Surgical Approach Does Not Impact Margin Status After Partial Nephrectomy for Large Renal Masses

Abimbola Ayangbesan, MD,¹ David M. Golombos, MD,² Ron Golan, MD,¹ Padraic O'Malley, MD,³ Patrick Lewicki, MD,¹ Xian Wu, MPH,⁴ and Douglas S. Scherr, MD¹

Abstract

Purpose: While surgical approach has recently been associated with positive surgical margin (PSM) after partial nephrectomy (PN) for small (<4 cm) renal masses, its impact on margin status for large (>4 cm) masses is unclear. We sought to evaluate the relationship between margin and surgical approach in patients undergoing PN for large renal masses.

Materials and Methods: Using the National Cancer Database (NCDB), we identified patients undergoing PN for pathological T_{1b} and T_{2a} renal-cell carcinoma diagnosed from 2010 to 2013. Conversions to open surgery were also included in our analysis. The primary outcome was surgical margin status. Multivariable regression modeling was performed to identify factors associated with PSM. A propensity score matching analysis was then performed to evaluate the impact of margin status on overall survival (OS).

Results: Of the 7495 patients undergoing PN for pT_{1b} and pT_{2a} renal masses over the study period, 504 (6.7%) had PSM. On multivariable analysis, surgical approach (laparoscopic or robot assisted vs open) was not significantly associated with surgical margin ($p=0.12$ and $p=0.44$, respectively). Tumor stage (T_{2a} vs T_{1b}) also showed no significant association ($p=0.18$). A subsequent multivariable analysis using clinical staging showed that surgical approach ($p=0.28$ and $p=0.54$, respectively), tumor stage ($p=0.78$), and conversion-to-open surgery ($p=0.98$) had no significant association with PSM. Propensity score matched analysis showed that PSM was not significantly associated with OS (hazard ratio 0.95 [95% confidence interval 0.47–1.92] $p=0.88$).

Conclusion: In a contemporary nation-wide cohort, surgical approach was not associated with an increased risk of PSM for large, noninvasive renal masses. Furthermore, increased size from T_{1b} to T_{2a} was not associated with an increased risk of PSM. These data suggest that surgical approach should be selected by surgeon comfort level with an individual tumor, rather than the size of the tumor itself.

Keywords: surgical margins, minimally invasive surgical procedures, nephron-sparing surgery, nephrectomy, kidney, carcinoma

Introduction

THERE HAS BEEN an increasing utilization of partial nephrectomy (PN) in the management of renal tumors over the past decade.¹ Cancer-specific outcomes between radical nephrectomy and PN have been shown to be comparable, with nephron preservation also conferring decreased risk of chronic renal insufficiency and initiation of dialysis with potentially improved overall and cardiovascular survival.^{2–5} For renal masses <4 cm, recent guidelines advocate that PN should be offered to all patients in whom an intervention is

indicated and possess a tumor amenable to this approach.^{6,7} Moreover, several studies have demonstrated the oncological and functional efficacy of PN in the surgical management of larger renal masses.^{8–10}

The ultimate goal of PN is the complete removal of tumor, while attaining cancer-free margins.¹¹ The effects of positive surgical margin (PSM) on oncologic outcomes after PNs remain unclear. Historically, margin status was not believed to impact oncologic outcomes,^{12–14} but several recent studies have suggested that PSMs play an important role in outcomes^{15–17} and may be influenced by surgical approach.¹⁸

¹Department of Urology, Weill Cornell Medicine, New York Presbyterian Hospital, New York, New York.

²Department of Urology, Stony Brook School of Medicine, Stony Brook, New York.

³Department of Urology, Dalhousie University, Halifax, Canada.

⁴Department of Healthcare Policy and Research, Weill Cornell Medicine, New York, New York.

Abstract presented at the 2017 AUA Annual Meeting.

While the influence of PSMs on oncologic outcomes remains highly contested, margin status nevertheless serves as a quality indicator for oncological control in PN.¹¹ Most of the available literature discussing PN and margin status, especially at the population level, has focused mainly on small renal masses.^{13,17,18} In this study, we sought to evaluate the relationship between PSMs and surgical approach in a national, contemporary cohort of patients undergoing PN for large (>4 cm) renal masses and to identify predictors of PSMs in this population, and secondarily to evaluate the impact of PSM on survival in this population.

