Preoperative predictors of surgical approach for partial nephrectomy

Jay D. Raman, MD,[1,3] Benjamin Smith, MD,[2] Jamie Messer, MD,[1]
Thomas J. Rohner, MD[1], Lewis E. Harpster, MD,[1] Carl T. Reese, MD[1]

[1]Division of Urology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania, USA
[2]College of Medicine, Penn State Milton S Hershey Medical Center, Hershey, Pennsylvania, USA

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Introduction: *To evaluate preoperative parameters of patients undergoing partial nephrectomy to determine variables that impact selection of operative approach.*

Materials and methods: *The charts of 229 consecutive patients undergoing partial nephrectomy were reviewed. Clinical data points and associated axial imaging were evaluated to determine factors which contributed to selection of an open (versus laparoscopic) operation.*

Results: *A total of 140 men and 89 women with a mean age of 57 years, body mass index (BMI) of 31, and glomerular filtration rate (GFR) of 82 mL/min/1.73 m^2 were included. Twenty-three percent of patients had prior abdominal surgery and 7% had a history of contralateral renal cell carcinoma (RCC). The mean tumor size was 3.4 cm (range, 0.7-11) with 23% of lesions being endophytic, 38% involving the collecting system, and 29% being hilar. Thirty-four patients (15%) had multifocal lesions. Overall, 130 patients underwent an open partial nephrectomy (OPN) and 99 a laparoscopic partial nephrectomy (LPN). On univariate analysis, preoperative GFR (p = 0.05), a history of contralateral RCC surgery (p = 0.02), tumor size (p = 0.04), renal sinus/collecting system involvement (p = 0.001), renal hilar location (p = 0.001), tumor multifocality (p = 0.004), surgeon laparoscopic case volume of < 25 cases (p = 0.03), and lack of fellowship laparoscopic training (p = 0.02) all were associated with an open surgical approach. In a logistic regression model incorporating these eight variables, only renal hilar location (OR 2.63, 95% CI 1.17-5.88, p = 0.02) remained significantly associated with OPN.*

Conclusions: *Many parameters including increasing BMI, preoperative GFR, prior abdominal surgery, endophytic tumor location, and renal sinus/collecting system involvement do not necessarily preclude a minimally invasive partial nephrectomy. In our experience, renal hilar tumors were over 2.5 fold more likely to be managed by OPN owing to the complexity of resection.*

Key Words: nephron sparing surgery, partial nephrectomy, open surgery, minimally invasive surgery

Introduction

Renal cell carcinoma (RCC) is the 3rd most common genitourinary malignancy accounting for almost 61,000 new cases and over 13,000 cancer related deaths in 2011.[1] Population based studies have implicated that the incidence of RCC has increased 3%-4% yearly since the 1970s.[2] Owing to the increased use of non-invasive abdominal cross-sectional imaging, this trend has been associated with detection of a greater proportion of incidental small renal masses (SRMs).[3,4] While surgical extirpation remains the gold standard for localized RCC, it is apparent that radical nephrectomy represents significant overtreatment for many of these SRMs. Nephron-sparing surgery confers equivalent oncologic and superior renal function outcomes when compared to radical nephrectomy for patients with renal tumors smaller than 4 cm.[5,6] Recent series have further highlighted that such benefits persist even when considering larger localized renal tumors up to 7 cm.[7]

Over the past decade, laparoscopic partial nephrectomy (LPN) has assumed a greater role in the management of SRMs. Contemporary series implicate that for experienced surgeons, LPN provides comparable oncologic and renal function outcomes to open partial nephrectomy (OPN).[8] Furthermore, LPN has been associated with lower narcotic requirements,

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Address correspondence to Dr. Jay D. Raman, Penn State Milton S. Hershey Medical Center, 500 University Drive, H055, Hershey, PA 17033-0850 USA

improved cosmesis, earlier resumption of diet, lower cost, and decreased hospital length of stay.[9] However, LPN is a challenging operative procedure with a technique that continue to evolve and a steep learning curve necessary to minimize ischemia times and associated complications.[10,11]

