibility but due to a higher risk of associated comorbidities and metabolic syndrome that make patients more prone to complications in the postoperative period such as wound infection, myocardial infarction, stroke, blood clots in the legs or lungs, etc.

Other limitations of our study include its retrospective nature, relatively small sample size, variability in recorded perinephric, subcutaneous, and visceral fat measurements based on imaging (ie, CT scan) level as well as methodology, and lack of consideration of confounding variables such as medical comorbidities that, as noted above, may also increase in prevalence with certain fat measurements. Our study cohort of 98 patients is relatively small with a small number of high-grade complications ( $n=5$ ) being our primary endpoint of analysis, so statistical calculations remain speculative with a high probability of type II error, which limits the ability for broad generalization of our results to the population. Despite these limitations, we feel that our results are helpful in determining and raising awareness to factors that may influence short-term outcomes after partial nephrectomy in a hypothesis-generating fashion that may be confirmed or validated in future well-planned prospective trials or studies, which is beyond the scope of our present study.

## 5. Conclusions

Increasing visceral fat is associated with more high-grade postoperative 30-day complications in patients undergoing LAPN or RAPN in the treatment of small renal masses suspicious for primary RCC. Future studies could examine larger cohorts

across multiple institutions using three-dimensional morphometrics to minimize imaging-related variability and improve accuracy. Alternative fat measurements including adiposity or sarcopenic obesity may also be useful prognostic variables to examine and evaluate in the future in this patient group when undergoing surgery in the treatment of renal malignancies.

## Acknowledgments

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## Statement of ethics

All ethical guidelines were followed according to the Texas Tech University Health Sciences Center Institutional Review Board, which reviewed and approved this study. All patient information was de-identified and secured in a protected network.

## Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

## Funding source

None.

## Author contributions

Kelan Nesbitt and Pranav Sharma both fully contributed to the development of this study, creation of the IRB protocol, data collection, statistical analysis, and construction, revision, and approval of the final manuscript.

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