

Research Article

PADUA and RENAL Nephrometry Score Systems could not Predict Postoperative Outcomes after Partial Nephrectomy of Small Renal Masses in a Danish Cohort

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- PADUA
- Partial nephrectomy
- RENAL
- Warm ischemia time
- Small renal mass

Abstract

Objective: We aimed to evaluate the efficacy of the two previously validated scoring systems PADUA (Preoperative Aspects and Dimensions Used for an Anatomical score), and RENAL (Radius, Exophytic/endophytic, Nearness, Anterior/posterior Location) in a Danish cohort, with regard to the postoperative outcomes after partial nephrectomy. We also evaluated the shortest distance between the margin of the tumor and renal vessels, termed DTV (Distance of the Tumor from renal hilus Vessel), as a possible novel and simple predictor of postoperative outcomes.

Patients and methods: We collected retrospective data on 153 consecutive patients who underwent partial nephrectomy for small renal masses from January 2010 to December 2014. The median age was 67 years (range 33-82), 99 men and 54 women. All CT scans were initially evaluated by a radiologist and then re-evaluated by one urologist with measurement of all features included in the PADUA and RENAL score systems, as well as DTV. Outcomes were: bleeding, warm ischemia time, length of hospital stay, complication rates, and change in the estimated glomerular filtration rate (e-GFR) from before to after surgery.

Results: Neither PADUA nor RENAL were statistically significant predictors of any outcome in this cohort. The same was true for DTV regarding bleeding ($p=0.18$), warm ischemia time ($p=0.58$), length of hospital stay ($p=0.87$), complication rate ($p=0.59$) and the changes in the e-GFR from before to after surgery ($p=0.34$).

Conclusion: Neither the PADUA, the RENAL score systems nor could the DTV accurately predict the peri-or postoperative outcomes in our Danish cohort after laparoscopic partial nephrectomy of small renal masses.

ABBREVIATIONS

ASA: American Society of Anesthesiologists; AUC: Area Under the Curve; BMI: Body Mass Index; CT: Computed Tomography; DM: Diabetes Mellitus; DTV: Distance of the Tumor from Renal Hilus Vessel; EBL: Estimated Blood Loss; EGFR: Estimated Glomerular Filtration Rate; LOS: Length of Hospital Stay; PADUA: Preoperative Aspects and Dimensions Used for an Anatomical Score; PN: Partial Nephrectomy; RENAL: Radius, Exophytic/Endophytic, Nearness, Anterior/Posterior Location; ROC: Receiver Operating Characteristic; WIT: Warm Ischemia Time

INTRODUCTION

The incidence of renal cell carcinomas has increased over the past two decades, largely because of the incidental detection of

small renal tumors resulting from an increased use of computed tomography (CT) [1-3]. Surgical management of these small tumors has shifted from radical nephrectomy to nephron-sparing surgery with partial nephrectomy (PN) with a comparable oncological outcome [4]. Complexity of tumor remains the most important factor when determining which surgical approaches are safe and feasible. Many nephrometry score systems have been developed in the last decades to evaluate the complexity of renal masses and link this complexity to surgical and oncological outcome after surgery. Two validated and widely used score systems to aid in the decision of the surgical approach for treatment of renal masses are the PADUA (Preoperative Aspects and Dimensions Used for an Anatomical score), and RENAL (Radius, Exophytic/endophytic, Nearness, Anterior/posterior Location) scoring systems [5,6].

The aim of this study is to evaluate the efficacy of these two score systems with regard to the postoperative outcomes, and to evaluate the distance of the tumor from renal hilus vessel (DTV) as a novel and very simple predictor of the postoperative outcome after partial nephrectomy for small renal masses.

