

Tumour contact surface area as a predictor of postoperative complications and renal function in patients undergoing partial nephrectomy for renal tumours

Vincenzo Ficarra* , Alessandro Crestani[†] , Riccardo Bertolo[‡] , Alessandro Antonelli[§], Nicola Longo[¶], Andrea Minervini* , Giacomo Novara^{††}, Claudio Simeone[§], Marco Carini* , Vincenzo Mirone[¶], Francesco Porpiglia[‡]  and Collaborators[‡]

*Urologic Section, Department of Human and Pediatric Pathology 'Gaetano Barresi', University of Messina, Messina, [†]Urology Unit, Academic Medical Centre Hospital 'Santa Maria della Misericordia', Udine, [‡]Division of Urology, San Luigi Gonzaga Hospital Orbassano, University of Turin, Turin, [§]Urology Unit, ASST, Spedali Civili di Brescia, University of Brescia, Brescia, [¶]Department of Urology, University of Federico II of Naples, Naples, ^{**}Department of Urology, Careggi Hospital, University of Florence, Florence, and ^{††}Department of Oncologic, Surgical and Gastrointestinal Sciences, Urologic Unit, University of Padua, Padua, Italy

[‡]Collaborators are listed in Appendix 1

Objectives

To evaluate the ability of original tumour contact surface area (CSA) to predict postoperative complications and renal function impairment in a series of patients who underwent elective partial nephrectomy (PN) for renal masses.

Materials and Methods

We analysed the clinical records of 531 consecutive patients who underwent elective PN because of a suspicion of kidney cancer at five academic, high-volume centres between January 2014 and December 2016. Each participating centre evaluated prospectively the radiological images to evaluate the CSA and to assign a PADUA score. Several expert surgeons performed the surgical procedures in each participating centre. Binary logistic regression was used to perform both univariable and multivariable analyses to identify predictors of postoperative complications. Linear regression analysis was used to identify independent predictors of absolute change in estimated glomerular filtration rate (eGFR; ACE).

Results

The median (interquartile range) CSA value was 14.2 (7.4–25.1) cm². A total of 349 tumours (65.7%) had a CSA ≤ 20 cm² and the remaining 182 (34.3%) had a CSA > 20 cm². PNs were performed using an open approach in 237 (44.6%) cases, a pure laparoscopic approach in 152 cases (28.6%), and

a robot-assisted approach in the remaining 142 cases (26.7%). Multivariable analyses found that only age (odds ratio [OR] 1.037, 95% confidence interval [CI] 1.018–1.057) and PADUA score (OR 1.289, 95%CI 1.132–1.469) were independent predictors of postoperative complications. Tumour CSA (OR 1.020, 95%CI 1.010–1.030) was found to be an independent predictor of postoperative complications only when PADUA score was removed from the model. Age (from –0.639 to –0.306; $P < 0.001$); body mass index (from 0.267 to 1.076; $P = 0.001$), age-adjusted Charlson score (from –3.193 to –0.259; $P = 0.02$), preoperative eGFR value (from –0.939 to –0.862; $P < 0.001$) and tumour CSA (from –0.260 to –0.048; $P = 0.005$) were found to be independent predictors of ACE.

Conclusions

Tumour CSA is an independent predictor of postoperative renal function. Conversely, at multivariable analysis, PADUA score outperformed tumour CSA to predict postoperative complications after PN. The complexity of The Leslie et al. formula for calculating tumour CSA is a potential limitation with regard to its diffusion and application in clinical practice.

Keywords

renal cell carcinoma, partial nephrectomy, nephrometry scores, peri-operative outcomes, pathological features

Introduction

The relationship between renal masses and the adjacent anatomical structures allows surgeons to evaluate the complexity of the planned partial nephrectomy (PN), improving patient selection criteria and aiding the preoperative counselling process. Specifically, predicting the risk of peri-operative complications and renal function impairment can assist the urologist in decision-making with regard to radical nephrectomy vs PN as well as on open vs laparoscopic (either pure or robot-assisted) PN procedures [1]. Moreover, the assessment of standardized and objective variables in a score significantly improved the real comparability among different PN series, regardless of the approach used [2].

