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External validation of four nephrometry scores for trans-peritoneal robotic partial nephrectomy

Bhavan Prasad Rai[1], Amit Patel[2], Ahmed Abroaf[1], Narin Suleyman[1], Shanmugasundaram Gowriemohan[3], Venkat Prasad[3], Nikhil Vasdev[1], Jim Adshead[1]

[1]*Department of Urology, Lister Hospital Stevenage, United Kingdom*
[2]*Department of Radiology, Lister Hospital Stevenage, United Kingdom*
[3]*Department of Anaesthetics, Lister Hospital Stevenage, United Kingdom*

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Corresponding author
Bhavan Rai
Department of Urology
Lister Hospital Stevenage
Marton Raod
TS43BW Middlesbrough
United Kingdom
phone: +44 798 539 67 49 ext. 0
urobhavan@gmail.com

Introduction External validation of four nephrometry scores (NS): Centrality index (C-index), arterial based complexity (ABC), preoperative aspects and dimensions used for an anatomical (PADUA) and radius expohytic/endophytic nearness anterior/posterior location (RENAL) scoring systems in patients who have undergone trans-peritoneal robotic assisted partial nephrectomy (RAPN).

Material and methods A prospective database for RAPN has been maintained. Individual NSs were performed on 3-dimensional reconstructions of MDCT/MRI studies retrospectively by a board certified uroradiologist. Univariate Cox Proportional-Hazard Regression Analysis was performed for each NSs to valuate its predictability for the following parameters: Warm Ischemia Time (WIT), Estimated Blood Loss (EBL), Operative Time (OT), Complication Rates and Positive Margin Rates.

Results 78 RAPNs were performed for suspected renal malignancies. The mean OT, EBL and WIT time was 186.5 minutes (SD – 33.8), 125.5 mls (SD – 188.91) and 16.7 minutes (SD – 5.6) respectively. The overall complication rate was 20.5% (16/78) of which only 2.6% (2/78) were Clavien Grade 3 or higher complications. The mean change in creatinine change at Day – 1 was 12.54 µmol/L (SD – 18.05). On the Cox regression analysis only the Centrality index predicted prolonged WIT with statistical significance: C-Index (0.02), ABC (0.2), PADUA (0.2), RENAL (0.9). ABC predicted operative time with statistical significance: C-index (0.45), ABC (0.0004), PADUA (0.25), RENAL (0.3). None of the NSs could predict overall complication: C-index (0.5), ABC (0.2), PADUA (0.13), RENAL (0.5). None of the NSs predicted EBL: C-index (0.3)0, ABC (0.8), PADUA (0.2), RENAL (0.7). None of the NSs predicted Positive Margin Rates: C-index (0.4), ABC (0.4), PADUA (0.9), RENAL (0.8).

Conclusions C-index was able to predict prolonged WIT. ABC was a strong predictor of OT. PADUA and RENAL were poor predictors for all measured parameters.

Key Words: robotic assisted partial nephrectomy ‹› nephrometry scores ‹› renal ‹› PADUA ‹› centrality index ‹› ABC

INTRODUCTION

Robotic Assisted Partial Nephrectomy (RAPN) is increasingly becoming the approach of choice in patients undergoing a partial nephrectomy. Peri-operative outcomes following RAPN hinge on meticulous surgical planning. Tumor and patient characteristics are vital determinants of adverse outcomes. Nephrometry models use quantitative parameters from morphological imaging modalities to stratify the anatomical and surgical complexity of renal masses. Apart from describing tumor complexity, nephrometry scores (NSs) are also a useful mode of clinical and academic communication. In contemporary urological practice, the radius expohytic/endophytic nearness anterior/posterior loca-

tion (RENAL), preoperative aspects and dimensions used for an anatomical (PADUA) and Centrality index (C-index) are commonly used nephrometry scores (NSs). The parameters: tumor size, polarity, exophytic rate and relationship to collecting system are used in the RENAL and PADUA scoring system [1, 2]. In C-index a mathematical formula is used to calculate the distance between the tumor periphery and the center of the kidney [3]. Spaliviero et al. more recently described the Arterial Based Complexity (ABC) Scoring System which is the based on the relationship of the renal tumor and arterial vasculature. Table 1 summarizes the components of the 4 NSs. Despite the obvious benefits of the existing NSs the evidence describing their predictability of outcomes, inter-observer variability and reproducibility is conflicting. In this study we externally validate the four NSs for the outcomes: Warm Ischemia Time (WIT), Estimated Blood Loss (EBL), Operative Time (OT), Complication Rates, Positive Margin Rates, and Change in creatinine at Day 1. Additionally, we also evaluate and compare the ease of using these NSs in regular clinical practice.

