Original Article

Comparison of RENAL, PADUA, and C-index scoring systems in predicting perioperative outcomes after nephron sparing surgery

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ABSTRACT

Introduction and Objective: The RENAL, PADUA and centrality index (C-index) nephrometry scoring systems (SS) have been individually evaluated for their role in predicting trifecta outcomes after nephron-sparing surgery (NSS). However, there is little data on their comparative superiority. The present study was designed to evaluate the predictive value of three SS and to assess interobserver reliability.

Materials and Methods: Fifty patients undergoing NSS at our center between January 2014 and April 2016 were included in the study. The demographic details were noted. Images (computed tomography [CT] scans or magnetic resonance imaging) were reviewed by a urologist and a radiologist independently and RENAL, PADUA, and C-index were calculated. The correlation between these scoring system and trifecta outcomes were calculated.

Results: The RENAL and PADUA score did not correlate with any of the perioperative parameters. However, C-index had a significant correlation with operative time (OT) ($P = 0.02$) and trifecta outcomes ($P < 0.05$). There was an excellent concordance between the two observers in scoring the RENAL score ($\alpha = 0.915$; intraclass correlation coefficient [ICC] = 0.814) and PADUA score ($\alpha = 0.816$; ICC = 0.689 [$P < 0.001$]). There was lesser although acceptable concordance in the calculation of C-index (ICC –0.552; α –0.711).

Conclusions: There is good correlation among all the 3 SS. C-index has lower reproducibility due to difficult mathematical calculation but correlated best with trifecta outcomes.

INTRODUCTION

The complexity of renal tumors remains the primary determinant based on which the urologists decide surgical approach and strategy for treatment. A number of SS have been reported to standardize and quantitate tumor complexity.[1-3] These scores may also have potential to influence treatment selection provided they predict operative outcomes. Radius exophytic/endophytic nearness anterior/posterior location (RENAL) nephrometry score and preoperative aspects and dimensions used for anatomic (PADUA) classification and SS involve similar components and methodology. They provide a comprehensive description of the tumor size, closeness to the collecting system, polarity, and anterior or posterior location. Each component is assigned by score, providing a continuous variable.[2,3] Another score known as centrality index (C-Index) represents simple, practical measurement and characterizes tumor centrality based on the ratio of the distance between the tumor and kidney center and tumor radius[1]

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/iju.IJU_247_17

Received: 13.08.2017, **Accepted:** 09.10.2017

Financial support and sponsorship: Nil

Conflicts of interest: There are no conflicts of interest.

A number of studies validate these scores independently for determining preoperative decision-making and also predicting the postoperative outcomes in laparoscopic and open nephron-sparing surgery (NSS).[4-6] However, there is a paucity of data comparing these SS in predicting trifecta outcomes in NSS. There have been conflicting reports showing the superiority of one score over the other.[4,7,8] In an earlier study, we found that mean tumor size and staging in our series was advanced as compared to that in available literature.[9] We designed this study to evaluate the predictive value of SS (RENAL, PADUA score, and C-index) in determining perioperative outcome in NSS and to determine interobserver reliability, reproducibility, and variation in scoring done by urologist versus radiologist.

MATERIALS AND METHODS

Fifty consecutive patients with renal masses undergoing NSS were enrolled. The demographics details were noted. All the patients' imaging, viz., CT scans were viewed by an urologist and radiologist, and RENAL nephrometry score (RNS), PADUA score[3] and C-index[1] were calculated independently by an urologist and a radiologist. Each observer was blinded to the results of the other observer's assessments. In addition to using absolute scores, RENAL and PADUA scores were calculated and categorized as described by Kutikov *et al*.[2] and Ficarra *et al*. respectively.[3] The C-index was categorized as <1, equal to 1 or >1.[1]

The operative characters were noted viz. Warm ischemia time (WIT), estimated blood loss (EBL), OT, postoperative complications in Clavien-Dindo format,[10] length of hospital stay (LOS), percent change in creatinine level and estimated glomerular filtration rate (eGFR) by Cockcroft-Gault Formula. This change in creatinine and eGFR was calculated at immediate postoperative period and at the last available follow-up of the patient. Histopathology was reviewed for type of renal tumor, margin status, and Fuhrman grading.[11]

The trifecta outcomes were defined as negative surgical margins, WIT of <30 min and minimal postoperative complications (Clavien–Dindo Grade 0–2). The patients achieving trifecta outcomes were computed. Comparison was made for the predictive value of all three scores for 50 patients.