The RENAL nephrometry score, the PADUA classification, and the centrality index represented the first-generation of renal tumour complexity scoring systems proposed in the literature [3–5]. A recent systematic review of the literature showed that the RENAL and PADUA scoring systems were the most popular and frequently used nephrometry scores. Interestingly, available validation studies of first-generation systems showed conflicting results, probably as a consequence of the heterogeneity of the evaluated series [1].

With the aim of improving the predictive ability of previous nephrometry scores, Leslie *et al.* [6] proposed the use of a novel imaging variable based on the calculation using CT scan data of the renal tumour contact surface area (CSA) with the adjacent parenchyma. This variable predicted adverse tumour characteristics and the most important peri-operative outcomes. Moreover, the CSA seems to outperform the PADUA score in the prediction of operating time, estimated blood loss (EBL), complications, length of stay (LOS) and $\geq 10\%$ decrease in estimated GFR (eGFR). Recently, Hsieh *et al.* [7] proposed a simplified formula to calculate the tumour CSA, confirming its role as a predictor of renal function impairment after PN. Although Haifler *et al.* [8] externally validated the previous formula based on the assumption that all the renal tumours can be modelled as a sphere, the original formula proposed by Leslie *et al.* is still lacking external validation.

In this setting, we decided to evaluate the ability of the original CSA proposed by Leslie *et al.* to predict postoperative complications and renal function impairment in a series of patients who underwent elective PN for renal masses.

Patients and Methods

We analysed the prospectively collected clinical records of 531 consecutive patients who underwent elective PN because of a suspicion of kidney cancer at one of five academic, high-volume centres (Brescia, Florence, Naples, Turin [Orbassano] and Udine, Italy) between January 2014 and December 2016. Prior to surgery, all patients underwent three-dimensional

abdominal CT or abdominal MRI to define the clinical stage and the anatomical characteristics of the tumours. All the radiological images were prospectively evaluated by each centre with the aim of assigning the PADUA score [4] and the tumour CSA, according to the formula described by Leslie *et al.* [6]. Briefly, this imaging variable was calculated applying three-dimensional rendering software during preoperative CT. Specifically, after measurement of tumour volume and percentage of tumour located within the renal parenchyma, the total surface area (TSA) of the tumour is calculated using the formula $4\pi r^2$ for surface area of a sphere, where r equals the tumour radius. The tumour CSA is calculated by multiplying the TSA by the percentage of intraparenchymal component ($CSA = TSA \times \text{percentage of intraparenchymal tumour}/100$). The CT protocol included pre-contrast and post-contrast (arterial, venous, excretory phase) images. Slice thickness was 0.5 mm, and volume rendering was performed using the phase (arterial or venous) that provided the clearest delineation between the tumour and the surrounding renal parenchyma.

Preoperative staging examination included also chest imaging (CT or X-ray), serum creatinine, serum electrolytes and liver function tests. Conversely, bone scan and brain imaging were performed when indicated by symptoms. Patients with bilateral renal tumours and/or synchronous metastases were excluded from the analyses; therefore, none of the patients received neoadjuvant or adjuvant treatment.

Either one or two expert surgeons performed the surgical procedures in each participating centre. Volume at each centre was defined according to the categories reported by Xia *et al.* [9]. Specifically, the volume was defined as very low (1–7 cases), low (8–14 cases), medium (15–23 cases), high (24–43 cases) and very high (≥ 44 cases).

In all cases, a tumour excision with (enucleoresection) or without (simple enucleation) a minimal rim of healthy parenchyma around the capsule was performed. The choice among the different nephron-sparing techniques as well as between the open, laparoscopic or robotic approach was based on the participant centre and surgeon preferences.

Patient records were extracted from each institutional database. For every patient, the following demographic and preoperative variables were recorded: age; gender; body mass index (BMI); Charlson comorbidities index (CCI); American Society of Anesthesiologists (ASA) score; clinical tumour size; PADUA score [4]; and tumour CSA [6]. Specifically, according to PADUA score, tumours were stratified into low-risk (score 6–7), intermediate-risk (score 8–9), and high-risk groups (score ≥ 10) [4]. The CSA values were categorized in two groups according to the proposed cut-off value of 20 cm^2 [6].

