Urologia Internationalis

Original Paper

Urol Int 2021;105:108–117
DOI: 10.1159/000510684

Received: April 17, 2020
Accepted: July 31, 2020
Published online: October 12, 2020

Nephrometry Scores: Can Preoperative Assessment of Sectional Imaging Really Mirror Intraoperative Renal Tumor Anatomy?

Luisa Egen[a] Karl-Friedrich Kowalewski[a] Philipp Riffel[b] Patrick Honeck[a] Maximilian C. Kriegmair[a]

[a]Department of Urology and Urological Surgery, University Medical Center Mannheim, Mannheim, Germany; [b]Department of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Mannheim, Germany

Keywords
Kidney cancer · Renal cell carcinoma · Partial nephrectomy · Nephrometry · RENAL · PADUA

Abstract
Introduction: To compare RENAL, preoperative aspects and dimensions used for an anatomical (PADUA) classification, and Mayo Adhesive Probability (MAP) scores with the respective intraoperative findings and surgeon's assessment in predicting surgical outcome of patients undergoing partial nephrectomy. ***Methods:*** Data of 150 eligible patients treated at the University Medical Center Mannheim between 2016 and 2018 were analyzed. Tumors were radiologically and intraoperatively assessed by PADUA, RENAL, and MAP scores and surgeon's assessment. Correlations and regression models were created to predict ischemia time (IT), major complications, and Trifecta (negative surgical margin, IT < 25 min, and absence of major complications). ***Results:*** There were strong correlations between radiological and intraoperative RENAL ($r = 0.68$; $p < 0.001$) and PADUA scores ($r = 0.72$; $p < 0.001$). Radiological RENAL, PADUA, and MAP scores and surgeon's assessment were independent predictors of Trifecta (OR = 0.71, $p = 0.015$; OR = 0.77, $p = 0.035$; OR = 0.65, $p = 0.012$; OR = 0.40, $p = 0.005$, respectively). IT showed significant associations with radiological RENAL, PADUA, and surgeon's assessment (OR = 1.41, $p = 0.033$; OR = 1.34, $p = 0.044$; OR = 3.04, $p = 0.003$, respectively). MAP score proved as only independent predictor of major complications (OR = 2.12, $p = 0.002$). ***Conclusion:*** Radiologically and intraoperatively assessed scores correlated well with each other. Intraoperative nephrometry did not outperform radiological scores in predicting outcome confirming the value of the existing systems. MAP score correlates well with surgeon's assessment of perirenal fat and major complications underlining the importance of perirenal fat characteristics.

Introduction

Partial nephrectomy (PN) has emerged as the gold standard for localized renal cell carcinoma (RCC). The preservation of nephrons leads to improved long-term renal function compared to radical nephrectomy (RN) without compromising oncological outcome [1, 2]. Despite its benefits, both open and minimally invasive PN inherit a higher risk of postoperative complications than

karger@karger.com
www.karger.com/uin

Maximilian C. Kriegmair
Department of Urology and Urological Surgery, University Medical Center Mannheim
Theodor-Kutzer-Ufer 1-3
DE–68167 Mannheim (Germany)
maximilian.kriegmair@medma.uni-heidelberg.de

RN [3], particularly the occurrence of intraoperative bleeding and postoperative hemorrhage as well as urine leakage [4]. The risk of complications predominately depends on the tumor anatomy (e.g., size or approximation to collecting system) and can be significant even in the hands of experienced surgeons [5]. Therefore, preoperative assessment of the tumor anatomy is essential [6]. Nephrometry scores have been introduced as a tool to preoperatively objectify the tumor anatomy and to anticipate the surgical difficulty [7]. This prediction of potential postoperative morbidity is also useful for patient counselling and treatment planning [7].

