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Article type : Original Article

Tumor Contact Surface Area as predictor of postoperative complications and renal function in patients undergoing partial nephrectomy for renal tumors

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Keywords: renal cell carcinoma, partial nephrectomy, nephrometry scores, perioperative outcomes, pathological features

Abstract

Objectives: to evaluate the ability of original tumor contact surface area (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.

Material and methods: we analyzed the clinical records of 531 consecutive patients who underwent elective PN because of a suspicion of kidney cancer at five academic, high-volume centers from January 2014 to December 2016. Each participant Center evaluated prospectively the radiologic images to assign the CSA and the PADUA score. Several expert surgeons performed the surgical procedures in each participant Center. Binary logistic regression was used to perform both univariable and multivariable analyses looking for predictors of postoperative complications. Linear regression analysis was used to identify independent predictors of absolute change in eGFR (ACE).

Results: The median value of CSA was 14.2 (IQR 7.4-25.1) cm^2. 349 (65.7%) tumors showed a CSA ≤ 20 cm^2 and the remaining 182 (34.3%) a CSA > 20 cm^2. PNs were performed using an open approach in 237 (44.6%) cases, a pure laparoscopic approach in 152 (28.6%), and a robot-assisted approach in the remaining 142 (26.7%). 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) turned out to be independent predictors of postoperative complications. Tumor CSA (OR 1.020 – 95%CI 1.010-1.030) resulted independent predictor of postoperative complications only when PADUA score was removed from the model. Age (from -0.639 to -0.306; p<0.001); BMI (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 tumor CSA (from -0.260 to -0.048; p=0.005) turned out to be independent predictors of ACE.

Conclusions: Tumor CSA is an independent predictor of postoperative renal function. Conversely, at multivariable analysis PADUA score outperformed tumor CSA to predict postoperative complications after PN. The complexity of Leslie's formula to calculate the tumor CSA value is a potential limitation of its diffusion and application in the clinical practice.

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's selection criteria and preoperative counseling process. Specifically, predicting the risk of perioperative complications and renal function impairment can assist the urologist in the decision-making on radical versus PN as well as on open versus laparoscopic (either pure or robot-assisted) PN procedures [1]. Moreover, the assessment of standardized and objective parameters in a score significantly improved the real comparability among different PN series regardless of the used approach [2].

The R.E.N.A.L. nephrometry score, the PADUA classification, and the Centrality index (CI) represented the first-generation of renal tumor complexity scoring systems proposed in the Literature [3-5]. A recent systematic review of the Literature showed that RENAL and PADUA scoring systems are the most popular and used nephrometry scores. Interestingly, available validation studies of first-generation systems showed conflicting results probably as consequence of the heterogeneity of the evaluated series [1].

Aimed to improve the predictive ability of previous nephrometry scores, Leslie et al proposed the use of novel imaging parameter based on the calculation on the computed tomography (CT) scan data of the renal tumor contact surface area (CSA) with the adjacent parenchyma. This parameter predicted adverse tumor characteristics and the most important perioperative outcomes. Moreover, the CSA seems to outperform the PADUA score in the prediction of operative (OR) time, estimated blood losses (EBL), complications, length of stay (LOS) and ≥10% decrease in estimated glomerular filtration rate (eGFR) [6]. Recently, Hsieh et al proposed a simplified formula to calculate the tumor CSA confirming its role as predictor of renal function impairment after PN [7]. While Haifler et al externally validated the previous formula based on the assumption that all the renal tumors can be modeled as sphere, the original Leslie's formula is still lacking of an external validation [8].