The following intra-operative variables were extracted by the collected multicentre database: operating time; warm

ischaemia time (WIT); EBL; and transfusion rate. Three-month postoperative complications were classified according to the modified Clavien system [10]. Postoperative complications were defined as minor (grade 1–2) or major (grade 3–4).

Preoperative and postoperative eGFR values were based on serum creatinine and calculated using the Chronic Kidney Disease Epidemiology Collaboration formula [11]. Renal function was assessed using the most recent eGFR prior to surgery and the eGFR calculated 3 months after the surgical procedure. Renal function dynamics were represented by the absolute change in eGFR (ACE) and percentage change in eGFR (PCE). ACE was calculated according the following formula: $ACE = eGFR_{\text{postoperative}} - eGFR_{\text{preoperative}}$. PCE was calculated using the formula, $PCE = (eGFR_{\text{postoperative}} - eGFR_{\text{preoperative}}) / eGFR_{\text{preoperative}}$. For each patient 3-month PCE >10% and >20% were calculated.

4Excised tumours were staged according to the 2009 version of the TNM classification [12]. In addition, the following histological features were collected: histological subtype according to the WHO classification [13], nuclear grade according to the Fuhrman classification [14], and surgical margin status. A positive surgical margin (PSM) was defined as cancer cells at the level of the inked parenchymal excision surface.

Statistical Analysis

Parametric continuous variables were reported as mean \pm SD, whereas median and interquartile range (IQR) was used for nonparametric continuous variables. The Mann–Whitney *U*-test and the Kruskal–Wallis *H*-test were used to compare two or more nonparametric continuous variables, respectively. The Pearson chi-squared test was used to compare categorical variables.

Binary logistic regression was used to perform both univariable and multivariable analyses looking for predictors of overall postoperative complications. Linear regression analysis was used to identify independent predictors of ACE.

The following preoperative covariates were included in multivariate models: age; BMI; comorbidity index; preoperative eGFR; PADUA score; and tumour CSA. Considering the potential risk of collinearity between PADUA score and tumour CSA, we tested the latter variable too after exclusion of the PADUA score.

Receiver-operating characteristic (ROC) curve analyses were used to compare PADUA score and tumour CSA as predictors of peri-operative and functional outcomes. Data were reported as areas under the curve (AUCs). Specifically, an AUC of 0.5–0.7 indicated a low accuracy, an AUC of 0.7–

0.9 indicated moderate accuracy, and an AUC >0.9 indicated greater accuracy.

For all statistical analyses, a two-sided *P* < 0.05 was considered statistically significant. All data were analysed with SPSS v. 23 statistical software (IBM Corp., Armonk, NY, USA).

Results

Overall, 531 patients were included in the present study. Each participating centre performed a mean of 35 procedures/year. The median (IQR) CSA value was 14.2 (7.4–25.1) cm². A total of 349 tumours (65.7%) showed a CSA \leq 20 cm² and the remaining 182 (34.3%) a CSA > 20 cm². The preoperative and pathological characteristics of 531 patients enrolled in the present study were reported in Table 1. Notably, patients with a tumour CSA > 20 cm² were significantly younger (*P* = 0.001) and more frequently symptomatic (*P* < 0.001) than those with a tumour CSA \leq 20 cm². Moreover, CSA > 20 cm² was significantly correlated with clinical tumour size (*P* < 0.001), PADUA score (*P* < 0.001), and PADUA risk stratification (*P* < 0.001).

The PNs were performed using an open approach in 237 (44.6%) cases, a pure laparoscopic approach in 152 cases (28.6%), and a robot-assisted approach in the remaining 142 cases (26.7%). Peri-operative outcomes, stratified according to the different approaches, are reported in Table 2.

Intra-operative features, stratified according to CSA categories, are summarized in Table 3. The presence of tumours with CSA > 20 cm² was significantly correlated with longer operating time (*P* = 0.001), a lower probability of a zero-ischaemia technique being performed (*P* < 0.001), longer WIT (*P* < 0.001) and greater EBL (*P* = 0.01) in comparison with tumours with CSA \leq 20 cm².