Table 1. *Summary of the components of the nephrometry scores*

Nephrometry scores	Components
RENAL (Radius expohytic/ endophytic nearness anterior/posterior location)	• Radius, • Exophytic/Endophytic • Nearness to collecting system/renal sinus • Anterior/Posterior Locator • Location relative to Polar Lines
PADUA (preoperative aspects and dimensions used for an anatomical)	• Radius, • Exophytic/Endophytic • Longitudinal Location in relation to sinus line • Relationship to Renal Rim • Relationship to Renal Sinus • Relationship to Collecting System
C-Index (centrality index)	• Numerical score based on the combination of tumor diameter and distance from tumor edge to the kidney center
ABC (arterial based complexity)	• Relationship of the renal tumor and arterial vasculature

MATERIAL AND METHODS

A prospective database for RAPN has been maintained at the Lister Hospital, Stevenage, United Kingdom since September 2012 to August 2015. Demographic data, intra-operative parameters, post-operative biochemical analysis and complication were recorded. All the procedures were performed by a single surgeon (JA). All patients underwent multi-detector computed tomography (MDCT) and/or magnetic resonance imaging (MRI) pre-operatively. Imaging technique and scoring: an independent board certified consultant uroradiologist (AP) calculated the four NSs for each patient retrospectively. The radiologist was blinded to patient characteristics, surgical approach and clinical outcomes. For a given renal lesion, individual scores were performed on multi-planar reconstructions of MDCT or MRI studies using Carestream™ imaging. All four scores for a given lesion were calculated during a single session. Pre-operative MDCT studies comprised of bi-phasic examinations with image acquisition during unenhanced and nephrographic phases (80–100s), with slice collimation ranging from 2 to 3 mm. MRI examinations included standard T2 weighted sequences acquired in both axial and coronal planes with additional multi-planar reconstructions of the dynamic Gadolinium enhanced sequences. For PADUA and RENAL scoring, accurate assessment of the tumor location related to the polar and renal sinus lines was performed on multi-planar reconstructions with the kidney appropriately manipulated to its maximum bipolar length i.e. by tilting the coronal plane to a more oblique angle in order to obtain a 'true' coronal of the kidney. The relationship of lesions to the renal sinus fat or collecting system was assessed using multi-planar reconstruction, subjectively choosing the plane which best outlined the relationship of the lesion. Measurements to calculate the C-index were performed on the reconstructed 'true' coronal images to ensure greater accuracy. ABC scoring was also derived using multi-planar reconstructions, making use of all available planes for detailed assessment.

Surgical technique

All procedures were performed with transperitoneal approach with robotic assistance. We have previously described our technique [4]. Primary Outcomes: Predictability of Individual NSs for the parameters: Warm Ischemia Time (WIT), Estimated Blood Loss (EBL), Operative Time (OT), Complication Rates and Positive Margin Rates. Secondary Outcomes: The reporting consultant uroradiologist was asked to rate individual NSs using the Likerts scale for the following domains on a scale of 1 to 5: “NS is reader-friendly?”,“NS takes minimal time to perform?”, “ NS is less reliant on 3D reconstruction for accurate assessment?” and “NS is intuitive to understand renal lesion anatomy?”.