MATERIALS AND METHODS

Data on 153 consecutive patients who underwent hand assisted partial nephrectomy at the Department of Urology, Zealand University Hospital, Roskilde, were included from January 2010 (when the department started performing PN routinely), to December 2014. Data were collected retrospectively from patient charts. In accordance with Danish legislation, we obtained permission to conduct this study from the Danish Health and Medicines Authority who authorized that specific written or verbal consent from each individual was not required. All patients had undergone a CT urography as well as either a thoracic x-ray or CT scan as part of their preoperative diagnostic work-up. Pathological T-stage was assigned according to the 2009 TNM classification [7]. All CT scans were initially evaluated for diagnosis and staging by a radiologist. Subsequently, for this study, one urologist carried out the measurements of all features included in the PADUA and RENAL score systems, as well as DTV which was measured as the shortest distance between the margin of the tumor and the renal vessels (Figure 1). All operations were performed by a team consisting of three surgeons.

To evaluate the surgical outcome according to learning curve, the cohort was divided into three equal groups (tertiles) over the study period with 51 patients in each group (Group 1: Jan 2010-May 2012; Group 2: May 2012-Nov 2013; Group 3: Nov 2013-Dec 2014).

Perioperative outcome collected from patient charts were: operating time, estimated blood loss (EBL), warm ischemia time (WIT), positivity of surgical margin, re-operation, length of hospital stay (LOS), body mass index (BMI), diabetes mellitus (DM), and arterial hypertension and American Society of Anesthesiologists (ASA) classification. Complications were

categorized into minor (Clavien score ≤ 2) or major complications (Clavien score > 2) [8]. Estimated glomerular filtration rate (eGFR) was collected from the patient charts as preoperative and 6 months postoperative values as a routinely calculated value from creatinine measurements according to Modification of Diet in Renal Disease formula without correction for race: $eGFR (ml/min/1.73m^2) = 175 \times (\text{standardized creatinine}/88.4) - 1.154 \times (\text{age}) - 0.203 \times (0.742 \text{ if female})$ (creatinine in $\mu\text{mol/l}$, age). Creatinine was measured by an automated enzymatic quantitative method (Dimension Vista 1500 system, Siemens Healthcare Diagnostics, Inc.).

Statistical analyses were conducted using independent t-tests for continuous variables, paired t-test for analysis of the pre- to postoperative changes in e-GFR, and chi-square tests or Fisher's exact test for categorical variables, as applicable. Kruskal-Wallis analyses were performed to evaluate the relationships between scoring systems regarding the perioperative outcomes and postoperative complications. Receiver operating characteristic (ROC) and area under the curve (AUC) were used to determine the accuracy of each scoring system. All statistical analyses were done using Statistical Analysis Software 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS AND DISCUSSION

The median of age was 67 years (range 33-82 years), with 99 men and 54 women included. Preoperatively, 17 patients (11%) were diagnosed with diabetes mellitus and 70 patients had arterial hypertension (46%). At evaluation before surgery, 40 patients (26%) presented with ASA 1, 76 patients (50%) with ASA 2 and 37 patients (24%) presented with ASA 3. The mean DTV (\pm SD) was 26 mm (\pm 12). The demographic and pathological features for the patients and the renal masses are shown in (Table 1).

Neither PADUA nor RENAL were significant predictors of any outcome, and there was no significant difference in the accuracy between PADUA, RENAL and DTV for prediction of outcomes (Table 2). The same was observed for DTV, (Figure 2).

In sub-analyses of the data, the tumor size was not a significant predictor of EBL ($p=0.36$), WIT ($p=0.38$), LOS ($p=0.28$) or complication rate ($p=0.78$), but involvement of renal sinus was significant predictor of both EBL and LOS. EBL increased by 85 ± 44 ml ($p=0.05$) in case of involvement, and LOS increased by 0.7 ± 0.3 days ($p=0.02$). Renal sinus involvement was a borderline significant predictor of pre- to postoperative change in e-GFR, which decreased by 4 ± 2 ml/min/cm² ($p=0.07$), but sinus involvement did not predict WIT ($p=0.22$), complication rate ($p=0.44$), surgical margin ($p > 0.05$) or re-operation ($p > 0.05$).