The dissemination of laparoscopy into surgical training[12] has contributed to an increasing number of urologists who may be comfortable with a minimally invasive approach with respect to partial nephrectomy for SRMs. Therefore, it is valuable for such surgeons to be aware of preoperative factors that can potentially contribute to selection of OPN versus LPN. Such considerations would not only facilitate appropriate patient counseling prior to surgery, but may also minimize the likelihood of intraoperative or postoperative complications during LPN. Within our institution, there exists a collaborative relationship among open and minimally invasive surgeons such that all radiographic films are reviewed prior to partial nephrectomy to determine optimal treatment approach. To date, however, selection of a particular modality for partial nephrectomy was loosely based on a compilation of patient, tumor, and surgeon-related variables. We therefore attempt to objectify this process and aid other urologists by presenting our experience with preoperative clinical and radiographic factors that contributed to the selection of an open versus laparoscopic approach for partial nephrectomy.

Materials and methods

Study population

Institutional review board (IRB) approval was obtained to review medical charts and radiographic studies of patients who underwent surgical intervention for an enhancing renal mass between January 2003 and April 2009. Of 715 identified cases, 397 underwent a radical nephrectomy, 258 a partial nephrectomy, and 60 thermal ablation (cryoablation or RFA). We specifically began analysis in 2003 as this represented a time point 18 months (and 15 cases) after the introduction of LPN at our institution. We, therefore, believed that collecting data at this point would obviate some inherent case selection bias associated with introduction of a novel procedure (LPN). OPN was accomplished either by a flank extraperitoneal approach or a transbdominal approach at the discretion of the operative surgeon. Patients younger than 18 years of age, those with a functional or anatomic solitary kidney, patients undergoing bilateral synchronous nephron-sparing surgery, and those without available cross-sectional imaging for review were excluded from analysis. With such criteria, we identified 229 patients who underwent an OPN (n = 130) or LPN (n = 99) that constituted our study cohort.

Clinical variables

Clinical data points included patient age, gender, race, body mass index (BMI), estimated glomerular filtration rate (eGFR), comorbid conditions, history of contralateral RCC surgery (thermal ablation, partial or radical nephrectomy), prior abdominal surgery, and year of surgery. The abbreviated Modification of Diet in Renal Disease Study (MDRD) formula, a function of serum creatinine and demographic variables, was used to assess preoperative eGFR: GFR (in mL/minute/1.73 m^2) = 186 x [serum creatinine $(mg/dL)^{-0.154}$] x $(age^{-0.203})$ x (0.742, if female) x (1.21, if African-American).[13] Comorbidities included diabetes, hypertension, as well as an aggregate of conditions as represented by the Charlson-Romano (CR) index.

Radiographic data

All preoperative computed tomography (CT) or magnetic resonance imaging (MRI) was reviewed by two authors. Variables of interest included tumor size (maximum diameter in cm), laterality, polar location (upper, interpolar, or lower), focality (uni- versus, multi-), depth of tumor, anterior versus posterior location, involvement of the renal sinus/collecting system, or abutment of the renal hilum. Depth of tumor was classified as follows: 1) Exophytic: ≥ 60% extension of tumor off the natural surface of the kidney; 2) Mesophytic: tumor extends 40% to 60% off the kidney; 3) Endophytic: ≤ 40% of the lesion extending off the kidney. Abutment of the renal hilum was defined by tumors adjacent to the main renal artery or vein or the first segmental branch from the either of these vascular structures.

Surgeon data

Our partial nephrectomy databases were also reviewed for surgeon-specific variables that may be determinants for surgical approach. Included in this group were number of years in practice, annual surgical volume, annual number of renal surgery cases, fellowship training in laparoscopy, and total number of laparoscopy cases performed (< or > 25 cases). The referral system at our hospital results in equal distribution amongst all new kidney cancer cases (unless specified by the patient and/or referring physician) amongst the four urologists included in this study. Interestingly, our two highest volume renal cancer surgeons readily incorporate both open and laparoscopic approaches into their practice.