In this scenario, we decided to evaluate the ability of 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 analyzed the prospectively collected clinical records of 531 consecutive patients who underwent elective PN because of a suspicion of kidney cancer at five academic, high-volume centers (Brescia, Italy; Firenze, Italy; Napoli, Italy; Torino (Orbassano), Italy; Udine, Italy;) from January 2014 to December 2016. Prior to surgery, all patients underwent three-dimensional abdominal CT scans or abdominal magnetic resonance imaging (MRI) to define the clinical stage and the anatomical characteristics of the tumors. All the radiologic images were prospectively evaluated by each participant center with the aim of assigning the PADUA score [4] and the tumor contact surface area (CSA), according to the formula described by Leslie et al [6]. Briefly, this imaging parameter was calculated applying 3-dimensional rendering software at the preoperative CT scan imaging. Specifically, after measurement of tumor volume and percentage of tumor located within the renal parenchyma,

the total surface area (TSA) of the tumor is calculated using the formula $4\pi r^2$ for surface area of a sphere, where r equals the tumor radius. The tumor CSA is calculated by multiplying the TSA with the percentage of intraparenchymal component (CSA = TSA x percentage of intraparenchymal tumor/100). The CT protocol included precontrast and postcontrast (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 tumor 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 tumors and/or synchronous metastases were excluded from the analyses. Therefore, none of the patients received neoadjuvant or adjuvant treatment.

One-Two expert surgeons performed the surgical procedures in each participant Center. Volume center was defined according to the categories reported by Xia et al [9]. Specifically, the volume Center was defined 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 tumor 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 center 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 tumor size, PADUA score [4] and tumor CSA [6]. Specifically, according to PADUA score, tumors 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 intraoperative variables were extracted by the collected multicentre database: OR time, warm ischemia time (WIT), EBL, and transfusion rate. Three-month postoperative complications were classified according to the modified Clavien system [10]. Postoperative complications were distinguished as minor (grade 1–2) and major (grade 3–4).

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

Excised tumors were staged according to the 2009 version of the TNM classification [12]. Moreover, the following histologic features were collected: histologic subtypes according to the World Health Organization classification [13], nuclear grade according to the Fuhrman classification [14], and surgical margin status. Positive surgical margin (PSM) was defined as cancer cells at the level of inked parenchymal excision surface.

Statistical analysis

Parametric continuous variables were reported as mean ± standard deviation (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-square 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, comorbidities index, preoperative eGFR, PADUA score and tumor CSA. Considering the potential risk of collinearity between PADUA score and tumor CSA, we tested the last parameter too after exclusion of the PADUA score.

The ROC curve analyses were used to compare PADUA score and tumor CSA as predictors of perioperative and functional outcomes. Data were reported as areas under the curve (AUC). Specifically, an AUC of 0.5–0.7 indicated a low accuracy, of 0.7–0.9 indicated moderate accuracy, and >0.9 indicated greater accuracy.

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

Results

Overall 531 patients were included in the present study. Each participant center performed a mean of 35 procedures/year. The median value of CSA was 14.2 (IQR 7.4-25.1) cm^2. 349 (65.7%) tumors showed a CSA ≤ 20 cm^2 and the remaining 182 (34.3%) a CSA > 20 cm^2. Preoperative and pathologic characteristics of 531 patients enrolled in the present study were reported in the table 1 (Table 1). Notably, patients with a tumor CSA>20 cm^2 resulted significantly younger (p=0.001) and more frequently symptomatic (p<0.001) than those with a tumor CSA≤20 cm^2. Moreover, CSA>20 cm^2 was significantly correlated with clinical tumor size (p<0.0001), PADUA score (p<0.0001), and PADUA risk stratification (p<0.0001).

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

Intraoperative features stratified according to CSA categories were summarized in table 3 (Table 3). Specifically, the presence of tumors with CSA > 20 cm^2 was significantly correlated with a longer OR time (p=0.001), a lower probability to perform a zero-ischemia technique (p<0.0001), a longer WIT (p<0.0001) and an higher EBL (p=0.01) in comparison with tumors with CSA ≤ 20 cm^2.

Three-month postoperative complications were recorded in 140 (26.4%) patients. According to modified Clavien system, 110 (20.7%) patients showed minor (grade 1-2) and 30 (5.7%) major (grade 3-4) complications. In details, complications were detected in 75 (21.5%) patients with tumor CSA ≤ 20 cm^2 and in 65 (35.7%) with CSA > 20 cm^2 (p<0.0001).