The most commonly used scores are the RENAL [8] and the preoperative aspects and dimensions used for an anatomical (PADUA) classification scores [9]. While these are based on preoperative anatomical and radiological characteristics, others focus on tumor surroundings, for example, the perinephric fat. This is important since properties of perinephric tissue such as adhesiveness may aggravate the mobilization of the kidney and isolation of the tumor during surgery [10]. In order to assess the adhesiveness of perinephric fat, the Mayo Adhesive Probability (MAP) score was developed [11]. All scoring systems have been validated in several studies concerning the predictive value of perioperative outcome parameters [7]. Especially RENAL and PADUA scores showed good correlations with ischemia time (IT) [12–14], complications [15, 16], and functional outcomes [17–19] in some studies. On the other hand, literature still remains controversial as not all studies support these findings [17, 19, 20]. These limitations might be explained by an insufficient depiction of the actual anatomical conditions by two-dimensional preoperative sectional imaging. Furthermore, some parameters such as approximations of the collecting system depend on the extent and quality of the radiological images [5]. Consequently, recent studies have proposed a simple semiquantitative surgeon's assessment as a predictor of perioperative outcome. Irrespective of its subjective nature, promising results have been obtained [21].

However, it remains unclear whether preoperative assessment based on radiological imaging correlates well with intraoperative findings regardless of a nephrometry system or a surgeon's assessment. This study aimed at comprehensively comparing the RENAL, PADUA, and MAP scores with the factual surgeon's assessment of intraoperative tumor anatomy and to evaluate their potential to predict postoperative outcomes of patients undergoing PN.

Materials and Methods

Study Design

Data of 309 consecutive RCC patients treated at the University Medical Center Mannheim at Heidelberg University between October 2016 and November 2018 were collected in a prospective maintained database. After exclusion of cases with treatment other than PN (75), conversion to RN (8), multiple tumors (12), and missing preoperative images and data (64), 150 patients were included in this study. A total of 115 (76.7%) OPNs and 35 (23.3%) RPNs were performed by 8 different surgeons. Clinical and demographic data including age, sex, BMI, and American Society of Anaesthesiologists (ASA) classification were assessed. The study was approved by the institutional review board (2013-830-MA).

Nephrometry Scores and Surgeon's Assessment

Using the preoperative CT or MRI scans, (preoperative/radiological) RENAL, PADUA, and MAP scores were assessed in a standardized manner following the instructions by Kutikov and Uzzo [8], Ficarra et al. [9], and Davidiuk et al. [11]. A specially trained rater analyzed the cohort, and the results were confirmed in correspondence with a urologist (MCK) and a uro-radiologist (JB). After each procedure, the operating surgeon filled a questionnaire containing all individual parameters incorporated in the nephrometry scores (from which the intraoperative scores were deducted) and questions regarding the subjective assessment of surgical complexity, risk of postoperative complications (both defined as low, intermediate, or high), and the adhesiveness of perinephric fat (none, moderate, or extensive).

Perioperative Outcome

Perioperative outcome parameters included operative time (OT), use of ischemia, warm ischemia time (WIT), estimated blood loss (EBL), opening of the collecting system, overall complication rate, major complication rate, and length of hospital stay. Complications were graded using the Clavien-Dindo classification [22]. A Clavien score >2 was regarded as a major complication. Trifecta achievement was defined as a combination of negative surgical margin, WIT <25 min, and absence of major complications [23]. Additionally, tumor pathology, malignancy, surgical margin, and tumor measurements in 3 dimensions were obtained from the pathological reports. Volume of the resected tissue and tumor volume were calculated using the ellipsoid formula ($V = \pi/6 \times a \times b \times c$) [24]. By deducting tumor volume from the volume of total resected tissue, the excisional volume loss was identified [25].

Statistical Analysis

Statistical analysis was performed using R version 3.5.2 (R project, R Foundation for Statistical Computing) and JMP (SAS Institute, Cary, NC, USA). Continuous data are reported as mean ± SD, while categorical variables are reported with absolute and relative frequencies. Pearson's correlation coefficient was calculated to evaluate correlations between radiological and intraoperative scores. Scatter plots as well as kernel density and rug plots are used for visualization. Thereby, correlation coefficients ≤0.35 were interpreted as low or weak correlation, values between 0.36 and 0.67 are considered as modest or moderate correlations, while r values higher than 0.67 represent a strong correlation [26]. Multivariable and univariable logistic regression models were applied to predict