Three-month postoperative complications were recorded in 140 patients (26.4%). According to the modified Clavien system, 110 patients (20.7%) had minor (grade 1–2) and 30 (5.7%) had major (grade 3–4) complications. Specifically, complications were detected in 75 patients (21.5%) with tumour CSA \leq 20 cm² and in 65 patients (35.7%) with CSA > 20 cm² (*P* < 0.001).

On univariable analyses, patient's age (odds ratio [OR] 1.032, 95% CI 1.014–1.051), clinical tumour size (OR 1.021, 95% CI 1.010–1.032), PADUA score (OR 1.344, 95% CI 1.200–1.505) and tumour CSA (OR 1.017, 95% CI 1.008–1.027) turned out to be predictors of postoperative complications. Multivariable analyses showed that only age (OR 1.037, 95% CI 1.018–1.057) and PADUA score (OR 1.289, 95% CI 1.132–1.469) were independent predictors of postoperative complications. Tumour CSA (OR 1.020, 95% CI 1.010–1.030) was an independent predictor of postoperative complications only when PADUA score was removed from the model (Table 4). The ROC curve analyses showed that both tumour CSA and

Table 1 Demographic and preoperative characteristics of 531 patients included in the analysis, stratified according to the contact surface area cut-off value of 20 cm².

Variables	Total cases (N = 531)	CSA ≤ 20 cm ² (N = 349)	CSA > 20 cm ² (N = 182)	P
Median (IQR) age, years	64 (55–72)	65 (57–72)	61.4 (52.4–69.4)	0.001
Men, n (%)	353 (66.5)	232 (66.5)	121 (66.5)	0.99
Median (IQR) BMI, kg/m ²	25.7 (23.6–28)	26 (23.8–28.3)	25.4 (23.3–27.1)	0.01
CCI, n (%)				
0	416 (78.3)	231(66.2)	138 (75.8)	0.02
>0	115 (21.7)	118 (33.8)	44 (24.2)	
Symptoms at diagnosis, n (%)				
Absent	461 (86.8)	316 (90.5)	145 (79.7)	<0.0001
Present	70 (13.2)	33 (9.5)	37 (20.3)	
Median (IQR) clinical size, cm	3.2 (2.3–4.4)	2.9 (2–3.5)	4.5 (4–6)	<0.0001
Median (IQR) PADUA score	8 (7–10)	7 (7–8)	10 (8–11)	<0.0001
PADUA risk stratification, n (%)				
Low	198 (37.3)	180 (51.6)	18 (9.9)	<0.0001
Intermediate	197 (37.9)	126 (36.1)	71 (39)	
High	136 (25.6)	43 (12.3)	93 (51.1)	
Median (IQR) CSA, cm ³	14.2 (7.4–25.1)	9.6 (5.1–14.1)	30.6 (25.1–44.7)	<0.0001
Median (IQR) eGFR, mL/min	82.2 (66.8–100.4)	81.3 (66.3–96.9)	83.7 (68.3–108.7)	0.16
ASA score, n (%)				
1	84 (15.8)	52 (14.9)	32 (17.6)	0.41
2	356 (67)	231 (66.2)	125 (68.7)	
3	90 (16.9)	65 (18.6)	25 (13.7)	
4	1 (0.2)	1 (0.3)	0	
Median (IQR) pathological size, cm	3 (2.3–4.3)	3 (2–3.5)	4.2 (3–5.4)	<0.0001
Histological subtype, n (%)				
Benign	109 (20.5)	81 (23.2)	28 (15.4)	0.02
Clear-cell	293 (55.2)	178 (51)	115 (63.2)	
Non-clear-cell	129 (24.3)	90 (25.8)	39 (21.4)	
pT, stage, n (%)				
pT1a	274 (64.9)	205 (76.5)	69 (44.8)	<0.0001
pT1b	101 (23.9)	41 (15.3)	60 (39)	
pT2	33 (7.8)	13 (4.8)	20 (12.9)	
pT3a	14 (3.3)	9 (3.4)	5 (3.2)	
Nuclear grade, n (%)				
Grade 1	56 (13.3)	35 (13.1)	21 (13.6)	0.02
Grade 2	248 (58.8)	161 (60.1)	87 (56.5)	
Grade 3	99 (23.5)	66 (24.6)	33 (21.4)	
Grade 4	19 (4.5)	6 (2.2)	13 (8.4)	
Surgical margins, n (%)				
Negative	412 (97.6)	261 (97.4)	151 (98.1)	0.66
Positive	10 (2.4)	7 (2.6)	3 (1.9)	

ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson comorbidity index; CSA, contact surface area; eGFR, estimated GFR; IQR, interquartile range.