BMI was not a significant predictor of EBL ($p=0.38$), WIT ($p=0.29$), LOS ($p=0.86$) or complication rate ($p=0.94$). Presence of an exophytic tumor was not a significant predictor of EBL ($p=0.55$), WIT ($p=0.16$), LOS ($p=0.88$), complication rate ($p=0.43$) or difference in the e-GFR before vs. after the surgery ($p=0.27$).

Patients with DM had a mean significant decrease in the e-GFR by 7 ± 2 ml/min/cm² ($p=0.01$), but DM was not significant predictor of any other outcomes. Presence of preoperative arterial hypertension, anterior or posterior location of the tumor or gender also was not significant predictors of any outcomes.

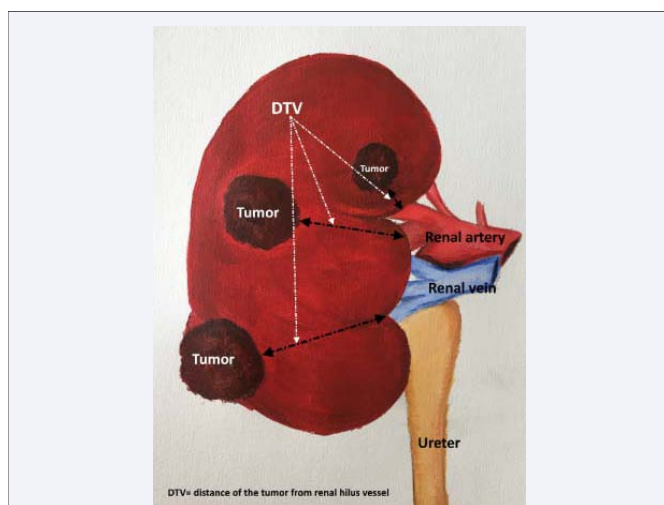


Figure 1 Measurements of the distance between the tumor margin and renalvessels (DTV).