Materials and Methods

Data source and patient selection

The National Cancer Database (NCDB), a joint program of the Commission on Cancer of the American College of Surgeons and the American Cancer Society, is a nationwide oncology outcomes database for more than 1500 Commission-accredited cancer programs in the United States and Puerto Rico that capture ~70% of all newly diagnosed cases of cancer.

We identified patients aged 18 years and older diagnosed with renal-cell carcinoma (RCC) from 2010 to 2013, who underwent PN and were found to have AJCC stage pT_{1b} or pT_{2a} RCC. We specifically chose 2010 as the starting year of this study because the surgical approach variable became available in NCDB. Patients with incomplete staging information, surgical margin status, or surgical treatment modality were excluded.

Demographic and clinical characteristics

Age at diagnosis, race, gender, insurance status, annual median income, geographic region, Charlson-Deyo comorbidity score, tumor size, tumor stage, tumor grade, tumor histology, surgical approach, hospital type, and surgical margin status were obtained using NCDB data. The primary outcome of the study was surgical margin status. PSM status was identified as residual tumor not otherwise specified (NOS) (1), microscopic (2), or macroscopic (3) residual tumor. Histologic subtypes of RCC were identified by their ICD-O-3 codes: 8140, 8310, and 8312 (clear cell); 8255, 8323, 8318, and 8319 (mixed, collecting duct, or sarcomatoid); 8260 (papillary); 8316 (cystic); and 8317 (chromophobe). Surgical approach was defined as either open partial nephrectomy (OPN), laparoscopic partial nephrectomy (LPN), robot-assisted partial nephrectomy (RAPN), or conversion-to-open partial nephrectomy (CPN). Treatment facility volume was divided into tertiles by volume of PNs performed within the institution. Institution type was classified as academic program or nonacademic.

Statistical analysis

Statistical analyses were performed using STATA version 14.1 (College Station, TX) and SAS version 9.4 (Cary, NC). Frequencies and proportions were used to characterize the study population. Demographic, facility-related, and prognostic characteristics were compared across three procedure groups using χ^2 tests. Multivariate logistic regression analysis was performed to identify factors independently associated with PSMs. Results from the multivariable logistic regression model are reported as odds ratios (ORs) with 95%

confidence intervals (CIs) and *p*-values. To evaluate impact of margin status on survival, a propensity score-matched analysis was employed to account for potential confounding factors in the relationship between margin status and overall survival (OS). We developed a multivariable logistic regression model to estimate a patient's propensity of having PSMs. Factors included in the logistic regression model were as follows: age at diagnosis, sex, race, median household income quartiles, quartiles of the percentage of individuals with less than a high school education, geography, Charlson-Deyo score, insurance, facility distance, center volume tertiles, facility location, facility type, year of diagnosis, surgical approach, laterality, histology, grade, tumor size using pathologic staging, and lymph vascular invasion. The estimated propensity score was then used to match patients with similar propensity to having PSMs based on 1:1 Greedy matching algorithm without replacement and with a caliper distance of 0.2 of the standard deviation of the logit propensity score. The success in achieving covariate balance was assessed using standardized differences of mean < 10% indicative of acceptable balance. We plotted Kaplan-Meier curves stratified by margin status for the propensity score-matched cohort and evaluated difference in OS between the groups with log-rank test. Subsequently, a conditional Cox proportional hazards model was constructed to assess the association between margin status and OS. The proportional hazards assumption of the Cox models was checked using the Schoenfeld residual method, with no evidence of violation found. Hazard ratio (HR) with 95% CI was reported. Follow-up times for patients were calculated from the time they got the cancer diagnosis to death, December 2012, or loss to follow-up, whichever came first. Patients diagnosed in 2013 were excluded from the survival analysis, given the absence of vital information and short follow-up time.

To account for excluded pT_{3a} patients staged at cT_{1b}/cT_{2a}, a sensitivity analysis was performed. We identified a new study cohort of 6555 patients and repeated the multivariable analysis evaluating factors associated with PSM. Furthermore, conversions to open surgery (*n* = 122) were also included in our analysis. All tests of significance were two sided and significant results were defined as *p* < 0.05.