Pathologic data

All specimens were reviewed by institutional pathologists. Staging was according to the American Joint Committee on Cancer (AJCC) and tumors were graded using Fuhrman criteria.[14] Positive surgical margins were defined as tumor cells touching the inked margin of the final specimen.

Statistical analysis

Univariate analysis was initially performed to determine which clinical, surgeon-specific, and radiographic variables were associated with a particular type of partial nephrectomy. Continuous and categorical variables were analyzed using the Mann-Whitney U and Pearson chi-square tests, respectively. For the chi-square test, odds ratios with 95% confidence intervals were used to quantify the magnitude and direction of any significant associations. Exact tests were employed when presented with small cell counts. The variables determined to have significant association on univariate analysis were incorporated into a logistic regression model. A process of backwards elimination was used which started with the full model including all variables. The variable with the largest p value greater than 0.15 was eliminated from the model at each step, and all variables eliminated from the model at the previous steps were added back and retained if their p value was less than 0.10.

Results

Clinical variables

Overall, 130 patients (57%) underwent an OPN, while 99 (43%) had a LPN. Table 1 highlights clinical and demographic characteristics of this surgical cohort stratified by surgical approach. A total of 140 men and 89 women with a mean age of 57 years and BMI of 31 were included in this study. 15 patients (7%) had a prior history of contralateral RCC therapy, and approximately 25% of this patient cohort had at least one prior abdominal operation. Mean preoperative estimated GFR for this group was 81.6 mL/min/1.73 m^2 with chronic kidney disease (CKD) stage distribution being CKD I (eGFR > 90) 38%, CKD II (eGFR 60-89) 45%, CKD III (eGFR 30-59) 16%, and CKD IV (eGFR 15-29) 1%. When stratified by year of surgery, the percentage of laparoscopically managed renal tumors increased from 23% (2003 and 2005) to 52% (2006 to 2009). On univariate analysis of preoperative clinical variables, a history of contralateral RCC surgery (p = 0.02) and baseline eGFR (p = 0.05) was associated with an open (versus laparoscopic) partial nephrectomy. Conversely, patient age, gender, race, BMI, comorbid conditions, prior abdominal surgery, year of surgery, and individual CKD stages (p = 0.13) all were not associated with a particular surgical approach.

Radiographic variables

Table 2 demonstrates imaging and pathologic characteristics of renal tumors managed by partial nephrectomy. The mean tumor size was 3.4 cm (range, 0.7 to 11) with a relatively equal distribution across the upper, middle, and lower poles of the kidney. Thirty-four patients (15%) had multifocal renal tumors, and 60% of tumors were located on the anterior surface of the kidney. Overall, 23% of tumors were endophytic, 38% involved the renal sinus/collecting system, and 29% were classified as renal hilar lesions. On univariate analysis of radiographic variables, tumor size (p = 0.04), multifocality (p = 0.004), renal sinus/collecting system involvement (p = 0.001), and renal hilar location (p = 0.001) were all associated with an open approach for partial nephrectomy. Tumor depth (p = 0.08), polar location (p = 0.15), and anterior (versus posterior) distribution (p = 0.53) however, were not associated with a particular surgical approach.

Surgeon variables

Amongst our four urologists managing kidney cancer, two had a cumulative laparoscopic case volume of at least 25 cases. One of these two urologists also had formal fellowship training in laparoscopy and endourology. The mean annual case volume for all four surgeons ranged between 680 and 870 cases, while the specific number of renal surgery cases ranged between 15 and 45 cases annually. On univariate analysis, lack of fellowship training in laparoscopy (p = 0.02) and cumulative laparoscopic case volume < 25 cases (p = 0.03) were associated with OPN, while annual case volume (p = 0.44), annual number of renal surgery cases (p = 0.19), and number of years in practice (p = 0.73) were not associated with specific approach.