Statistical analyses were performed using SPSS v 22.0 (IBM, NewYork USA) and Microsoft Excel 2007. Discrete categorical data were represented in the form of either a number or a percentage. Continuous data, assumed to be normally distributed, were written as in the form of its mean and standard deviation when it was skewed it was written in the form of its median and interquartile range, as per the requirement. The normality of quantitative data was checked by measures of Kolmogorov–Smirnov tests of normality. For normally distributed data, means of three Groups of (RNSs) (low, intermediate, and high) were compared using One-Way ANOVA followed by *post hoc* multiple comparisons test. For skewed data, Kruskal–Wallis test followed by Mann–Whitney U-test for two groups was applied. To compare the 2 groups for normally distributed Student's *t*-test was applied to compare two groups. Proportions were compared using Chi-square or Fisher's exact test, depending on their applicability for 2 Groups. Spearman or Pearson correlation coefficients were calculated to see the relationship of different variables. For time-related variables of Skewed data Wilcoxon-Signed rank test was applied; for normally distributed data paired *t*-test was carried out. To see the reliability of intraobserver error; intraclass correlation coefficient (ICC) and Cronbach's α was calculated. The concordance was rated as excellent for Cronbach α >0.9, good for Cronbach α 0.8–0.9, and acceptable for Cronbach α 0.7–0.8. All the statistical tests were two-sided and were performed at a significance level of $P < 0.05$.

RESULTS

Twenty-seven tumors were located on the right side. Forty-seven NSS out of 50 were done robotically and 3 patients were operated laparoscopically. Majority (48%) of patients (24/50) were detected incidentally. Other clinical presentations included pain (38%), lower urinary tract symptoms (8%), recurrence (2%), Von Hippel–Lindau during follow-up (2%) and hematuria (2%). Majority tumors were stage T1 tumors (80%). Eighteen percent patients were stage T2 and only 1 patient was stage T3a with renal vein thrombosis. Majority of tumors (70%) were clear-cell carcinoma. Tumor margin was positive in 2 (4%) patients.

More than one renal artery was present in 9 (18%) patients and 8 patients had more than one renal vein (16%). The mean operating time (OT) was 157.24 ± 54.205 min, WIT was 25.98 ± 11.58 min, and EBL was 212.50 ± 160.06 ml. Complications were graded as per Clavien–Dindo grading. Median follow-up was 8 months (Range-3–22 months). The mean eGFR of the patient cohort at last follow-up was not significantly different than mean preoperative eGFR. One patient had new onset of CKD III. Complications occurred in 22 patients. Majority (24%) of perioperative complications were of Grade 1, 16% Grade 2 with only 4% patients having grade 3 complications. Mean scores (RENAL, PADUA, and C-index) showed no significant difference and are as follows: RENAL: Urologist = 7.84 ± 2.12 (4–12); Radiologist = 7.36 ± 2.11 (4–11). C-index: Urologist = 1.34 ± 0.62 (0.4-3.00); radiologist = 1.10 ± 0.50 (0.11–2.67) and PADUA: Urologist-9.64 ± 2.22,(6–14) and Radiologist = 8.64 ± 1.94 (6–13).

Correlations were calculated among various scores with respect to various parameters such as OT, WIT, EBL,

Clavien–Dindo complications, tumor size and also the scores determined by radiologist and urologist. All the SS had good correlation among themselves and with tumor size. Pearson Correlation coefficient for RENAL-C-Index was .530 ($P < 0.0005$) and RENAL–PADUA was 0.910 ($P < 0.0005$) and C-index-PADUA was .471 ($P < 0.001$). There was a significant correlation between the C-index and OT ($\sigma = -0.327$, $P = 0.02$). However, no significant correlation was observed between the other scores and EBL, OT, WIT and complications. Thirty-six (72%) patients achieved trifecta outcomes. Out of all the scores only, C-index was associated with trifecta outcomes [Table 1].

There was an excellent concordance between the two observers in scoring RENAL scores. Cronbach $\alpha = 0.915$ and ICC = 0.814 ($P < 0.001$). The ICC and Cronbach α values for all the scores are given in Table 2. The kappa for anterior/posterior agreement was 0.644 ($P < 0.001$). From the analysis, it is clear that minimum concordance was in exophytic/endophytic component and maximum between the "radius". There was good concordance between the two observers in scoring the PADUA score. Cronbach $\alpha = 0.816$ and ICC = 0.689 ($P < 0.001$). The concordance for subcomponents revealed the highest concordance with tumor size and lowest with determination of relation to renal sinus. Among the three scores, the least concordance was between the C-index although it also showed acceptable ICC (0.552) and Cronbach α (0.711). The calculation of C component was the determinant which showed poor concordance.