Statistical analysis

Univariate Cox Proportional-Hazard Regression Analysis was performed for each NSs to evaluate its

Table 2. *Demographics*

Number of patients (n)	78
Mean Age (SD) in years	58.3 (11)
M:F	3:1
Mean (SD) and Median (Range) Operative Time (minutes)	186.5 (33.8), 180 (120–270)
Mean (SD) and Median (Range) Estimate Blood Loss (mls)	125.5 (188.91), 100 (10–1500)
Mean (SD) and Median (Range) Warm Ischemia Time (minutes)	16.7 (5.6), 16 (9–34)
Mean tumor size (range) (cm)	25.9 (9.8), 25 (12–70)
Mean preoperative Cr (creatinine) (range) (mg/dL)	82.5 (25.5), 79 (46–199)
Mean postoperative Cr (creatinine) (range) (mg/dL)	95.37 (27.03), 94 (45–210)
Mean % change from serum Cr (mg/dL)	12.54 (18.05), 12 (0–50)
Overall Complications • Clavien 1 • Clavien 2 • Clavien 3 • Clavien 4 • Clavien 5	16 8 6 2 (Selective Embolization of left renal artery after presentation with hematuria pneumothorax) 0 0
Positive Margin N (%)	4 (5%)
Histopathology RCC - Clear cell - Papillary - Chromophobe Benign - Oncocytoma - Angiomyolipoma - Others	 39 15 4 7 5 8

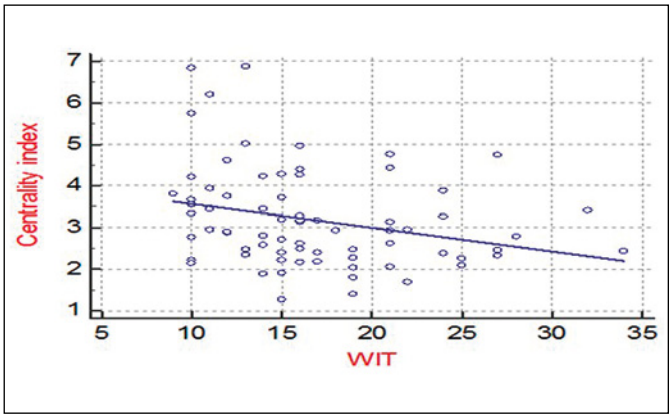

Figure 1. *Cox regression analysis – Centrality index (C-index) predicted prolonged warm ischemia time (WIT).*

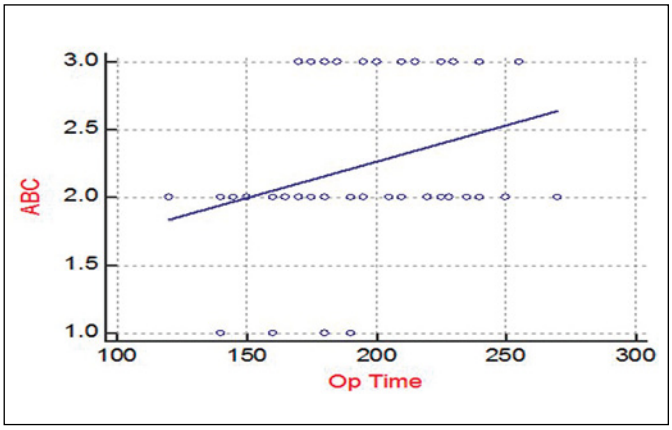

Figure 2. *Cox regression analysis – Arterial based complexity (ABC) predicted operative time.*

predictability for the following parameters: Warm Ischemia Time (WIT), Estimated Blood Loss (EBL), Operative Time (OT), Complication Rates and Positive Margin Rates. A p-value of less than 0.05 was considered significant.

RESULTS

A total of 78 RAPNs were performed for suspected renal malignancies. The mean age was 58.3 yrs. (SD – 11).The male: female ratio was 3:1. The mean tumor size was 25.9 mm (SD 9.8, range 12–70 mm). The mean operative time, EBL and WIT time was 186.5 minutes (SD – 33.8), 125.5 mls (188.91) and 16.7 minutes (5.6) respectively. Overall complication rate was 20.5% (16/78) of which only 2.6% (2/78) were Clavien Grade 3. The Clavien 3 complications were a pneumothorax and bleeding requiring selective embolization. There were no Clavien 4 or 5 complications. None of the patients required a radical nephrectomy or conversion to an open procedure. Four (5%) patients had a positive margin rate (Table 2).