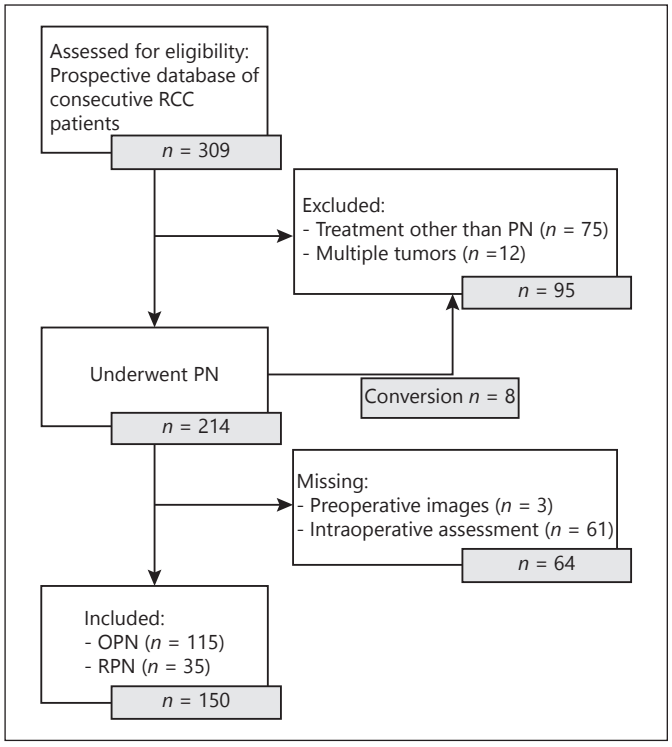


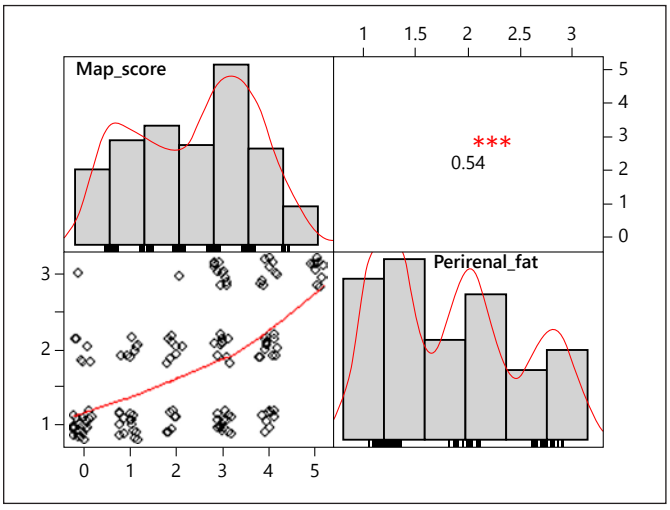
Fig. 1. Flowchart of eligible patients. RCC, renal cell carcinoma; PN, partial nephrectomy.

the occurrence of binary outcomes such as Trifecta, major complications, and IT. Regression models are presented as suggested previously [27, 28]. For visualization purposes, univariable regression is presented by receiver operating characteristic (ROC) curves with the corresponding area under the curve (AUC). Multivariable regression models were based on clinically and statistically important factors. Therefore, these models included age, sex, BMI, approach, ASA score, and 1 radiological or intraoperative score. A p value of <0.05 was considered statistically significant.

Results

Study Population

A total of 150 patients were eligible for analysis (see flowchart, Fig. 1). Median patient age was 63.5 years (21–89) and mean BMI was 27.4 kg/m^2 (SD, 4.4 kg/m^2). Overall, 76.7 percent (n = 115) of patients underwent OPN and 23.3 percent (n = 35) had RPN. Detailed baseline characteristics of included patients can be found in online suppl. Table 1 (see www.karger.com/doi/10.1159/000510684 for all online suppl. material). Trifecta was achieved in 77.3% (n = 116) of patients and 20 patients (13.3%) experienced major complications (Clavien >2). Information on the postoperative course is listed in Table 1.



Color version available online

Fig. 2. Correlation and distribution between MAP score and surgeon's assessment of perirenal fat. *** indicates a p value of <0.001. Scatter plots and kernel density plots with rug plots are used to visualize the distribution of score and assessment. MAP, Mayo Adhesive Probability.