Results

Between 2010 and 2013, 7495 patients underwent PN for pT_{1b} and pT_{2a} renal masses. Of these, 2813 (37.5%), 882 (11.8%), and 3800 (50.7%) underwent RAPN, LPN, and OPN, respectively. Patient demographics, hospital characteristics, and baseline clinicopathological features stratified by surgical approach can be found in Table 1. Overall, PSMs were observed in 504 (6.7%) cases. On multivariable analysis (Table 2), surgical approach (LPN or RAPN vs OPN) was not significantly associated with PSM (*p* = 0.12 and *p* = 0.44, respectively). Likewise, tumor stage (T_{2a} vs T_{1b}) showed no significant association (*p* = 0.18). Significant predictors of PSM include age > 60 years (OR 1.57 [95% CI 1.01–2.44] *p* = 0.05), African-American race (OR 1.52 [95% CI 1.06–2.17] *p* = 0.02), education level (OR 1.48 [95% CI 1.03–2.14] *p* = 0.03), rural setting (OR 4.82 [95% CI 2.45–9.46] *p* < 0.001), PN at a nonacademic center (OR 1.57 [95% CI 1.15–2.15] *p* = 0.004), mixed histology (OR 1.84 [95% CI 1.04–3.24] *p* = 0.04), and undifferentiated tumor grade (OR 2.42 [95% CI 1.26–4.65] *p* < 0.01).

TABLE 1. DEMOGRAPHICS AND BASELINE CHARACTERISTICS OF PATIENTS UNDERGOING PARTIAL NEPHRECTOMY FROM 2010 TO 2013 STRATIFIED BY SURGICAL APPROACH

<i>Variable</i>	<i>No. of RAPN (%)</i>	<i>No. of LPN (%)</i>	<i>No. of OPN (%)</i>	<i>p</i>
Overall	2813 (37.5)	882 (11.77)	3800 (50.7)	
Age				0.36
<50	541 (19.2)	183 (20.8)	688 (18.1)	
50–59	800 (28.4)	229 (26.0)	1039 (27.3)	
60–79	1357 (48.2)	430 (48.8)	1915 (50.4)	
80+	115 (4.1)	40 (4.5)	158 (4.2)	
Sex				0.70
Male	1853 (65.9)	594 (67.4)	2507 (66.0)	
Female	960 (34.1)	288 (32.7)	1293 (34.0)	
Race				0.29
White	2326 (82.7)	726 (82.3)	3101 (81.6)	
African American	379 (13.5)	110 (12.5)	522 (13.7)	
Other	108 (3.8)	46 (5.2)	177 (4.7)	
Income				<0.001
<38,000	451 (16.1)	148 (16.9)	687 (18.1)	
38,000–62,999	1408 (50.2)	373 (42.5)	1893 (50.0)	
63,000+	944 (33.7)	356 (40.6)	1208 (31.9)	
Education				0.07
<7%	659 (23.5)	225 (25.6)	883 (23.3)	
7–20%	1690 (60.3)	492 (56.0)	2207 (58.3)	
≥21%	456 (16.3)	161 (18.3)	699 (18.5)	
Geography				<0.001
Metro	2284 (83.4)	753 (87.8)	3012 (81.2)	
Rural	42 (1.5)	19 (2.2)	63 (1.7)	
Urban	414 (15.1)	86 (10.0)	636 (17.1)	
CCI				0.03
0	1907 (67.8)	621 (70.4)	2510 (66.1)	
1	690 (24.5)	191 (21.7)	936 (24.6)	
2+	216 (7.7)	70 (7.9)	354 (9.3)	
Insurance				0.003
Private	1462 (52.5)	442 (50.9)	1829 (48.9)	
Government	1249 (44.8)	399 (45.9)	1751 (46.8)	
Uninsured	76 (2.7)	28 (3.2)	159 (4.3)	
Facility distance				<0.001
<10	990 (35.3)	351 (40.0)	1406 (37.1)	
10–25	1028 (36.7)	255 (29.0)	1469 (38.8)	
25+	786 (28.0)	272 (31.0)	916 (24.2)	
Center volume				<0.001
High	921 (32.7)	275 (31.2)	1358 (35.7)	
Intermediate	1052 (37.4)	306 (34.7)	1161 (30.6)	
Low	840 (29.9)	301 (34.1)	1281 (33.7)	
Facility location				<0.001
Northeast	629 (23.8)	297 (35.8)	920 (25.7)	
Midwest	766 (29.0)	151 (18.2)	888 (24.8)	
South	880 (33.3)	280 (33.7)	1300 (36.3)	
West	365 (13.8)	102 (12.3)	477 (13.3)	
Facility type				<0.001
Academic/research	1488 (56.4)	470 (56.6)	2185 (61.0)	
Nonacademic	1152 (43.6)	360 (43.4)	1400 (39.1)	
Year of diagnosis				<0.001
2010	363 (12.9)	189 (21.4)	855 (22.5)	
2011	623 (22.2)	245 (27.8)	1005 (26.5)	
2012	809 (28.8)	212 (24.0)	1032 (27.2)	
2013	1018 (36.2)	236 (26.8)	908 (23.9)	
Side				0.51
Left	1428 (50.8)	440 (49.9)	1874 (49.3)	
Right	1385 (49.2)	442 (50.1)	1926 (50.7)	