Primary outcomes (Table 3)

Imaging suitable for 3D reconstruction was available for 74 cases. On the Cox regression analysis only the Centrality index predicted prolonged WIT with statistical significance: C-Index (0.02) (Figure 1), ABC (0.2), PADUA (0.2), RENAL (0.9) were all poor predictors of WIT. ABC predicted the operative time with statistical significance: ABC (0.0004) (Figure 2). C-index (0.45), PADUA (0.25), RENAL (0.3) were all poor predictors of operative time. None of the NSs predicted EBL: C-index (0.3)0, ABC (0.8), PADUA (0.2), RENAL (0.7). None of the NSs predicted Positive Margin Rates: C-index (0.4), ABC (0.4), PADUA (0.9), RENAL (0.8). None of the NSs could predict overall complication: C-index (0.5), ABC (0.2), PADUA (0.13), RENAL (0.5). Secondary Outcomes: (Table 4) ABC scored the highest for the domains Reader

Table 3. *Primary outcomes: predictability of nephrometry scores*

	WIT (warm ischemia time)	Operation time	EBL (Estimated Blood Loss)	Positive Margins	Complications	Day 1 – Change in creatinine
C-index (centrality index)	✓	×	×	×	×	✓
ABC (arterial based complexity)	×	✓	×	×	×	×
RENAL (radius expohytic/endophytic nearness anterior/posterior location)	×	×	×	×	×	×
PADUA (preoperative aspects and dimensions used for an anatomical)	×	×	×	×	×	×

✓ – Significant Predictor; × – Insignificant Predictor

Table 4. *Secondary outcomes: ratings on ease of scoring individual nephrometry scores*

	ABC (arterial based complexity)	C-index (centrality index)	RENAL (radius expohytic/endophytic nearness anterior/posterior location)	PADUA (preoperative aspects and dimensions used for an anatomical)
Reader friendly	5	1	3	3
Minimal time	5	1	3	3
Less reliant on 3D recon	3	1	2	2
Intuitive to understand anatomy	4	5	4	4
TOTAL	17	8	12	12

friendly (5/5), Minimal time (5/5) and less reliance on 3-D reconstruction (3/5). C-index scored the highest on the domain intuitive to understanding anatomy (5/5). ABC secured the high overall score of 17/20 and C-Index was the worst performer with a score of 8/20. The RENAL and PADUA scored similarly with a score of 12/20.

DISCUSSION

In this study we evaluated the predictability of four widely used NSs. Centrality index predicted WIT reliably. ABC predicted operative time with statistical significance. PADUA and RENAL nephrometry scores were poor predictors of all parameters. None of the NSs were able to predict estimated blood loss, complication rates or positive margin rates. In the current series none of the four NSs reliably predicted all the set outcomes. A number of reasons can be attributed to this observation. Individual surgical techniques have specific nuances influencing peri-operative outcomes variably. The RENAL nephrometry score was initially developed using a heterogeneous cohort of patient undergoing open, laparoscopic and robotic assisted partial and radical nephrectomy [2]. The PADUA score was designed in patients undergoing open retroperitoneal partial nephrectomy [1]. The C-index scores were designed in patients who underwent trans-peritoneal laparoscopic partial nephrectomy [3]. ABC was designed using a heterogeneous cohort of patients undergoing open, laparoscopic and robotic assisted partial nephrectomy [5]. It is therefore plausible that these NSs are not universally applicable for all techniques and approaches. Perhaps the rationale for the C-index score being a good predictor for WIT in our series, is that our robotic assisted transperitoneal approach more closely resembled the techniques employed in describing the C-index nephrometry scores, even though they adopted a conventional laparoscopic approach. The existing nephrometry models appear to lack inclusion of vital patient and tumor characteristics which could potentially impact post-operative outcomes and to that extent lack face validity. Patient factors such as body habitus, obesity and comorbid status have all been implicated in adversely influencing outcomes after robotic assisted partial nephrectomy. Naeem N. et al. in a comparative study reported higher estimated blood loss, longer median operative time and warm ischemia time in patients with BMI's of more than 30 when they underwent a robotic partial nephrectomy [6]. Guillotreau J. et al. reported a higher post-operative complication rates in patient undergoing RAPN with higher American Society of Anesthesiology (ASA) score and a higher Charlson comorbidity index [7]. The overall complication rate in our series was 20.5% with the gross majority being Clavien I and II grade complications. It is plausible