Table 2 Peri-operative outcomes stratified according to the different approaches used to perform partial nephrectomy.

Variables	Open PN (n = 237)	Laparoscopic PN (n = 152)	Robot-assisted PN (n = 142)	P
Median (IQR) operating time, min	127 (106–165)	80 (65–100)	135 (110–172)	<0.001
Zero ischaemia, n (%)	89 (37.6)	50 (32.9)	49 (34.5)	0.62
Median (IQR) WIT, min	14 (10–19)	16 (14–20)	18 (14–25)	<0.001
Median (IQR) EBL, mL	150 (100–300)	100 (50–150)	100 (50–177)	<0.001
Intraoperative transfusion, n (%)	8 (3.4)	1 (0.7)	4 (2.8)	0.22
Major (Grade 3–4) postoperative complications	19 (8)	6 (3.9)	5 (3.5)	0.10
ACE	–6 (–19 to +5.2)	–7.2 (–19.7 to (–0.5)	–6.3 (–15.6 to (–0.4)	0.43

ACE, Absolute change in estimated GFR; EBL, estimated blood loss; IQR, interquartile range; PN, partial nephrectomy; WIT, warm ischaemia time.

PADUA score have a low accuracy to predict overall complications (AUC 0.61 vs 0.64; $P = 0.38$).

The median (IQR) value of preoperative eGFR was 82.2 (66.8–100.4) mL/min/1.73 m². The median (IQR) 3-month

eGFR was 81 (64–100) with a median (IQR) ACE value of –6.5 (–18 to +1.5). Three months after surgery, 136 patients (25.6%) had a PCE > 20%. Specifically, 77 cases (22.1%) had a tumour CSA ≤ 20 cm² and 59 (32.4%) had a tumour CSA

Table 3 Intra-operative features of 531 patients included in the analysis, stratified according to the CSA cut-off value of 20 cm².

Variables	Total cases (N = 531)	CSA ≤ 20 cm ² (N = 349)	CSA > 20 cm ² (N = 182)	P
Approach, n (%)				
Open	237 (44.6)	155 (44.4)	82 (45.1)	0.50
Laparoscopic	152 (28.6)	105 (30.1)	47 (25.8)	
Robot-assisted	142 (26.7)	89 (25.5)	53 (29.1)	
Median (IQR) operating time, min	119 (90–150)	113 (85–145)	120 (90–170)	0.001
Ischaemia, n (%)				
Zero	188 (35.4)	156 (44.7)	32 (17.6)	<0.001
Warm	343 (64.6)	193 (55.3)	150 (82.4)	
Early unclamping technique, n/total (%) (n = 343)	95/343 (27.7)	59/193 (30.1)	36/150 (24)	0.17
Median (IQR) WIT, min (n = 343)	16 (12–20)	15 (10–19)	18 (15–23)	<0.001
Median (IQR) EBL, mL	100 (50–200)	100 (50–200)	150 (50–300)	0.01
WIT, n (%)				
≤20 min	262 (76.4)	163 (84.5)	99 (66)	<0.001
>20 min	81 (23.6)	30 (84.5)	51 (34)	
Haemostatic agents, n (%)				
Not used	67 (12.6)	46 (13.2)	21 (11.5)	0.58
Used	464 (87.4)	303 (86.8)	161 (88.5)	
Median (IQR) LOS, days	6 (5–7)	6 (5–7)	6 (5–8)	0.06
Median (IQR) postoperative eGFR, mL/min	81 (64–100)	82 (67.4–101)	77 (59–94)	0.08
PCE > 10%, n (%)	223 (42)	136 (39)	87 (47.8)	0.05
PCE > 20%, n (%)	136 (25.6)	77 (22.1)	59 (32.4)	0.009

EBL, estimated blood loss; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LOS, length of hospital stay; PCE, percentage change in eGFR; WIT, warm ischaemia time.

Table 4 Univariable and multivariable analyses to predict overall postoperative complications.