At univariable analyses, patient's age (OR 1.032 – 95%CI 1.014-1.051), clinical tumor size (OR 1.021 – 95%CI 1.010-1.032), PADUA score (OR 1.344 – 95%CI 1.200-1.505) and tumor 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) turned out to be independent predictors of postoperative complications. Tumor CSA (OR 1.020 – 95%CI 1.010-1.030) resulted independent predictor of postoperative complications only when PADUA score was removed from the model (Table 4). The ROC curve analyses showed that both tumor CSA and PADUA score have a low accuracy to predict overall complications (AUC 0.61 Vs 0.64; p=0.38).

The median value of preoperative eGFR was 82.2 ml/min/1.73 m^2 (IQR 66.8-100.4). The median value of 3-mo eGFR was 81 (IQR 64-100) with a median value of ACE of -6.5 (IQR -18 to +1.5). Three months after surgery 136 (25.6%) patients showed a PCE greater than 20%. Specifically, 77 (22.1%) cases had tumor CSA ≤ 20 cm^2 and 59 (32.4%) tumor CSA > 20 cm^2, respectively (p=0.009). Table 5 showed multivariable analyses 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 Charlson score (from -3.193 to -0.259; p=0.02), preoperative eGFR value (from -0.939 to -0.862; p<0.001) and tumor 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 tumor CSA and PADUA score to predict the 3-mo PCE > 20% (AUC 0.58 Vs 0.56; p=0.49).

Discussion

Tumor CSA calculated according to the Leslie's formula is an independent predictor of post-operative renal function in patients who underwent PN for suspicious renal masses. However, this imaging parameter failed to predict overall post-operative complications in the same setting of patients.

The tumor CSA was originally described in 2015 by Leslie et al 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 to categorize the tumor CSA according to the cut-off value of 20 cm^2, demonstrating its role as independent predictors of OR time ≥ 4 hours, EBL > 500 ml, overall complications, LOS ≥ 4 days and ≥10% decrease of eGFR [6]. No external validation of tumor CSA calculated according to the Leslie's formula was previously published. The present study for the first time tested the ability of the Leslie's original formula to predict postoperative complications and renal func-

tion in an external series of patients who underwent PN for renal tumors. Differently from the original Leslis's study, we used both PADUA score and tumor CSA as continuous variables. Conversely, Leslie et al categorized their cases in two subgroups according to the cut-off value of 20 cm^2.[1, 4].

According to our data, the tumor CSA outperformed PADUA score to predict the ACE. Conversely, PADUA score outperformed the tumor CSA to predict 3-mo postoperative overall complications. The ROC curve analyses confirmed that both systems show low accuracy to predict overall complications and 3-mo PCE > 20%.

Therefore, both the systems could be appropriately used to evaluate the complexity of the renal tumor suitable for PN and counsel patients about the risk of perioperative complications. The main limitation of the tumor CSA is the complexity to calculate this parameter requiring the software imaging.

To simplify the CSA calculation, recently, Hsieh et al proposed a mathematical model assuming that renal tumors modeled as spheres [7]. According to this model, the CSA was calculated by the formula CSA=2 x p x r (tumor radius) x d (depth of intraparenchymal part of the tumor). In a small cohort of patients with a mean CSA of 30 cm^2 and a median RENAL nephrometry score of 7, the Hsieh's formula predicted the renal function impairment better than RENAL nephrometry score [7]. Recently, Haifler et al performed the first external validation of the Hsieh's formula in a series of 257 tumors with a median CSA of 14.5 cm^2 and a median RENAL nephrometry score of 9. At multivariable analysis the CSA turned out to be an independent predictor of ACE together with nephrometry score, EBL and patient's age [8]. Preoperative characteristics of patients/tumors included in the two previous studies seem to be different from those enrolled in our study. In particular, cases included in the Hsieh's study had a significantly higher value of both CSA and clinical tumor size in comparison with our series. Similarly, the Haifler's population seem to be composed by a higher percentage of patients with clinical tumors > T1 in comparison with our series.