Table 1: Comparison of scoring systems with respect to trifecta outcomes

Parameters	Trifecta outcomes		*P*
	Positive	Negative	
Mean RENAL	7.64±2.10	8.36±2.17	0.246
Mean PADUA	9.47±2.26	10.07±2.13	0.370
Mean C-index	1.47±0.65	1.04±0.41	0.05

RENAL=Radius exophytic/endophytic nearness anterior/posterior location, PADUA=Preoperative aspects and dimensions used for anatomic

Table 2: Concordance between urologist's and radiologist's score using Cronbach α and intraclass correlation coefficient: radius exophytic/endophytic nearness anterior/posterior location, preoperative aspects and dimensions used for anatomic and C-index

Indices	Cronbach α (CI)	ICC (CI)
RENAL		
Radius	0.939 (0.892-0.965)	0.884 (0.805-0.933)
Exophytic/endophytic	0.692 (0.458-0.825)	0.529 (0.297-0.703)
Nearness to sinus fat or collecting system	0.863 (0.759-0.922)	0.759 (0.612-0.856)
Location in relation to polar lines	0.777 (0.606-0.873)	0.635 (0.435-0.775)
RENAL score	0.915 (0.851-0.952)	0.844 (0.740-0.908)
PADUA		
Tumor size	0.949 (0.910-0.971)	0.903 (0.836-0.944)
Endophytic	0.688 (0.451-0.823)	0.525 (0.291-0.700)
Sinus line	0.793 (0.634-0.882)	0.656 (0.465-0.789)
Renal rim	0.742 (0.545-0.853)	0.589 (0.374-0.744)
Renal sinus	0.202 (−0.406-0.547)	0.112 (−0.169-0.377)
Collecting system	0.759 (0.576-0.863)	0.612 (0.404-0.760)
PADUA score	0.816 (0.674-0.896)	0.689 (0.508-0.812)
C-index		
C	0.260 (−0.304-0.580)	0.150 (−0.132-0.409)
R	0.940 (0.895-0.966)	0.888 (0.810-0.935)
C-index	0.711 (0.491-0.836)	0.552 (0.326-0.718)

RENAL=Radius exophytic/endophytic nearness anterior/posterior location, PADUA=Preoperative aspects and dimensions used for anatomic, CI=Confidence interval, ICC=Intraclass correlation coefficient

DISCUSSION

A number of studies have assessed the existing SS for their role in predicting the trifecta outcomes after nephron sparing surgery.[1-3] In our cohort of 50 patients all 3 scores: RENAL (RNS), PADUA, and C-index were calculated. The RNS did not correlate with any of the perioperative parameters. However, C-index had significant correlation with OT ($P = 0.02$) and was also associated with trifecta outcomes ($P < 0.05$). There was excellent concordance between the urologist and the radiologist in scoring RNS; Cronbach α was 0.915 and ICC was 0.814 ($P < 0.001$). There was good concordance between the two observers in scoring the PADUA score. Cronbach $\alpha = 0.816$ and ICC = 0.689 ($P < 0.001$). Among the three scores, the least concordance was between the two observers the calculation of C-index although it showed an acceptable ICC (0.552) and Cronbach α (0.711).

Esen *et al.* have already validated that RENAL and PADUA score influence surgical treatment strategy for localized renal masses.[5] High RENAL and PADUA scores increased the likelihood of an open NSS. However, the predictive value of these SS in predicting the perioperative outcomes is still controversial.[4,7,8] In fact, with the advent of robotic surgery more and more data have been compiled recently with NSS being offered to patients with larger tumors or highly complex tumors.[12,13]

Okhunov *et al.* conducted a study to establish reliability of these SS and assess relationships between these three SS and perioperative and postoperative variables.[4] They found that there were no significant associations between any of the three SS assessed and the occurrence of complications, OT, or EBL (EBL). All the scores were associated with WIT, percent change in creatinine level, and tumor size. In our series, all the SS had good correlation among themselves and with tumor size. There was significant correlation between the C-index and OT in our study ($P = 0.02$). However, no significant correlation was observed between the other scores (viz. RENAL and PADUA) and EBL, OT, WIT, and complications. Yeon *et al.* have also found that RENAL and PADUA score do not predict perioperative outcomes, namely, complications, WIT, and EBL.[7]

No significant correlation was found by Okhunov *et al.*[4] between the PADUA and RENAL scoring system and LOS.

However, C-Index showed a significant relationship with LOS. Patients with lower scores had longer hospital stay. In our series, there was no correlation between any of these scoring system and LOS [Table 3]. The comparison between their series and ours is shown in Table 3.

Regarding the prediction of trifecta outcomes Acar *et al*. have found that there was no statistically significant difference between RENAL, PADUA, and C-index between the trifecta positive and negative groups.[8] In our series, only C-index was found to have association with trifecta outcomes, and RENAL/PADUA scoring system had no association with trifecta outcomes [Table 1].

Plausible reason for this poor correlation of these SS with these combined outcome measures is that these SS were primarily devised for predicting tumor complexity and anticipatory difficulty to be encountered during NSS. However, the actual difficulty encountered during surgery depends on a number of factors such as surgeon's experience, hilar anatomy, vascular anomalies encountered and tumor characteristics.[14] Postoperative complications also depend on patient's age and comorbidities. Thus, these SS alone may not be reflective of perioperative outcomes.