Table 1. Perioperative data (values are given as mean and SD in brackets or percentage and number in brackets)

Surgical approach	
OPN, % (n)	76.7 (115)
RPN, % (n)	23.3 (35)
OT (in min±SD)	147.7±43.5
Use of ischemia, % (n)	85.3 (128)
WIT (min±SD)	18.6±6.8
EBL (mL±SD)	404.0±557.8
OCS, % (n)	49.3 (74)
Transfusions, % (n)	9.3 (14)
Positive surgical margin, % (n)	1.5 (2)
Occurrence of complications, % (n)	28.7 (43)
Major complications (Clavien ≥3), % (n)	13.3 (20)
Postoperative complications Clavien-Dindo, % (n)	
1	30.2 (13)
2	23.2 (10)
3a	25.6 (11)
3b	18.6 (8)
4a	2.3 (1)
Trifecta achievement, % (n)	77.3 (116)
Excisional volume loss (cm^3 ± SD)	21.4±21.2

OT, operative time; WIT, warm ischemia time; EBL, estimated blood loss; OCS, opening of the collecting system.

Correlation of Radiological and Intraoperative Scores

Correlation analyses revealed statistically significant associations between all obtained scores (radiological and intraoperative PADUA and RENAL scores; all p values

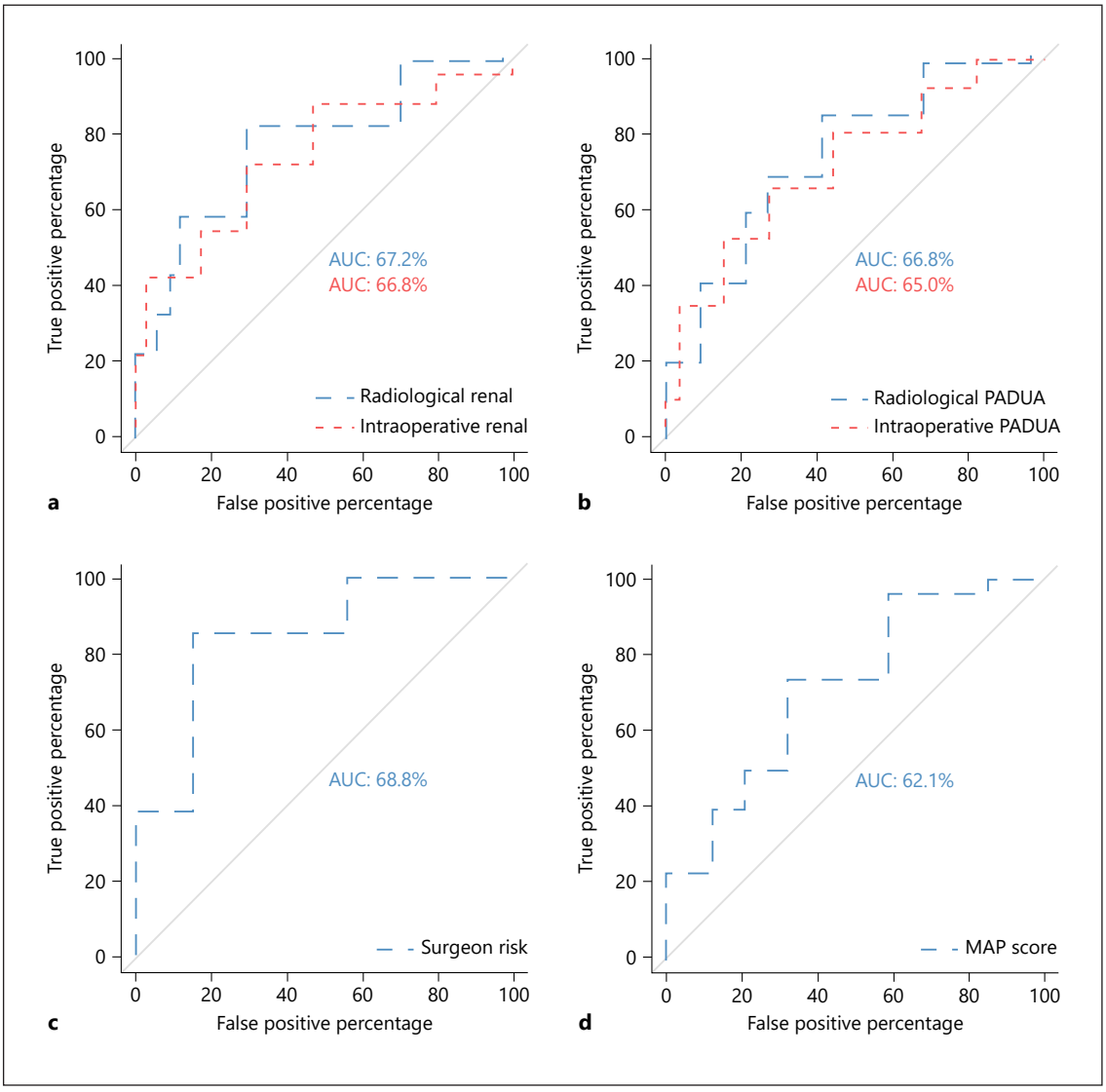


Fig. 3. AUCs of radiological and intraoperative RENAL (**a**) and PADUA (**b**) scores, surgeon's assessment (**c**), and MAP score (**d**) for predicting Trifecta. PADUA, preoperative aspects and dimensions used for an anatomical; MAP, Mayo Adhesive Probability; AUC, area under the curve.

<0.001). Strength of correlations seemed dependent on the way of obtainment as both radiologically and both intraoperatively acquired RENAL and PADUA scores showed the highest correlations with each other ($r = 0.85$, $r = 0.86$ respectively). Furthermore, all scores revealed significant correlations with the surgeon's assessment (all p values <0.001). However, with correlation coefficients ranging from 0.35 to 0.45, the association of the scores to the subjective assessment appeared weaker than the association of the respective scores with each other (see Table 2). Furthermore, a significant correlation between the MAP score and the intraoperative surgeon's rating on perinephric fat adhesiveness could be observed ($r = 0.506$, $p < 0.001$; Fig. 2).

Regression Analyses