Pathology

Over 80% of renal tumors were histologically confirmed RCC with a similar distribution between open and laparoscopic cases. Of the RCC lesions, over 75% were pT1a tumors, 15% were pT1b tumors, and 10% were staged ≥ pT2. An open surgical approach was associated with more advanced pathology (p = 0.03). Positive surgical margins occurred in six cases (2.6%) with no difference between surgical approach (2.3% open versus 3.0% laparoscopic, p = 0.73).

Predictors for method of partial nephrectomy

Logistic regression methodology was used to create a model based upon the preoperative clinical, surgeon-related, and radiographic variables that were found to be significantly associated with the type of partial nephrectomy on univariate analysis. The variables

TABLE 1. **Clinical and demographic characteristics of this surgical cohort stratified by surgical approach**

Variable	All patients (n = 229)	Open (n = 130)	Laparoscopic (n = 99)	p value
Age (mean)	57.1	57.4	56.8	0.78
[median; range]	(59); 21-93	(59); 21-93	(58) 21-82	
Gender (no., %)				
Male	140 (61.1%)	81 (62.3%)	59 (59.6%)	0.68
Female	89 (38.9%)	49 (37.7%)	40 (40.4%)	
Race (no., %)				
Caucasian	213 (93)	122 (94)	91 (92)	0.54
African American	6 (3)	3 (2)	3 (3)	
Hispanic	7 (3)	4 (3)	3 (3)	
Asian	1 (1)	1 (1)	0 (0)	
Other	2 (1)	0 (0)	2 (2)	
BMI (mean)	30.5	30.3	30.8	0.56
[median; range]	(30); 21-50	(30); 21-50	(30); 22-45	
CR index (mean)	2.5	2.6	2.3	0.17
[median); range]	(2); 0-10	(2); 0-8	(2); 0-10	
HTN (no., %)				
No	90 (39)	47 (36)	43 (43)	0.26
Yes	139 (61)	83 (64)	56 (57)	
Diabetes (no., %)				
No	184 (80)	101 (78)	83 (84)	0.25
Yes	45 (20)	29 (22)	16 (16)	
Hx contralateral RCC surgery (no., %)				
No	214 (93)	116 (90)	98 (99)	0.02
Yes	15 (7)	14 (10)	1 (1)	
Prior abdominal surgery (no., %)				
No	175 (77)	96 (74)	79 (79)	0.34
Yes	54 (23)	34 (26)	20 (21)	
Preop Cr (mean)	1.05	1.12	0.97	0.02
[median; range]	(0.9); 0.4-9.9	(0.98); 0.4-9.9	(0.9); 0.5-3.44	
Preop GFR (mean)	81.6	78.4	85.7	0.05
[(median); range]	(81.0); 20-171	(79); 30-170	(85.5); 20-171	
Year of surgery				
2003-2005	70	54	16	
2006-2009	159	76	83	0.08

incorporate into the model included: preoperative GFR, prior contralateral RCC therapy, tumor size, tumor focality, renal sinus/collecting system involvement, abutment of the renal hilar vasculature, fellowship training in laparoscopy, and cumulative laparoscopic case volume.

In the regression model incorporating these eight variables, only renal hilar location (odds ratio [OR] 2.63, 95% CI 1.17-5.88, p = 0.02) remained significantly associated with open nephron sparing surgery.

