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The impact of nephrometry score on partial nephrectomy rates and survival

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Aim: To evaluate the utility of the nephrometry score (NS) and its effects on survival using our experiences with renal tumor data.

Materials and methods: Data from 220 patients who underwent renal tumor surgery between 2002 and 2008 were analyzed retrospectively. The exclusion criteria were lack of preoperative tomography films or pathological data and loss of patients for follow-up. Preoperative computed tomography of the patients was evaluated according to the R.E.N.A.L. NS system at www.nephrometry.com, and low, moderate, and high complexity groups were compared. A cut-off point of 8 for the NS was determined and patients were grouped. Kaplan-Meier and logistic regression tests were used for survival analysis.

Results: Seventy patients were included in the study. Of these, 49 (70%) were treated with radical nephrectomy and 21 were treated with partial nephrectomy (30%). Low, moderate, and high complexity scores were calculated in 20 (28.5%), 22 (31.4%), and 28 (40%) of the patients, respectively. Partial nephrectomy surgeries comprised 85% (n = 17) of the low complexity group and 18.1% (n = 4) of the moderate group. Univariate analysis showed that pathological stage and complexity group were significant factors indicating survival; pathological stage was the only independent factor.

Conclusion: The NS is an objective method in the evaluation of patients with renal tumors and may be a promising means of increasing partial nephrectomy rates in moderately complex cases. Although pathological stage, rather than the NS, is an independent factor for survival, the NS may be a useful preoperative tool.

Key words: Nephrometry, renal tumors, partial nephrectomy, survival

Nefrometri skorunun parsiyel nefrektomi ve sağkalım üzerine etkisi

Amaç: Nefrometri skorunun (NS) kullanılabilirlik ve sağkalım üzerine olan etkisini değerlendirmesi

Yöntem ve gereç: Renal tümor cerrahisi uygulanan 220 hastanın verileri retrospektif olarak analiz edildi. Dışlama kriteri preoperatif tomografi veya patoloji verilerinin olmaması ve hastanın takip sırasında kaybedilmesiydi. Hastaların preoperatif bilgisayarlı tomografileri www.nephrometry.com'daki R.E.N.A.L. NS'ye göre değerlendirildi ve düşük, orta, yüksek kompleks gruplar karşılaştırıldı. NS için kestirim noktası (8) belirlendi ve hastalar gruplandırıldı. Sağkalım analizleri için Kaplan Meier ve lojistik regresyon testleri kullanıldı.

Bulgular: Çalışmaya 70 hasta alındı. Bunların 49'u (% 70) radikal nefrektomi ve 21'i (% 30) parsiyel nefrektomi ile tedavi edildi. Düşük, orta ve yüksek komplekslik skorları sırasıyla 20 (% 28,5), 22 (% 31,4) ve 28 (% 40) hasta olarak hesaplandı. Parsiyel nefrektomi operasyonları düşük komplekslik grubunun % 85'ini (n = 17) ve orta karmaşıklık grubunun % 18.1'ini (n = 4) kapsıyordu. Tek değişkenli analize göre, patolojik evre ve NS sağkalımı gösteren anlamlı faktörler iken; multivaryant analizde patolojik evre bağımsız olan tek faktördü.

Sonuç: NS renal tümörlü hastaların değerlendirilmesinde objektif bir metottur ve orta komplekslikteki hastalarda PN oranlarının artması anlamında ümit verici olabilir. NS ile karşılaştırıldığında, patolojik evrenin sağkalım için bağımsız faktör olmasına rağmen NS yararlı bir preoperatif kriter olabilir.

Anahtar sözcükler: Nefrometri, renal tümör, parsiyel nefrektomi, sağkalım

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Introduction

Detection of organ-confined and incidental renal cell carcinoma (RCC) has increased with the use of advanced imaging techniques in the last 2 decades. The radical nephrectomy (RN), described by Robson in 1963, has been the gold standard for all renal masses to improve tumor control (1). Recently, the partial nephrectomy (PN), the gold standard for nephron-sparing therapy, was reported to be safe and to have equivalent oncological results to RN for renal tumors of less than 4 cm (2). According to tumor node metastasis staging, PN was also suggested for pT1b renal tumors in some studies because of its equivalent cancer control (3). Although nephron-sparing surgery (NSS) has favorable oncological outcomes and advantages for postoperative renal function (4), it has been performed in only a small portion of patients with renal neoplasm (5). Despite the fact that radiological tumor characteristics can be more important in surveying and choosing the best treatment modality, only tumor size has been considered in defined predictive nomograms and prognostic factors (6). Currently, there are no published studies with completed external validation regarding radiological tumor characteristics, which could be useful in choosing RN, PN, or another treatment modality.