Variables	Univariable analyses		Multivariable analysis including PADUA score		Multivariable analysis without PADUA score	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Gender						
Male	Referent					
Female	0.919 (0.609–1.387)	0.68				
Age (continuous)	1.032 (1.014–1.051)	0.001	1.037 (1.016–1.058)	<0.0001	1.037 (1.016–1.037)	<0.001
BMI (continuous)	0.974 (0.930–1.019)	0.25	0.977 (0.929–1.027)	0.35	0.977 (0.930–1.026)	0.35
CCI score						
0–1	Referent		Referent		Referent	
>1	1.060 (0.699–1.609)	0.78	0.943 (0.593–1.499)	0.80	0.965 (0.612–1.520)	0.87
Symptoms						
Absent	Referent					
Present	1.332 (0.772–2.301)	0.30				
Clinical tumour size (continuous)	1.021 (1.010–1.032)	<0.001				
Preoperative eGFR (continuous)	0.992 (0.984–1.001)	0.07	0.999 (0.992–1.006)	0.70	0.998 (0.991–1.005)	0.65
PADUA score (continuous)	1.344 (1.200–1.505)	<0.001	1.296 (1.135–1.480)	<0.0001		
PADUA risk						
Low	Referent					
Intermediate	2.373 (1.439–3.912)	0.001				
High	3.838 (2.276–6.472)	<0.001				
Tumour CSA (continuous)	1.017 (1.008–1.027)	<0.001	1.010 (0.998–1.021)	0.10	1.020 (1.010–1.031)	<0.001
Tumour CSA						
≤20 cm ²	Referent					
>20 cm ²	2.030 (1.365–3.017)	<0.001				

BMI, body mass index; CCI, Charlson comorbidity index; CSA, contact surface area; eGFR, estimated GFR; OR, odds ratio.

> 20 cm² (P = 0.009). Table 5 shows the multivariable analyses conducted to identify predictors of ACE. Age (from –0.639 to –0.306; P < 0.001), BMI (from 0.267 to 1.076; P = 0.001), age-adjusted CCI score (from –3.193 to –0.259; P = 0.02), preoperative eGFR value (from –0.939 to –0.862;

P < 0.001) and tumour CSA (from –0.260 to –0.048; P = 0.005) turned out to be independent predictors of ACE. The ROC curve analyses showed overlapping low accuracy between tumour CSA and PADUA score to predict 3-month PCE > 20% (AUC 0.58 vs 0.56; P = 0.49).

Table 5 Multivariable analysis to identify independent predictors of absolute change in eGFR.

Variables	B (95% CI)	P
Age (continuous)	-0.114 (-0.639 to -0.306)	<0.001
BMI (continuous)	0.064 (0.267-1.074)	0.001
CCI score (continuous)	-0.047 (-3.133 to -0.259)	0.02
Preoperative eGFR (continuous)	-0.925 (-0.939 to -0.862)	<0.001
PADUA score (continuous)	0.019 (-0.690 to 1.738)	0.39
Tumour CSA (continuous)	-0.063 (-0.260 to -0.048)	0.005

BMI, body mass index; CCI, Charlson comorbidity index; CSA, contact surface area; eGFR, estimated GFR.

Discussion

Tumour CSA, calculated according to the formula proposed by Leslie *et al.*, is an independent predictor of postoperative renal function in patients who underwent PN for suspicious renal masses; however, this imaging variable failed to predict overall postoperative complications in the same patient cohort.

The CSA of the tumour was originally described in 2015 by Leslie *et al.* [6] and tested in a series of 200 patients who underwent traditional or robot-assisted PN for suspicious renal masses. In their original study, the authors proposed categorizing tumour CSA according to the cut-off value of 20 cm², demonstrating its role as an independent predictor of operating time ≥ 4 h, EBL > 500 mL, overall complications, LOS ≥ 4 days and $\geq 10\%$ decrease of eGFR. No external validation of tumour CSA calculated according to the Leslie *et al.* formula has been published previously. The present study tested, for the first time, the ability of Leslie *et al.*'s original formula to predict postoperative complications and renal function in an external series of patients who underwent PN for renal tumours. Unlike the original study by Leslie *et al.*, we used both PADUA score and tumour CSA as continuous variables. Conversely, Leslie *et al.* categorized their cases in two subgroups according to the cut-off value of 20 cm². [1,4].