For prediction of Trifecta, both scores, PADUA and RENAL for radiological and intraoperative assessment, as well as the MAP score and surgeon's assessment were significant factors on univariable analyses. On multivariable analysis, however, both intraoperative scores did not predict Trifecta (Table 3). Additionally, according to both

Table 2. Correlation of radiological and intraoperative scores and surgeon's assessment. Strength of correlation given as Pearson's correlation coefficient

	PADUA rad	RENAL rad	PADUA intraoperative	RENAL intraoperative	Surgeon risk
PADUA rad	1				
p value	–				
RENAL rad	0.86	1			
p value	<0.001	–			
PADUA intraoperative	0.72	0.66	1		
p value	<0.001	<0.001	–		
RENAL intraoperative	0.70	0.68	0.85	1	
p value	<0.001	<0.001	<0.001	–	
Surgeon risk	0.35	0.37	0.47	0.45	1
p value	<0.001	<0.001	<0.001	<0.001	–

PADUA, preoperative aspects and dimensions used for an anatomical.

univariable and multivariable analyses, the open approach was significantly associated with a smaller chance of Trifecta achievement (OR = 0.16, CI = 0.04–0.69, $p = 0.015$). Regarding major complications, the univariable analysis identified both RENAL and MAP scores and the surgeon's assessment to be predictive markers. However, only the MAP score proved as significant independent predictor of major complications on multivariable analysis (OR = 2.12, CI = 1.31–3.41, and $p = 0.002$, see online suppl. Table 2). With respect to the prediction of IT, radiological scores outperformed intraoperative scores on both uni- and multivariable analyses. Radiological scores as well as the surgeon's assessment were the only independent predictors for IT of 25 min or more (online suppl. Table 3).

ROC curves created from univariable logistic regression showed comparable prediction capability of each score with area under the curve ranging from 49.9 to 70.2 percent. Figure 3a–d shows the ROC curves analyzing the accuracy of the scores in predicting Trifecta achievement, ROC curves showing the predictive accuracy of major complications, and IT of ≥25 and ≥20 min are presented as online suppl. Figures 2a–d, 3a–d, and 4a–d, respectively.