Regarding validation of the SS, Montang *et al*. found ICC of 0.92 between two urologists and concluded high fidelity of the RENAL scoring system.[15] In another similar study by Kolla *et al*. concordance among 3 observers was 94%, 76%, 66%, 80%, and 54% for the R, E, N, A, and L components, respectively.[16] The corresponding kappa values for each of these 5 components were 0.95, 0.86, 0.76, 0.84, and 0.73, respectively. They also concluded that RNS has good interobserver reliability with L component having least agreement which needs to be kept in mind while scoring. In our series, we found 'E' (exophytic) component in RENAL score to be least concordant of all the components. This difference is likely due to inherent interobserver as well as intraobserver bias.

One of the detailed studies by Spaliviero *et al*. which included 90 CT scans read by 5 observers.[17] One radiology fellow, one radiology resident, 2 urology fellows, and one secondary school student were asked to rate C-index, PADUA, and RENAL score. They found that agreement using C-Index method (ICC = 0.773) was higher than with PADUA (ICC = 0.677), or RENAL (ICC = 0.660).

Our results are in contradiction to above study with C-index showing least agreement between the two observers (Cronbach α = 0.711). The plausible reason for the same is that the difficulty encountered in calculating the C component of C-index on axial scans. They have used reconstructed coronal CT scans for calculating the C-index instead of thin slice axial scans. Determination of two separate variables x and y and further application of Pythagoras theorem to determine c from x and y inherently inducts multiple mathematical steps. However, regarding reproducibility of REANL and PADUA scores, we agree with the results of Hew *et al*. and Spaliviero *et al*. that RENAL and PADUA scores are highly reproducible.[17,18]

Spaliviero *et al*. also stated that agreement between reference and secondary school student was lower than with other physicians although the differences were not statistically significant.[17] They concluded clinical experience reduces interobserver variability of existing nephrometry systems. Although not an outcome of our study, we agree with the above conclusions and believe the premise that increasing experience of the observers in calculating a particular score will lead to increase in agreement.

An interesting find in our study was that all mean scores by urologist were higher than those calculated by radiologist. Although this difference was not statistically significant, it might be possible that the urologist tend to overestimate the subcomponents of the scoring system in anticipated difficulty during the surgery.

Table 3: Summary of studies on comparing radius exophytic/endophytic nearness anterior/posterior location, preoperative aspects and dimensions used for anatomic and C-index

Study	Scoring system	Indices	OT	WIT	EBL	Complications	LOS	Tumor size
Okhunov *et al*.[4]	RENAL	Rho	0.01	0.32	−0.01	0.01	0.00	NR
		P	0.935	0.001	0.936	0.885	0.982	NR
	PADUA	Rho	−0.06	0.25	−0.04	−0.04	−0.02	NR
		P	0.562	0.016	0.691	0.667	0.814	NR
	C-index	Rho	−0.04	−0.44	0.09	−0.06	0.21	NR
		P	0.706	0.001	0.376	0.526	0.039	NR
Present study	RENAL	Rho	0.081	0.106	0.150	0.145	−0.078	0.514
		P	0.576	0.463	0.298	0.315	0.590	0.000
	PADUA	Rho	0.052	0.156	0.250	0.178	−0.066	0.414**
		P	0.718	0.278	0.080	0.216	0.651	0.003
	C-index	Rho	−0.327*	−0.215	−0.051	−0.060	−0.017	−0.373**
		P	0.020	0.133	0.727	0.677	0.907	0.008

P<0.05 is considered statistically significant. *Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed).NR=Not reported, OT=Operative time, WIT=Warm ischemia time, EBL=Estimated blood loss, LOS=Length of hospital stay, RENAL=Radius exophytic/endophytic nearness anterior/posterior location, PADUA=Preoperative aspects and dimensions used for anatomic

The strengths of this study are that it is a prospective study. The tumor diameter and complexity of the tumors in our study are higher as compared to that in the contemporary series, thereby strengthening evidence for performing NSS for such tumors. To the best of our knowledge, this is the second study comparing all three SS in predicting trifecta outcomes. The limitations of this study include a small sample size and a short follow-up period. There is inherent observer bias among various observers.

CONCLUSIONS

C-index fared better than other two SS in predicting trifecta outcomes; however, it is difficult to calculate and has highest interobserver variability.

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How to cite this article: Sharma AP, Mavuduru RS, Bora GS, Devana SK, Palani K, Lal A, *et al*. Comparison of RENAL, PADUA, and C-index scoring systems in predicting perioperative outcomes after nephron sparing surgery. Indian J Urol 2018;34:51-5.