According to our data, tumour CSA outperformed PADUA score in predicting ACE. Conversely, PADUA score outperformed tumour CSA in predicting 3-month overall postoperative complications. The ROC curve analyses confirmed that both systems had low accuracy for predicting overall complications and 3-month PCE > 20%.

Both systems could therefore be used to evaluate appropriately the complexity of renal tumours and their suitability for PN in order to plan the treatment and to counsel patients about the risk of peri-operative complications. The main limitation of tumour CSA is that it is complex to calculate, requiring imaging software.

To simplify the CSA calculation, recently, Hsieh *et al.* [7] proposed a mathematical model assuming that renal tumours

could be modelled as spheres. According to this model, the CSA was calculated using the formula $CSA = 2 \times p \times r$ (tumour radius) $\times d$ (depth of intraparenchymal part of the tumour). In a small cohort of patients with a mean CSA of 30 cm² and a median RENAL nephrometry score of 7, the Hsieh *et al.* formula predicted renal function impairment better than RENAL nephrometry score [7]. Recently, Haifler *et al.* [8] performed the first external validation of the Hsieh *et al.* formula in a series of 257 tumours with a median CSA of 14.5 cm² and a median RENAL nephrometry score of 9. At multivariable analysis CSA was found to be an independent predictor of ACE, together with nephrometry score, EBL and patient age. Preoperative characteristics of patients/tumours included in the two previous studies seem to be different from those enrolled in the present study. In particular, cases included in the study by Hsieh *et al.* had a significantly higher value of both CSA and clinical tumour size in comparison with the present series. Similarly, the population in the study by Haifler *et al.* comprised a higher percentage of patients with clinical tumours > T1 in comparison with the present series.

More recently, Suk-Ouichai *et al.* [15] performed a second external validation of the formula proposed by Hsieh *et al.* in a series of 419 patients who underwent PN for solitary renal tumours. They demonstrated that the simplified formula to estimate CSA was not strongly associated with functional outcomes after PN and was not an independent predictor of endophytic tumours.

Although interesting, in our opinion, the simplified formula proposed by Hsieh *et al.* is not appropriate for evaluating the CSA of numerous non-spherical renal tumours. For this reason, we used the original formula by Leslie *et al.* to obtain the CSA in our patients.

Available data are still not definitive to compare tumour CSA with the first generation of nephrometry scores. In their original paper, Leslie *et al.* concluded that a CSA > 20 cm² was a better predictor of peri-operative and functional outcomes in comparison with PADUA score ≥ 10 [6]. In the present study, CSA was superior to PADUA score for predicting functional outcomes, but was less able to predict overall complications.

The use of categorical variables instead of continuous variables could influence the interpretation of the predictive role of these numerical variables. Moreover, the inclusion of variables providing similar information concerning the anatomical and topographic characteristics of renal tumours could produce a collinearity event in the multivariable models, influencing the correct interpretation of the results.

Limitations of the present study include retrospective analysis of data and the lack of central imaging review to assign the PADUA scores and to calculate the tumour CSA area.

Moreover, we did not calculate the amount of sacrificed healthy parenchyma during the extirpative phase of the procedure. However, in all cases, the authors minimized excisional volume loss by performing a simple enucleation or a minimal PN. Last, as with the imaging features, the pathology slide review was not centralized.

In conclusion, tumour CSA value correlated with important postoperative variables such as operating time, the zero-ischaemia technique, WIT, EBL and PCE > 20%. At multivariable analyses, tumour CSA was found to be an independent predictor of postoperative renal function. Conversely, PADUA score outperformed tumour CSA in predicting postoperative complications after PN. Both tumour CSA and PADUA score, however, had a low accuracy in predicting postoperative complications and renal functional impairment. The complexity of the formula by Leslie et al. to calculate the tumour CSA value is a potential limitation of its diffusion and application in clinical practice.

Conflicts of Interest

None declared.