The nephrometry score (NS), first described by Kutikov et al., depends on the anatomical features of renal tumors, which are visible using tomography (7). The primary end point of this study was to describe partial nephrectomy rates according to complexity groups and evaluate whether this scoring system might be useful in determining the best method of treatment. Our secondary goal was to identify the relationship between this scoring system and survival outcomes.

Materials and methods

Between 2002 and 2008, 220 patients who underwent RN or PN with solid renal masses were analyzed retrospectively. Preoperative radiological documentation and pathological reports were available for 70 of these patients. Exclusion criteria for the study were lack of preoperative computerized tomography (CT) films or pathological reports, or loss of patients for follow-up. All of the preoperative CTs of the patients were scored according to the R.E.N.A.L. nephrometry score (R.E.N.A.L. NS, at www.nephrometry.com). The R.E.N.A.L. NS consists of the (R)adius (tumor size at maximal diameter), (E)xophytic/endophytic properties of the tumor, (N) earness of tumor's deepest portion to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor, and (L)ocation relative to the polar line. The suffix h (hilar) is assigned to tumors that abut the main renal artery or vein. Based on the nephrometry sum, all of the renal tumors were divided into 3 groups: low (4 to 6 points), moderate (7 to 9 points), and high (10 to 12 points) complexity lesions (7). An open approach was taken in all of the cases. All of the patients were evaluated postoperatively every 3 to 6 months for the first 2 years after the procedure, and every 6 months thereafter, with physical examination, chest radiography, abdominal computed tomography, blood chemistry panel, and, if indicated, radionuclide bone scanning.

All of the eligible data were collected using SPSS 15.0 software. For disease-specific survival analysis, the patients were divided into 2 groups according to the cut-off point found with the receiver operating curve (lesion complexity score of 4-8 vs. 9-12). As the known pathological stage is a strong predictor of survival, all of the preoperative parameters were evaluated by pathological stage, and pT1 and pT2 were grouped independently from pT3. Clinical findings suggested as prognostic factors were grouped as age (<57 vs. ≥57), sex (male vs. female), tumor side (left vs. right), tumor size (≤7 cm vs. >7 cm), and diagnosis (incidental vs. symptomatic), and these were included in the univariate analysis. Significant parameters in the univariate analysis were reevaluated in the multivariate analysis. Kaplan-Meier tests were used for the univariate analysis, while logistic regression analysis was used for the multivariate analysis. $P < 0.05$ was accepted as significant. Complications were not assessed in this study, but none of the deaths that may affect survival analysis were related to complications.

Results

A total of 70 patients, 37 men (52.9%) and 33 women (47.1%), were included in the study. Mean age at diagnosis was 56.4 ± 10.6 years. The mean follow-up time was 57.2 ± 26.9 months. The demographics of the patients are summarized in Table 1.

Table 1. The demographic data of the patients (* indicates mean ± standard deviation).

		Total
Age*		56.4 ± 10.6
Sex	Men	37 (52.8%)
	Women	33 (47.1%)
Side	Right	39 (55.7%)
	Left	31 (44.2%)
Pain	-	41 (58.5%)
	+	29 (41.4%)
Hematuria	-	57 (81.4%)
	+	13 (18.5%)
Palpable mass		0
Type of presentation	Symptomatic	38 (54.2%)
	Incidental	32 (45.7%)
Localization	Upper	17 (24.2%)
	Middle	24 (34.2%)
	Lower	28 (40%)
	Diffuse	1 (1.4%)
Radiological cystic appearance	-	63 (90%)
	+	7 (10%)
Radiological size		6.34 ± 2.68
Operation type	RN	49 (70%)
	PN	21 (30%)
Stage	T1	36 (51.4%)
	T2	16 (22.8%)
	T3	18 (25.7)
Pathologic size*		6.34 ± 2.84
Perirenal fat invasion	-	55 (78.5%)
	+	15 (21.4%)
Adrenal involvement	-	68 (97.1%)
	+	2 (2.8%)
Renal vein invasion	-	63 (90%)
	+	7 (10%)
Necrosis	-	67 (95.7%)
	+	3 (4.2%)
Pathologic type	Clear cell	52 (74.2%)
	Papillary	1 (1.4%)
	Collecting duct	4 (5.7%)
	Sarcomatoid	2 (2.8%)
	Multilocular cystic	1 (1.4%)
	Oncocytoma	6 (8.5%)
	Chromophobe	1 (1.4%)
	Unclassified	3 (4.2%)
Fuhrman grade	1	16 (22.8%)
	2	39 (55.7%)
	3	14 (20%)
	4	1 (1.4%)

Low, moderate, and high nephrometry scores were calculated for 20 (28.5%), 22 (31.4%), and 28 (40%) patients, respectively (Table 2). RN was performed in 49 cases (70%), and 21 patients were treated with PN (30%). PN rates were 85% (n = 17) in the low complexity group and 18.1% (n = 4) in the moderate group. All of the patients with high complexity lesions were treated with RN. There was a shift to lower complexity groups in the total score when compared with tumor size only. The overall PN rate was 12.2%.