Discussion

The concept of renal preservation has increasingly emerged as a central tenet in the management of renal cortical neoplasms.[15] Contemporary data has implicated a link between CKD and cardiovascular events, risk of hospitalization, and all cause mortality.[16] These associations coupled with evidence that patients undergoing radical nephrectomy are more likely develop CKD emphasizes that nephron sparing

TABLE 2. **Imaging and pathology data for renal tumors managed by partial nephrectomy**

Variable	All patients (n = 229)	Open (n = 130)	Laparoscopic (n = 99)	p value
Imaging data				
Size cm (mean)	3.4	3.6	3.0	0.04
[median; range]	(3.0); 0.7-11	(3.1); 1.2-11	(2.7) 0.7-10.1	
Location (no., %)				
Upper	71 (31)	48 (37)	25 (25)	0.15
Middle	67 (30)	38 (30)	29 (29)	
Lower	89 (39)	44 (34)	45 (45)	
Multifocal (no., %)				
No	195 (85)	103 (79)	92 (93)	0.004
Yes	34 (15)	27 (21)	7 (7)	
Anterior (no., %)				
No	92 (40)	55 (42)	37 (37)	0.53
Yes	137 (60)	75 (58)	62 (63)	
Tumor depth (no., %)				
Endophytic	53 (23)	38 (29)	17 (17)	0.08
Mesophytic	88 (38)	53 (41)	36 (36)	
Exophytic	88 (38)	39 (30)	46 (46)	
Renal sinus/collecting system (no., %)				
No	142 (62)	68 (52)	74 (75)	0.001
Yes	87 (38)	62 (48)	25 (25)	
Hilar (no., %)				
No	163 (71)	79 (61)	84 (85)	0.001
Yes	66 (29)	51 (39)	15 (15)	
Final pathologic data				
Histology (no., %)				
RCC	191 (83)	109 (84)	82 (83)	0.88
Clear cell	141 (62)	80 (62)	61 (62)	
Papillary	41 (18)	25 (19)	16 (16)	
Chromophobe	9 (4)	4 (3)	5 (5)	
Benign	38 (17)	21 (16)	17 (17)	
Stage (no., %)*				
pT1a	148 (77)	80 (73)	68 (83)	0.03
pT1b	26 (14)	16 (15)	10 (12)	
pT2	7 (4)	6 (6)	1 (1)	
pT3a	9 (5)	6 (6)	3 (4)	
pT3b	1 (1)	1 (1)	0 (0)	
Fuhrman grade (mean)	1.9	1.9	1.8	0.45
[median; range]	(2.0); 1-4	(2.0); 1-4	(2.0); 1-4	

*distribution for 191 patients with pathologically confirmed RCC

surgery should be considered in the management of RCC, specifically as it relates to small renal masses.[6,17,18] While urologists increasingly are embracing the principle of kidney sparing surgery for SRMs, the surgical approach and means to achieve this goal remains a debate. In particular, an impetus in the surgical community is incorporation of minimally invasive techniques to manage diseases. With respect to nephron sparing surgery, several retrospective studies have implicated lower narcotic requirements, improved cosmesis, earlier resumption of diet, and shorter hospital duration for patients managed by LPN

compared to OPN.[9,19] Such benefits, however, often need to be balanced against a higher complication profile for LPN even in the hands of expert minimally invasive surgeons.[11]

A concern amongst many "open" and "minimally invasive" surgeons is that each group is married to a particular approach without adapting operative strategy to patient and lesion characteristics. This dichotomy between surgical disciplines, however, is increasingly blurred for urologists completing contemporary urologic residency and fellowship training.[12] Such trainees are amply versed in partial nephrectomy techniques with the growth of laparoscopy and robotics facilitating an increased utilization of such modalities to manage more complex renal masses.[11,20,21] With such a surgical armamentarium, an important consideration is appropriate selection of operative approach for nephron sparing surgery that maintains oncologic outcomes while minimizing surgical morbidity.