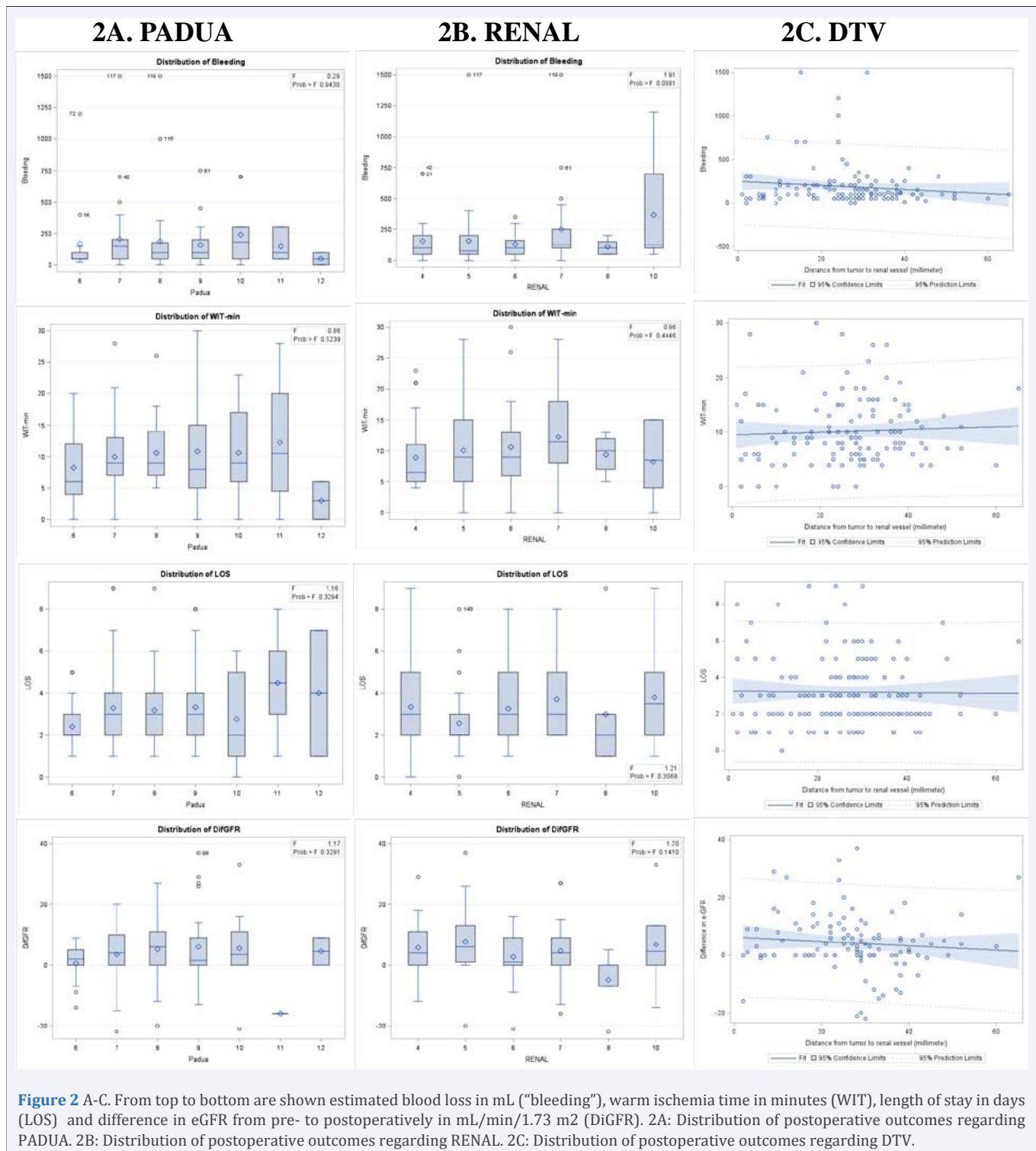


Figure 2 A-C. From top to bottom are shown estimated blood loss in mL ("bleeding"), warm ischemia time in minutes (WIT), length of stay in days (LOS) and difference in eGFR from pre- to postoperatively in mL/min/1.73 m² (DiGFR). 2A: Distribution of postoperative outcomes regarding PADUA. 2B: Distribution of postoperative outcomes regarding RENAL. 2C: Distribution of postoperative outcomes regarding DTV.

Comparing groups across the learning curve, patients who underwent partial nephrectomy in Group 2 had a significantly lower WIT of 4 ± 1 min ($p=0.0009$) compared to group 1, while those who underwent surgery in Group 3 had a significant increase in WIT 3 ± 1 min ($p=0.01$). Overall complication rates also decreased significantly in Group 3 compared to Group 1 and Group 2 ($p=0.02$). There were no significant differences between groups regarding EBL ($p=0.38$), LOS ($p=0.17$), re-operation

rate ($p=0.47$), surgical margin ($p=0.35$), pre- to postoperative difference in e-GFR ($p=0.18$) or operation time ($p=0.67$). There were no significant differences in the PADUA ($p=0.51$) or RENAL ($p=0.33$) classifications or DTV ($p=0.84$) through the study period.

In multivariate analysis with adjustment of WIT, tumor size, EBL, renal sinus involvement and re-operations rate, the LOS increased by 1.4 days, only when patients get re-operation (SE

0.6; 95% CL 0.15 – 2.81, p=0.02). Renal sinus involvement was neither significant predictor of pre- to postoperative change in e-GFR (p=0.20) nor on EBL (p=0.11). DM remains a poor predictor on pre- to postoperative change in e-GFR, the e-GFR decreased 6 ml/min/1.73m², if patients had DM prior to surgery (SE 3.1; 95% CL -12.29 – 0.2, p=0.05).