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

Although interesting, in our opinion the simplified Hsieh's formula could be not appropriate to evaluate the CSA of numerous non-spherical renal tumours. For such reason, the original Leslie's formula was used to get CSA in our patients.

Available data are still not definitive to compare tumor CSA with the first-generation of nephrometry scores. In their original paper, Leslies et al concluded that CSA >20 cm^2 was a better predictor of perioperative and functional outcomes in comparison with PADUA score ≥10 [6]. In our study, CSA was superior to PADUA score to predict functional outcomes but less able to predict overall complications.

The use of categorical variables instead of continuous one could be a potential difference in the interpretation of predictive role of these numerical variables. Moreover, the inclusion of parameters doing similar information concerning the anatomic and topographic characteristics of renal

tumors 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 score and calculate the tumor 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 the excisional volume loss performing a simple enucleation or a minimal PN. Last, similarly to the imaging features, the pathology slides review was not centralized.

Conclusions

Tumor CSA value was correlated to some important postoperative parameters such as OR, no ischemia technique, WIT, EBL and PCE greater than 20%. At multivariable analyses, tumor CSA resulted a independent predictor of postoperative renal function. Conversely, PADUA score outperformed tumor CSA to predict postoperative complications after PN. However, both tumor CSA and PADUA score showed a low accuracy to predict postoperative complications and renal functional impairment. The complexity of Leslie's formula to calculate the tumor CSA value is a potential limitation of its diffusion and application in the clinical practice.

Conflicts of interest

None declared

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Table 1: Demographic and preoperative characteristics of 531 patients included in the analysis stratified according to the CSA cut-off value of 20 cm^2

Variables	Total cases (n=531)	CSA ≤ 20 cm^2 (n=349)	CSA > 20 cm^2 (n=182)	P Value
Median (IQR) Age, years	64 (55 – 72)	65 (57 – 72)	61.4 (52.4 – 69.4)	0.001
Male gender (%)	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
Charlson comorbidity index, n (%)				0.02
- 0	416 (78.3%)	231(66.2%)	138 (75.8%)	
- >0	115 (21.7%)	118 (33.8%)	44 (24.2%)	
Symptoms at diagnosis, n (%)				<0.0001
- absent	461 (86.8%)	316 (90.5%)	145 (79.7%)	
- 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				<0.0001
- low	198 (37.3%)	180 (51.6%)	18 (9.9%)	
- intermediate	197 (37.9%)	126 (36.1%)	71 (39%)	
- high	136 (25.6%)	43 (12.3%)	93 (51.1%	
Median (IQR) Contact Surface Area (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 (%)				0.41
- 1	84 (15.8%)	52 (14.9%)	32 (17.6%)	
- 2	356 (67%)	231 (66.2%)	125 (68.7%)	

- 3 - 4	90 (16.9%) 1 (0.2%)	65 (18.6%) 1 (0.3%)	25 (13.7%) 0	
Median (IQR) pathological size, cm	3 (2.3-4-3)	3 (2-3.5)	4.2 (3-5.4)	<0.0001
Histologic subtype, n (%) - benign - clear cell - non clear cell	 109 (20.5%) 293 (55.2%) 129 (24.3%)	 81 (23.2%) 178 (51%) 90 (25.8%)	 28 (15.4%) 115 (63.2%) 39 (21.4%)	0.02
pT, stage, n (%) - pT1a - pT1b - pT2 - pT3a	 274 (64.9%) 101 (23.9%) 33 (7.8%) 14 (3.3%)	 205 (76.5%) 41 (15.3%) 13 (4.8%) 9 (3.4%)	 69 (44.8%) 60 (39%) 20 (12.9%) 5 (3.2%)	<0.0001
Nuclear Grade, n (%) - grade 1 - grade 2 - grade 3 - grade 4	 56 (13.3%) 248 (58.8%) 99 (23.5%) 19 (4.5%)	 35 (13.1%) 161 (60.1%) 66 (24.6%) 6 (2.2%)	 21 (13.6%) 87 (56.5%) 33 (21.4%) 13 (8.4%)	0.02
Surgical margins, n (%) - negative - positive	 412 (97.6%) 10 (2.4%)	 261 (97.4%) 7 (2.6%)	 151 (98.1%) 3 (1.9%)	0.66