Discussion

Correlations

There were high correlations between radiological scores with the respective intraoperative score. To our knowledge, this is the first study to report on the relation between radiological and intraoperative findings. Nowadays, radiological evaluation provides high resolution imaging, while intraoperative evaluation can be complicated due to complex anatomy with adjacent tissue. Thus, minor differences between the 2 assessments are reasonable. Still, a reliable, precise, and safe evaluation whether tumors are organ confined or locally advanced can be more accurate during surgery as tissue feeling and palpation are possible. In addition, also radiological RENAL and PADUA scores as well as intraoperative RENAL and PADUA scores showed a strong correlation. This is in line with a previous study conducted by Bylund et al. [20] reporting on data of 162 PN patients with similar findings. RENAL and PADUA scores correlated strongly featuring a correlation coefficient of 0.79 which was comparable to our results. Sharma et al. [21] compared the RENAL score with a subjective surgeon's rating and identified a statistically significant correlation. Similarly, Khene et al. [29] analyzed a subjective assessment given pre- and postoperatively by the surgeon in comparison with RENAL, PADUA, and the MAP score. They observed good correlations for all scores, with RENAL showing the strongest correlation with the preoperative assessment [29].

Prediction of Trifecta

Trifecta is an integrated variable compromising major objectives of surgical RCC treatment: the oncologically safe resection, functional preservation by reducing IT, and minimizing complications. Hence, the prediction of

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Table 3. Logistic regression model for evaluating the association between nephrometry scores and Trifecta. Multivariable models consisted of age, gender, BMI, ASA score, approach, and one of the scores at a time (e.g., radiological RENAL)

Variable	Direction and unit	Univariable analyses						Multivariable analyses					
		coefficient	SE	wald χ^2	*p* value	odds ratio	95% CI	coefficient	SE	wald χ^2	*p* value	odds ratio	95% CI
Intercept*													
Age <65 years	Yes versus no	0.11	0.20	0.32	0.5710	1.25	0.58–2.68						
Men	Yes versus no	0.003	0.21	0.0001	0.9909	1.01	0.43–2.33						
BMI <25 kg/m^2	Yes versus no	−0.06	0.21	0.08	0.7828	0.89	0.40–1.99						
ASA ≤2	Yes versus no	0.16	0.21	0.56	0.4562	1.37	0.60–3.14						
Approach	OPN (1) versus RAPN (2)	−0.93	0.38	5.97	**0.0146**	0.16	0.04–0.69						
RENAL rad	Increasing units	−0.40	0.13	9.15	**0.0025**	0.67	0.52–0.86	−0.34	0.14	5.92	**0.0149**	0.71	0.54–0.94
RENAL intra	Increasing units	−0.32	0.11	7.94	**0.0048**	0.73	0.58–0.91	−0.22	0.12	3.23	0.0721	0.80	0.63–1.02
PADUA rad	Increasing units	−0.34	0.12	8.86	**0.0029**	0.71	0.57–0.89	−0.26	0.12	4.47	**0.0346**	0.77	0.60–0.98
PADUA intra	Increasing units	−0.29	0.11	6.97	**0.0083**	0.75	0.60–0.93	−0.18	0.12	2.16	0.1413	0.84	0.66–1.06
MAP score	Increasing units	−0.29	0.13	4.86	**0.0275**	0.75	0.58–0.97	−0.43	0.17	6.38	**0.0115**	0.65	0.48–0.91
Surgeon assessment	Increasing units	−1.05	0.30	12.35	**0.0004**	0.35	0.20–0.63	−0.91	0.32	7.85	**0.0051**	0.40	0.22–0.76