Discussion

Partial nephrectomy is considered the gold standard of

care in guidelines from both the American and the European Urological Associations [9,10]. The surgical approach of open or laparoscopic techniques may depend on patient history including previous abdominal surgery, as well as the surgeon's preferences. The planning and feasibility of partial nephrectomy now depends strongly on the anatomical features of the renal masses. Due to higher complication rates associated with partial compared to radical nephrectomy, this procedure should be limited to high volume center with high experience [11]. Many nephrometry

Table 1: Perioperative data, complications, pathological features of the renal masses and PADUA/RENAL classification information.

Perioperative data	e-GFR, mean± SD (95% CL) (mL/min/cm ²)	Before surgery	76 ± 16 (73-79)
		After surgery	71 ± 17 (68-74)
		Difference pre- to postoperatively	4 ± 10 (3-6)
	EBL in mL mean ± SD (95% CL)		176 ± 241 (135-217)
	Operation time minutes, mean ± SD (95% CL)		119 ± 34 (113-125)
	Warm ischemia time, minutes, mean ± SD (95% CL)		10 ± 6 (9-11)
	Length of stay in days, mean ± SD (95% CL)		3 ± 2 (3-4)
	DTV in mm, median, mean ± SD (95% CL)		28, 26 ± 12 (24-28)
	PADUA Score, median, mean± SD (95% CL)		8, 8 ± 1.3 (7.8-8.3)
	RENAL Score, median, mean± SD (95% CL)		6, 5.8 ± 1.6 (5.5-6.0)
Complications	Clavian score, N (%)	1	112 (73%)
		2	24 (16%)
		3a	9 (5.9%)
		3b (3 patients required endoscopic insertion of JJ catheter, 2 patients with wound infection)	5 (3.3%)
		4a (2 patients required dialysis)	2 (1.3%)
		5 (one patient died)	1 (0.65%)
		Re-operation, N (%)	No
	Yes (3 patients required endoscopic insertion of JJ catheter, 2 patients with wound infection required revision of the wound not under general anesthesia, 2 patients required insertion of central venous catheter to hemodialysis, one patient get nephrectomy due to severe bleeding and died one the 3rd. Postoperative day)	8 (5%)	
Tumor characteristics	Laterality of tumor N (%)	Left side	85 (56%)
		Right side	68 (44%)
	Tumor size in cm, N (%)	4	105 (69%)
		4.1-7	27 (18%)
		>7	22 (14%)
		T stage, N (%)	pT1a
		pT1b	19 (12%)
		pT2	16 (10%)
		pT3	10 (6.5%)
	Surgical resection margins, N (%)	Benign lesions	26 (17%)
		Negative margins	145 (95%)
		Positive margins	8 (5%)
PADUA & RENAL	Longitudinal (polar) location, N (%)	Middle	59 (39%)
		Superior/inferior	94 (61%)

	Exophytic rate, N (%)	<50%	44 (29%)
		>50%	84 (55%)
		Endophytic	25 (16%)
	Renal rim involved, N (%)	Lateral	102 (67%)
		Medial	51 (33%)
	Renal sinus, N (%)	Involved	79 (51.63%)
		Not involved	74 (48.36%)
	Urinarycollecting system, N (%)	Dislocated/infiltrated	30 (19.60%)
		Not involved	123 (80.39%)
	Face, N (%)	Anterior	60 (39.21%)
		Posterior	93 (60.78%)
	Location of mass relative to polar lines, N (%)	50% across polar line/entirelybetween polar lines/crosses axialmidline	30 (19.60%)
		Entirelybelowlower polar/above upper polar line	75 (49.01%)
		Crosses polar line	48 (31.37%)

Abbreviations: eGFR: estimated Glomerular Filtration Rate; EBL: Estimated Blood Loss; DTV: Distance of the Tumor from renal hilus Vessel

Table 2: Accuracies of PADUA, RENAL and DTV scores regarding outcomes, and p-value for difference between accuracies.