In this study of 229 renal lesions managed by partial nephrectomy, we sought to identify preoperative clinical, surgeon-related, and imaging characteristics that contributed to management by either an open or laparoscopic approach. With respect to clinical variables, we observed that prior contralateral RCC surgery ($p = 0.02$) and preoperative estimated GFR ($p = 0.05$) were more likely to be associated with an open surgical approach. Interestingly, several other variables that historically would have been indications for OPN (i.e. higher BMI and prior abdominal surgery) were not associated with a particular treatment modality. Reviewing associated radiographic imaging highlighted that tumor size ($p = 0.04$), multifocality ($p = 0.004$), renal sinus/collecting system involvement ($p = 0.001$), and abutment to the renal hilar vasculature ($p = 0.001$) all were associated with OPN. When considering surgeon-specific variables, we observed that a fewer cumulative laparoscopic cases ($p = 0.03$) and lack of fellowship training in laparoscopy ($p = 0.02$) were associated with an open approach. When incorporating these variables in a logistic regression model, however, only renal hilar location independently was associated with OPN with a 2.6 fold greater likelihood of being managed by an open versus laparoscopic approach. Furthermore, review of the overall positive margin rate of 2.6% with similar outcomes for OPN and LPN underscores that the quality of the operation was not compromised when selecting treatment approach.

Accepting that nephron sparing surgery should be considered for all SRMs, we believe that our findings provide urologists managing renal tumors a means to objectify the decision making process for partial nephrectomy approach. In our experience, preoperative clinical variables contributed minimally to surgical technique, while radiographic data had significant bearing on operative approach. Other groups have recently made similar observations. In 2009, Kutikov and Uzzo introduced the concept of the R.E.N.A.L nephrometry score as a means to more accurately characterize salient radiographic anatomy of renal masses.[22] This same group subsequently evaluated patterns of surgical treatment for renal masses as a function of the tumor's Nephrometry score.[23] Here, they observed that a large tumor size predicted OPN versus minimally invasive surgery (MIS)-PN, while a difficult location (as defined by polar lines) demonstrated the smallest predictive ability. Additionally, a lower "N" score (nearness to sinus/urothelium) was most predictive of MIS-PN versus OPN. Hayn and colleagues further applied the R.E.N.A.L. nephrometry score retrospectively to patients with renal tumors managed by LPN and observed that a higher score was associated with an increased estimated blood loss, warm ischemia time, and length hospital stay.[24] They, therefore, concluded that such considerations may be helpful in counseling patients and may stratify tumors based on the technical difficulty of performing LPN. While our study does not utilize a scoring system, the observations are similar and further underscores that certain tumor characteristics may encourage use of an open versus minimally invasive approach for partial nephrectomy.

We feel that the approach to a renal mass should start with consideration of whether the lesion can be managed by nephron sparing surgery. Thereafter, the urologist should examine whether nephron sparing surgery can be accomplished safely by minimally invasive techniques. Using variables that we have defined in this study or in the context of a nephrometry score would aid in objectifying the decision for surgical approach for partial nephrectomy. Such an approach allows optimum sparing of the renal unit while tailoring therapy to minimize surgical morbidity. We acknowledge several limitations. Firstly, the retrospective nature of the study fails to account for patient specific variables that may have contributed to treatment choice beyond what we measured. Secondly, our study does not calculate nephrometry scores, which may better objectively quantify the complexity of a renal lesion. However, in that system, different lesions may be classified similarly due to the aggregate nature of the scoring system. Additionally, hilar location (which was highly predictive for OPN in our

study) lacks a true score in the described R.E.N.A.L. model. Thirdly, the collaborative approach of our group to review films to determine optimal treatment approach (open versus laparoscopic) may not be generally applicable. Indeed, in our study, surgeon-specific factors were not associated with treatment approach on multivariate analysis potentially due to this internal referral system. Finally, our analysis included cases prior to the introduction of robotic assisted partial nephrectomy. Indeed, such technology has been increasingly incorporated for SRMs and may likely increase the complexity of lesions that can be approached via minimally invasive surgery.

Conclusions

An increasing volume of renal lesions can be managed by nephron sparing surgery. Many parameters including increasing BMI, preoperative GFR, prior abdominal surgery, endophytic tumor location, and renal sinus/collecting system involvement do not necessarily preclude a minimally invasive partial nephrectomy. In our experience, renal hilar tumors were over 2.5 fold more likely to be managed by open partial nephrectomy likely owing to the complexity of resection. □

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