The multivariable model consisted of age, gender, BMI, ASA score, approach and one of the scores at a time (e.g., radiological RENAL). ASA, American Society of Anaesthesiologists; CI, confidence interval; SE, standard error; PADUA, preoperative aspects and dimensions used for an anatomical; MAP, Mayo Adhesive Probability.
* Intercept is defined as a mathematical constant for each model; not specified for there is no clinical interpretation. Coefficient (β) is defined as the mathematical weighting of each variable in the model. SE is defined as standard error, the estimated error of the mathematical weighting. Wald^2 is defined as [|coefficient|/standard error]^2. The higher the value, the higher the predictive value of the variable. Odds ratio is the change in odds of transfusion for each unit change of the variable while controlling for other variables in the model. 95% CI is defined as the 95% confidence interval for the estimated odds ratio [27].

this variable inherits valuable information for patient counselling on the anticipated therapeutic success. In our cohort, the Trifecta success rate was 77.3%, and all radiological scores and the subjective surgeon's rating were independent predictors for Trifecta achievement.

In a multi-institutional study by Harke et al. [30], comparing Trifecta achievement between OPN and RPN for entirely endophytic tumors, PADUA score was identified as the only independent predictor of Trifecta. However, in this study, no other nephrometry score was included in the analysis. Complementarily, Khene et al. [31] analyzed the predictive potentials of RENAL and MAP scores for Trifecta achievement. They found the MAP score to be an independent predictor of Trifecta achievement on multivariable analysis, while RENAL score presented a significant association only on univariable analysis [31]. This aspect is supported by the results obtained by Sharma et al. [21]. They divided their study population into 2 groups according to the Trifecta status (Trifecta positive and negative patients). The surgeon's rating significantly correlated with the 2 subgroups, while there was no such link regarding the RENAL score. It was argued by the authors that the postoperative evaluation by the surgeon can more adequately predict Trifecta achievement as it comprises pre- and intraoperative factors [21]. Another study conducted by Khene et al. [29] revealed limited predictive potentials for all scores analyzed (RENAL, PADUA, and MAP scores), while again the surgeon's rating seemed to be superior in predicting Trifecta outcomes. In 2018, Sharma et al. [21, 32] compared nephrometry scores for their capability of predicting different perioperative outcome parameters. Neither RENAL nor PADUA scores showed significant correlations with Trifecta achievement or any other tested variable [21, 32]. These findings mirror the results acquired by Acar et al. [33]. None of the scores (RENAL, PADUA, and C-Index) were predictive of Trifecta. Furthermore, Acar et al. [33] found the length of hospitalization to be the only parameter differing between the groups of Trifecta-positive and Trifecta-negative patients. This, however, cannot be used as a predictor as it is, naturally, a belated postoperative variable and inevitably affected by the occurrence of complications. Furthermore, the R-status which is part of Trifecta has usually no impact on the immediate postoperative course.

Overall, there is a critical view on the scores for their predictive potential regarding Trifecta achievement, while a trend can be observed toward favoring the surgeon's rating. In our study, however, the radiological scores were capable of predicting Trifecta. Yet, we also identified the subjective surgeon's assessment as independent predictor with the highest accuracy. The attempt at objectifying this assessment by generating intraoperative nephrometry scores generated equivocal results. As these scores have been developed for evaluation on radiological imaging, they showed limited applicability to the intraoperative situs. Further studies are needed in order to determine which score or assessment incorporates the highest potential for predicting Trifecta outcomes.

Prediction of Major Complications

Major complications are most relevant for the postoperative course of the patient. In the presented study, only the MAP score was an independent predictor for complications on multivariable analysis. In contrast, the RENAL score (radiological and intraoperative) and the surgeon's assessment were predictors on univariable analysis only. In the literature, the association of perioperative complications and nephrometry scores shows equivocal results. Upon its initial presentation, the PADUA score and the respective risk groups were associated with an increased risk for postoperative complications [9]. These results were supported by a number of subsequent studies for the individual scores [13, 34, 35] and their risk group stratification [36]. Other authors have obtained differing results [37, 38]. In some studies, no associations of neither RENAL nor PADUA scores were found [17, 19], while in comparison, the surgeon's assessment proved as the only significant predictor of postoperative complications [29].

With regard to the MAP score, it seems to be agreed upon that this is a predictor of the presence of adherent perinephric fat [39]. However, the occurrence or grade (according to the Clavien classification) of complications could not be related to neither adherent perinephric fat nor the MAP score [40, 41]. In contrast to that, we found the MAP score to be the only independent predictor of major complications, outperforming not only all other nephrometry scores but also the surgeon's subjective rating. Possibly, the MAP score has been underestimated with respect to predicting major complications. These results underline that tumor surroundings should not be neglected when evaluating tumor risk potential.