	PADUA AUC (95% CL)	RENAL AUC (95% CL)	DTV AUC (95% CL)	P- value
Surgicalresection margins	0.63 (0.48-0.79)	0.65 (0.50-0.80)	0.62 (0.42-0.83)	0.98
Re-operation	0.57 (0.37-0.77)	0.62 (0.39-0.86)	0.60 (0.49-0.70)	0.83
Warmischemia time	0.52 (0.42-0.62)	0.59 (0.49-0.69)	0.57 (0.47-0.67)	0.33
Estimatedbloodloss	0.49 (0.39-0.59)	0.54 (0.43-0.64)	0.54 (0.44-0.64)	0.54
Operation time	0.55 (0.45-0.66)	0.49 (0.39-0.60)	0.55 (0.44-0.66)	0.96
Complications	0.57 (0.42-0.72)	0.58 (0.40-0.77)	0.51 (0.36-0.66)	0.63
Change in e-GFR	0.52 (0.43-0.62)	0.51 (0.41-0.61)	0.49 (0.39-0.59)	0.54

Abbreviations: eGFR: estimated Glomerular Filtration Rate

score systems may help the surgeon to take the decision how to perform PN, or to refer the patients with high nephrometry score to a high volume center to perform the procedure [5,6].

We analyzed our cohort of patients undergoing laparoscopic partial nephrectomy to evaluate retrospectively the benefit of nephrometry score systems in surgical decision making. We found that neither the PADUA score system nor the RENAL score predicted strongly the surgical outcomes. We hypothesized that the single measure of distance between the tumor margin and the renal vessel would influence postoperative outcomes, but this could not be confirmed based on this study. This result may be due to the surgeons' experience with laparoscopic technique prior to starting partial nephrectomy at our institute at 2010, resulting in good perioperative and postoperative outcomes throughout the study period and across classification scores. Some other studies have, just as the present study, also reported negative findings regarding PADUA and RENAL score systems [12], in contrast to the original papers reporting PADUA and RENAL score systems as predictors of the postoperative outcome [5,6].

In our cohort, involvement of the renal sinus was a statistically significant predictor of increased EBL as well as LOS, while the distance between the tumor mass margin and renal vessel was not. Thus, in our experience there was no minimum distance

between the renal mass and the renal sinus for performing partial nephrectomy safely with minimal risk for bleeding.

In our cohort, BMI was not a significant predictor of postoperative outcome, corroborating other studies [13,14]. The gender also did not predict postoperative outcome in our cohort, contrary to Abdullah et al., [13]. Who reported that male gender was a significant predictor on postoperative outcome in obese patients undergoing partial nephrectomy.

The efficacy of PADUA, RENAL and DTV was not statistically significant in our study (Table 2). Thus in our experience, the validated PADUA and RENAL scores which include multiple measurements did not perform better as predictors of outcome than one simple measurement (DTV). The accuracy and quality of reporting the score systems can differ between observers, depending on experience, but the agreement of reporting PADUA and RENAL score systems was previously reported as high by three different observers [15], where reporting one measurement was more accurate than many measurements.

Increased experience with performing PN over the study period leads to a small but statistically significant decrease in WIT and complications rate in Group 2, while the WIT increased again in Group 3; however, the complications rate were still lower

than in Group 1. This increase in the WIT may be explained by the inclusion of new surgeons with less experience, and possibly an increase over time in the complexity of the renal masses where partial nephrectomy was planned.

The limitations of our study include the small number of patients, the retrospective nature of the study, as well as the inclusion of patients in the period of our initial experience, which can bias outcomes, especially EBL and WIT. Prospective studies are needed to evaluate the nephrometry score systems and their accuracy on large cohorts with small renal masses.

CONCLUSION

PADUA and RENAL score systems poorly predict the postoperative outcome in our Danish cohort of laparoscopic partial nephrectomy for small renal masses, and did not perform better than the single distance measurement between the tumor mass and renal vessels. Involvement of the renal sinus was significant predictor to increase EBL and LOS only in univariate analysis. DM was the only predictor of a pre- to postoperative decrease in e-GFR in univariate and multivariate analysis.

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