Pathological stage and complexity groups according to the cut-off point were significant in the univariate disease-specific survival analysis (P = 0.001 and P = 0.043, respectively) (Table 3 and Figure 1a and 1b). Insignificant parameters in the univariate analysis were age (P = 0.63), sex (P = 0.73), tumor side (P = 0.58), diagnosis (P = 0.52), and tumor size (P = 0.12). In the multivariate analysis, pathological stage was the only independent factor, while the complexity groups did not reach significance (P = 0.034 vs. P = 0.521).

Table 2. The distribution of the patients according to the NS.

	1	2	3
R	19 (27.1%)	22 (31.4%)	29 (41.4%)
E	31 (44.2%)	30 (42.8%)	9 (12.8%)
N	19 (27.1%)	27 (38.5%)	24 (34.2%)
	a	p	x
A	33 (47.1%)	34 (48.5%)	3 (4.2%)
L	11 (15.7%)	24 (34.2%)	35 (50%)
	Low (4-6)	**Moderate (7-9)**	**High (10-12)**
T	20 (28.5%)	22 (31.4%)	28 (40%)

Table 3. The results of significant parameters in the disease-specific survival analysis.

	P-value (Kaplan-Meier)	Estimate	Standard deviation	95% confidence interval	P-value (Logistic regression)	Hazard ratio
Pathological stage	**0.001**				**0.034**	6.2
Group A		127.2	10.7	106.2-148.3		
Group B		35.9	8.2	19.8-51.9		
Complexity group	**0.041**				0.521	1.6
Group 1		127.2	16.2	95.4 -159		
Group 2		66.9	8.7	49.7-84.1		

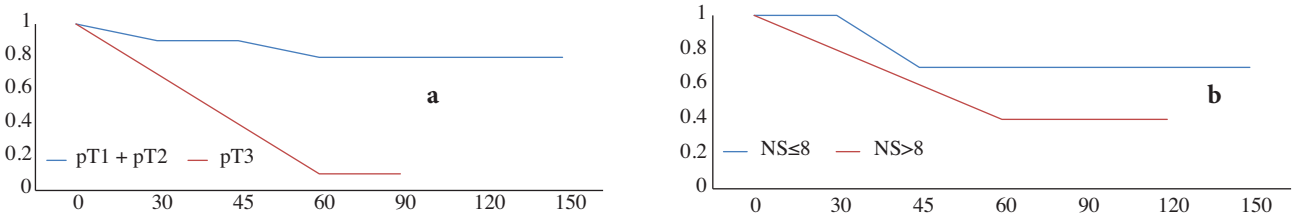

Figure. Kaplan-Meier graphics of a) the pathologic stage and b) the NS.

Discussion

In recent years, the detection of renal tumors has increased to 60% with the greater use of quality imaging techniques (8). In general, RN has been performed to increase tumor control because uro-oncologists have evaluated all of the renal masses, except angiomyolipomas, as renal cell cancer until the results of the histopathological analysis are known. Despite the advantage of tumor control after RN, the procedure is associated with increased risk of chronic renal failure and its associated conditions, such as cardiovascular morbidity, hospitalization, and death (9,10). The cancer-specific, metastasis-free survival and the local or distant recurrence rates after PN and RN have been demonstrated to be similar (3). The risk of chronic renal failure is less for PN, and the procedure has a more positive impact on quality of life (11). The ideal patient for PN has been defined as a patient with a solitary, exophytic, and easily resectable tumor of up to 4 cm in diameter, but few patients fit all of these conditions (12). The characteristics of aggressive-appearing tumors have not been defined clearly and tumor size remains the only preoperative predictive value. However, the surgical margins, local recurrences, and cancer-related death rates are not predicted by tumor size in localized RCC (13,14). Becker et al. (15) proposed consideration of a tumor's tomography presentation and the surgeon's technical ability, rather than tumor size, when making decisions about whether PN could be performed instead of RN (16). However, despite all of the advantages of PN, there are limitations to the use of this treatment modality based on tumor size, tumor location, and the experience of the surgeon.

The NS system described here accounts for almost all of the anatomical signs that are generally considered before the procedure. Moreover, it is easy to use and could be applied during daily practice. Recent reports have mentioned a similar cancer-specific survival after PN in appropriate patients who had larger tumors (14). Results of another retrospective study showed that in selected patients with stage T1b-T3N0M0 RCC, PN provided equivalent intermediate-term oncological efficacy and superior renal function outcomes when compared to RN (17). Additionally, excellent cancer-specific outcomes at 5 and 10 years have been shown after PN for renal tumors of up to 7 cm (18). However, oncological safety was less evident in RCC of greater than 7 cm when PN was performed (19). The main reason for these limitations was the lack of a standardized descriptive system to characterize renal tumor anatomy.