Prediction of Ischemia Time

Aim of PN is the reduction of IT in order to minimize parenchymal and functional loss [42, 43]. The role of off-clamp resection remains controversial as latest RCTs reveal similar postoperative outcomes compared to the procedure under arterial clamping [44, 45]. Moreover, IT is a widely accepted measure of tumor complexity as difficult lesions require a longer time to be excised under

ischemic conditions [7]. Many studies have already investigated the potential of nephrometry to predict IT. A systematic review by Klatte et al. [7] confirmed that the majority supports strong correlations between RENAL and PADUA scores with the extent of IT. Bylund et al. [20] even attributed a stronger association to the scores than to its individual parameters such as tumor size and location. Only few acquired controversial results or no statistically significant associations [19, 46]. Our findings are in line with the general view in the literature as we found radiological RENAL score and PADUA score to effectively predict IT with high accuracy. However, our intraoperative scores did not reaffirm such link.

To our knowledge, there are no studies comparing the surgeon's assessment to the length of IT. We found the surgeon's risk assessment to strongly correlate with IT. This association appears as plausible consequence as a challenging procedure may more often be accompanied by a prolonged postoperative course. Yet, this association was not expressed in the intraoperatively acquired nephrometry rating, which leads us to the assumption that not only anatomical factors contribute to the surgeon's intraoperative perception of anticipated complications.

Analogous to our results regarding Trifecta, radiological tumor examination yielded promising results in predicting tumor complexity, while intraoperative nephrometry performed inferiorly. As the surgeon's assessment is also in accordance with IT, it seems to be a complex composition of not only anatomical features. It is yet to be seen what factors contribute to the surgeon's perception of tumor complexity and risk stratification.

Limitations

This study is not devoid of limitations. First, the postoperatively completed assessment of intraoperative tumor anatomy might induce a certain degree of bias as surgeons could possibly overestimate tumor complexity. In order to reduce this bias, surgeons were asked to fill the questionnaire instantly after the procedure was finished and before potential complications could be observed during the postoperative course. Furthermore, surgeons were not aware of the value of each score given to the respective tumor preoperatively/radiologically. The strong correlations between pre- and intraoperative scores hint that the applied method did not limit the quality of our results. In addition, no prediction of long-term functional or oncological outcomes was analyzed. Yet, these are no primary considerations of nephrometry. Our findings were drawn from a medium-sized sample of 150 patients, which might affect external validity of the results to some extent.

Conclusion

These data provide a comprehensive comparison of radiological and intraoperatively determined nephrometry scores with a subjective surgeon's rating. The scores correlate well with each other. Minor differences are possibly attributable to the fact that nephrometry was developed for radiological examination of renal tumors. Radiological scores seem applicable for postoperative risk stratification and were not outperformed by intraoperative assessment. The MAP score correlates well with surgeon's assessment of the perirenal fat and can predict major complications underlining the importance of perirenal fat characteristics.

Statement of Ethics

The study was approved by the institutional review board of Heidelberg University, Medical Faculty Mannheim (2013-830-MA).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding.

Author Contributions

All authors met all of the following criteria: (1) substantial contributions to conception and design and/or acquisition of data and/or analysis and interpretation of data, (2) authors participated in drafting the article or revising it critically for important intellectual content; and (3) authors gave final approval of the version to be published.

In detail, authors contributed to the following parts of the study: study conception and design: Egen, Kowalewski, Kriegmair, and Honeck; acquisition of data: Egen, Kowalewski, Riffel, and Kriegmair; analysis: Egen and Kowalewski; analysis and interpretation of data: Egen, Kowalewski, Riffel, and Kriegmair; drafting of manuscript: Kowalewski, Riffel, Honeck, and Kriegmair; critical revision: Riffel, Honeck, and Kriegmair. Without the help of each of the authors, the conduction of the study would not have been possible or would have led to a significant reduction in quality.

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