References

- Klatte T, Ficarra V, Gratzke C et al. A literature review of renal surgical anatomy and surgical strategies for partial nephrectomy. *Eur Urol* 2015; 68: 980–92
- Ljungberg B, Bensalah K, Canfield S et al. EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol* 2015; 67: 913–24
- Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol* 2009; 182: 844–53
- Ficarra V, Novara G, Secco S et al. Preoperative aspects and dimensions used for an anatomical (PADUA) classification of renal tumours in patients who are candidates for nephron-sparing surgery. *Eur Urol* 2009; 56: 786–93
- Simmons MN, Ching CB, Samplaski MK et al. Kidney tumor location measurement using the C index method. *J Urol* 2010; 183: 1708–13
- Leslie S, Gill IS, de Castro A et al. Renal tumor contact surface area: a novel parameter for predicting complexity and outcomes of partial nephrectomy. *Eur Urol* 2014; 66: 884–93
- Hsieh PF, Wang YD, Huang CP et al. A mathematical method to calculate tumor contact surface area: an effective parameter to predict renal function after partial nephrectomy. *J Urol* 2016; 196: 33–40.
- Haifler M, Ristau BT, Higgins AM et al. External validation of contact surface area as a predictor of postoperative renal function in patients undergoing partial nephrectomy. *J Urol* 2018; 199: 649–54
- Xia L, Pulido JE, Chelluri RR et al. Hospital volume and outcomes of robot-assisted partial nephrectomy. *BJU Int* 2018; 121: 900–7
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation on a cohort of 6,336 patients and results of a survey. *Ann Surg* 2002; 240: 205–13
- Levey AS, Inker LA. Assessment of glomerular filtration rate in health and disease: a state of the art review. *Clin Pharmacol Ther* 2017; 102: 405–19
- Greene FL, Gospodarowicz M, Wittekind C et al. *American Joint Committee on Cancer (AJCC) staging manual*. 7 edn. Philadelphia, PA: Springer, 2009.
- Eble JN, Sauter G, Epstein JI et al., eds. *Pathology and genetics of tumors of the urinary system and male genital organs. World Health Organization classification of tumors*. Lyon, France: IARC Press; 2004.
- Fuhrman S, Lasky LC, Limas L. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol* 1982; 6: 655–63
- Suk-Ouichai C, Wu J, Dong W et al. Tumor contact surface area as a predictor of functional outcomes after standard partial nephrectomy: utility and limitations. *Urology* 2018; 116: 106–13

Appendix 1

Antonino Infererra (Department of Human and Paediatric Pathology ‘Gaetano Barresi’, Urology Section, University of Messina), Marta Rossanese (Department of Human and Paediatric Pathology ‘Gaetano Barresi’, Urologic Section, University of Messina), Enrica Subba (Department of Human and Paediatric Pathology ‘Gaetano Barresi’, Urology Section, University of Messina), Giuseppe Basile (Department of Human and Paediatric Pathology ‘Gaetano Barresi’, Urology Section, University of Messina), Gianluca Giannarini (Urology Unit, Academic Medical Centre Hospital ‘Santa Maria della Misericordia’, Udine, Italy), Alessandro Veccia (Urology Unit, ASST, Spedali Civili di Brescia, University of Brescia, Italy), Fabio Esposito (Department of Urology, University of Federico II of Naples, Italy), Silvia Lucarini (Department of Urology, Careggi Hospital, University of Florence, Italy), Riccardo Campi (Department of Urology, Careggi Hospital, University of Florence, Italy), Andrea Mari (Department of Urology, Careggi Hospital, University of Florence, Italy).

Correspondence: Vincenzo Ficarra, Department of Human and Paediatric Pathology ‘Gaetano Barresi’, Urologic section - University of Messina, via Consolare Valeria 1, 98124 Messina, Italy.

e-mail: vficarra@unime.it

Abbreviations: CSA, contact surface area; PN, partial nephrectomy; eGFR, estimated GFR; ACE, absolute change in estimated GFR; OR, odds ratio; EBL, estimated blood loss; LOS, length of stay; TSA, total surface area; BMI, body mass index; CCI, Charlson comorbidity index; ASA, American Society of Anesthesiologists; WIT, warm ischaemia time; PCE, percentage change in eGFR; IQR, interquartile range; ROC, receiver-operating characteristic; AUC, area under the curve; OR, odds ratio.