Table 2: Perioperative 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 Value**
Median (IQR) OR, min	127 (106-165)	80 (65-100)	135 (110-172)	<0.001
No ischemia, 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
absolute change in eGFR (ACE)	-6 (-19 – (+5.2)	- 7.2 (-19.7 – (-0.5)	- 6.3 (-15.6 – (-0.4)	0.43

Table 3: Intraoperative features of 531 patients included in the analysis stratified according to the CSA cut-off value of 20 cm^2

Variables	Total cases (n=531)	CSA ≤ 20 cm^2 (n=349)	CSA > 20 cm^2 (n=182)	P Value
Approach, n (%) - open - laparoscopic - robot-assisted	 237 (44.6%) 152 (28.6%) 142 (26.7%)	 155 (44.4%) 105 (30.1%) 89 (25.5%)	 82 (45.1%) 47 (25.8%) 53 (29.1%)	0.50
Median (IQR) OR, min	119 (90-150)	113 (85-145)	120 (90-170)	0.001
Ischemia, n (%) - zero - warm	 188 (35.4%) 343 (64.6%)	 156 (44.7%) 193 (55.3%)	 32 (17.6%) 150 (82.4%)	<0.0001
Early unclamping technique, n/tot (%) (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)	<0.0001
Median (IQR) EBL, ml	100 (50-200)	100 (50-200)	150 (50-300)	0.01
WIT, n (%) - ≤ 20 - > 20	 262 (76.4%) 81 (23.6%)	 163 (84.5%) 30 (84.5%)	 99 (66%) 51 (34%)	<0.0001
Hemostatic agents, n (%) - not used - used	 67 (12.6%) 464 (87.4%)	 46 (13.2%) 303 (86.8%)	 21 (11.5%) 161 (88.5%)	0.58
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 greater than 10%, n (%)	223 (42%)	136 (39%)	87 (47.8%)	0.05
PCE greater than 20%, n (%)	136 (25.6%)	77 (22.1%)	59 (32.4%)	0.009

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

	Univariable analyses		Multivariable analysis including PADUA score		Multivariable analysis without PADUA score	
Variables	**OR (95% CI)**	**P Value**	**OR (95% CI)**	**P Value**	**OR (95% CI)**	**P Value**
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)	<0.0001
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
Charlson 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 tumor size (continuous)	1.021 (1.010-1.032)	<0.001				
Preoperative eGRF (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					
- interm.	2.373 (1.439-3.912)	0.001				
- high	3.838 (2.276-6.472)	<0.001				
Tumor CSA (continuous)	1.017 (1.008-1.027)	<0.001	1,010 (0,998-1,021)	0.10	1.020 (1.010-1.031)	<0.0001
Tumor CSA						
- ≤ 20 cm^2	Referent					
- > 20 cm^2	2.030 (1.365-3.017)	<0.001				

Table 5: Multivariable analysis to identify independent predictors of absolute change in eGFR (ACE)

Variables	B (95% CI)	P Value
Age (continuous)	-0.114 (-0.639 - -0.306)	<0.0001
BMI (continuous)	0.064 (0.267 – 1.074)	0.001
Charlson score (continuous)	-0.047 (-3.133 - -0.259)	0.02
Preop eGFR (continuous)	-0.925 (-0.939 - -0.862)	<0.0001
PADUA score (continuous)	0.019 (-0.690 – 1.738)	0.39
Tumor CSA (continuous)	-0.063 (-0.260 - -0.048)	0.005