The complications most likely to occur after or during PN may be predictable using this method. Urine leakage can be evaluated more accurately when measuring the tumor depth. The degree of bleeding may be predictable by scoring polar lines and endo/exophytic properties. Using parameters similar to the NS, the preoperative aspects and dimensions used for an anatomical (PADUA) classification of renal tumors was developed for prediction of these complications (20).

The description of PN rates in each complexity group was the primary end point of this study. Kutikov et al. published rates of 88%, 84%, and 46.6% for low, moderate, and high complexity groups, respectively (7). Our rates were much lower than these overall, with significant differences for the moderate and high complexity groups. Our high complexity group was composed mainly of patients with tumor diameters greater than 7 cm. We did not think that performing PN in 46% of these cases would be possible. The data presented in the study by Kutikov et al. might have consisted of tumors in solitary kidneys or, based on Becker's suggestions, perhaps the group was more experienced than we were (15). Our overall PN rates were comparable to those of Hollenbeck et al. (12.2 vs.

9.6, respectively) (5). However, as a self-criticism, this could be higher due to the use of the NS. We think that the PN system will be most helpful in patients who have renal tumors with diameters between 4 and 7 cm.

Another issue, observed in Table 2, is the grouping of a small subset of patients who fell between the groups. The number of patients in the R1 column, which represents tumor size below 4 cm, was 19. However, the low complexity group contained 20 patients; therefore, 1 patient who had a renal tumor of greater than 4 cm in diameter was included in the low complexity group and was much more likely to receive PN. The same situation occurred with 1 patient in the R3 column who was included in the moderate complexity group. We found that RN was performed on the R2 patient who was included in the low complexity group. We had previously made our treatment decisions based on tumor size, and therefore, when we evaluated these findings together, the use of complexity groups and the NS to determine the course of treatment was likely to increase elective PN rates in all of the groups due to the higher PN rates in the lower complexity groups. All of the patients included in the low complexity group were eligible for PN. In addition, patients in the R2 group who exhibited low complexity were also candidates for PN. In conclusion, the NS can be useful in treatment decisions for renal tumors of between 4 and 7 cm or over 7 cm in size.

Prognostic factors and nomograms are used to predict the likelihood of cancer in patients with renal masses. Clinical signs, tumor-related factors, various laboratory findings, age, and sex are important prognostic factors in RCC. Independently, pathological stage, histologic subtype, Fuhrman grade, and tumor size are the important parameters. However, factors that have independence on the multivariate analysis are the most useful and powerful. Pathological stage has proven to be the single most important prognostic factor for RCC. Various molecular markers, such as high levels of CA-9 and Ki-67, lymph node involvement, and systemic metastasis, are other factors for poor survival (21). Several factors were combined for improving predictive capacity, and the nomogram created by Lane included factors of age, sex, CT size of the renal mass, local symptoms at diagnosis, and history of smoking. This method was designed for use in choosing the best treatment modality (RN or PN) for renal tumors no larger than 7 cm (22). According to another study, the treatment modality decision should not depend on tumor size alone because small measurement errors in CT size could cause errors (23). In general, pathologic size is not the same as CT size, and there has been controversy about the significance of this difference (24,25). In another algorithm, the score was based on stage, size, grade, and necrosis (SSIGN score) to predict survival (26). The UCLA Integrated Staging System consisted of pathological stage, Eastern Cooperative Oncology Group (ECOG) performance status, Fuhrman grade, and histological subtypes. RCC histological subtype is an important prognostic feature; papillary and chromophobe RCCs are less aggressive than clear cell RCC (22). Another study by Kattan et al. used size, tumor subtype, stage, and preoperative symptoms to develop a postoperative prognostic nomogram that predicted recurrence and death (27). The centrality index was first described by Gill et al. (28). Complexity groups, which account for tumor size and anatomical location, had significance in univariate analysis; however, the NS was not an independent factor in our study. Additional analysis indicated that these nomograms consisted of multiple independent factors. This was the first study to evaluate a spectrum including tumor depth, tumor polarity, and tumor size. Combining these parameters showed no independently significant variables at the end of the study. As has been shown previously, pathological stage was one of the most important independent prognostic factors for renal tumor outcome in this study. Depending only on anatomical signs in imaging is not sufficient to predict survival, but it is superior to the use of radiological tumor size alone. We suggest adding complexity groups in place of tumor size in the nomograms described above to improve accuracy.

Use of tumor size as a basis for treatment decisions in RCC can be insufficient and misleading. In an effort to increase objectivity in determining which treatment is the better choice, the NS is useful, although it is not an independent factor indicating survival. The NS may be effective for increasing partial nephrectomy rates, especially in patients with moderately complex lesions.

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