that we were unable to demonstrate a positive correlation between the NSs and complications due our low major complication rate. In this study we had two Clavien IIIa complications, one of which was a pneumothorax. This was in a patient with kyphosis and was thought be secondary to her ventilatory issues bearing no relation to the tumor characteristics. Interestingly the patient who had post-operative bleeding requiring embolization had low NSs of RENAL 6A, PADUA 7, ABC 2 and C-index 6.19. There is increasing evidence that tumor characteristics, such as surrounding adherent tumor fat and overall perinephric fat adversely affect over all outcomes in patients undergoing robotic partial nephrectomy. Khene Z.E. et al. reported in a series of 202 patient undergoing RAPN significantly higher operative time, blood loss, transfusion, conversion and radical nephrectomy rates if they had associated adherent perirenal fat (APF) [8]. Macleod L.C. et al. measured abdominal wall fat in anterior, posterior, posterolateral, and lateral orientation, and perinephric fat in anterior, posterior, medial, and lateral orientation and evaluated their influence in a patient who underwent a RAPN [9]. They concluded only perinephric fat in particular medial and posterior fat was associated with increased EBL and operative time. Other factors that could possibly influence outcomes are complexity of renal vasculature and right or left sided procedure. An ideal NS must be reproducible, with minimal inter-observer variability and must be simple to use in day to day practice. Amongst the four NSs, ABC was the easiest to use and C-index was the most difficult to use with overall scores of 17/20 and 8/20 respectively in this series. Spaliviero M. et al. reported interobserver variability of RENAL, PADUA and C-index with intra-class correlation coefficients for 0.773, 0.677 and 0.660 respectively thus C-index having a strong agreement between observers and PADUA/RENAL scores having moderate agreement [10]. In the recently reported ABC score the exact matching amongst observers was only in 70% of the cases [5, 11]. The strengths of this study are that all surgical and outcome data has been maintained prospectively. The nephrometry scores were however calculated retrospectively, however this was inevitable as the study was based on a traditional cohort relative to the more recently described scoring systems such as the Arterial Based Scoring system. In this study a detailed assessment of the renal masses was performed using multiplanar reconstructions. We believe this allowed more accurate scoring, particularly in assessing the tumor relationship with polar/renal sinus lines, renal sinus fat and the collecting system. Image reconstructions manipulated into the 'true' coronal plane also allowed for more accurate measurements when calculating the C-index. This also highlights that accurate scoring does require a trained uro-radiologist. A limitation of the study is that the NSs were calculated by a single uro-radiologist and therefore inter-observer variability could not be assessed. Future NSs must take into consideration additional patient and tumor factors in order to be deemed reliable. This may perhaps make NSs exhaustive; however, it is still essential for the models to be comprehensive and accurate. There is an argument that existing NSs have been adopted into mainstream clinical and academic practice without appropriate evaluation. Future research in the form of prospective collaborative studies or large volume single series are required to validate the use of NSs in mainstream practice. Furthermore, there is a need for an international consensus on the best NS to predict outcomes in order to maintain consistent and standardized reporting.

CONCLUSIONS

In this study all the patients underwent a robotic assisted partial nephrectomy. Centrality index (C-index) was a reliable predictor of warm ischemia time (WIT). Arterial based complexity (ABC) was able to predict operative time. Radius expohytic/endophytic nearness anterior/posterior location (RENAL) and preoperative aspects and dimensions used for an anatomical (PADUA) scoring systems were poor predictors of all outcomes measured. None of the nephrometry scores (NSs) were able to predict estimated blood loss, complication rates or positive margin rates. The C-index was the most difficult to calculate. Future nephrometry scores must take into consideration with patient and other tumor factors. Scoring systems must undergo robust internal and external validation possibly in a prospective collaborative setting before being adopted into mainstream practice.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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