(continued)

TABLE 1. (CONTINUED)

Variable	No. of RAPN (%)	No. of LPN (%)	No. of OPN (%)	p
Histology				<0.001
Clear cell	1809 (64.3)	585 (66.3)	2672 (70.3)	
Papillary	707 (25.1)	195 (22.1)	725 (19.1)	
Chromophobe	216 (7.7)	72 (8.2)	278 (7.3)	
Mixed	66 (2.4)	27 (3.1)	100 (2.6)	
Cystic	15 (0.5)	3 (0.3)	25 (0.7)	
Grade				0.11
Well differentiated	256 (11.9)	73 (10.6)	314 (10.5)	
Moderately differentiated	1211 (56.2)	404 (58.9)	1664 (55.5)	
Poorly differentiated	625 (29.0)	181 (26.4)	929 (31.0)	
Undifferentiated	64 (3.0)	28 (4.1)	89 (3.0)	
Size				<0.001
pT _{1b}	2627 (93.4)	795 (90.1)	3398 (89.4)	
pT _{2a}	186 (6.6)	87 (9.9)	402 (10.6)	
LVI				0.63
Negative	2197 (96.4)	705 (95.8)	2912 (96.5)	
Present	81 (3.6)	31 (4.2)	105 (3.5)	
Margin status				0.01
Positive	220 (7.8)	49 (5.6)	235 (6.2)	
Negative	2593 (92.2)	833 (94.4)	3565 (93.8)	

CCI=Charlson comorbidity index; LPN=laparoscopic partial nephrectomy; LVI=lymphovascular invasion; OPN=open partial nephrectomy; RAPN=robot-assisted partial nephrectomy.

Upon running a subsequent multivariable analysis on the newly identified, clinically staged cohort of 6555 patients from the sensitivity analysis (Appendix Table A1), surgical approach (LPN or RAPN vs OPN) was not significantly associated with PSM ($p=0.28$ and $p=0.54$, respectively), nor was tumor stage (T_{2a} vs T_{1b} , $p=0.78$) (Table 3). Moreover, conversion-to-open surgery showed no significance (CPN vs OPN, $p=0.98$) (Table 4).

After excluding 3470 patients from the OS analysis attributable to being diagnosed in 2013 or for having more than one malignancy, 263 patients (6.5%) had a PSM within the cohort of 4025 patients (Appendix Table A2). In the unmatched cohort, significant differences existed in terms of margin status by surgical approach ($p=0.02$), patient age ($p=0.002$), insurance type ($p=0.01$), center volume ($p<0.001$), facility type ($p<0.001$), tumor histology ($p=0.002$), and grade ($p=0.02$). However, after 1:1 propensity score matching, the 243 (matching rate: 92.4%) patients with a PSM to patients with negative surgical margin, the groups were well balanced, and none of the aforementioned variables retained their significance. Kaplan-Meier curves illustrating OS are shown in Figure 1. Margin status was not significantly associated with OS in the propensity score-matched cohort (HR 0.95 [95% CI 0.47–1.92] $p=0.88$).

Discussion

There has been a rapid adoption and increasing use of minimally invasive surgical techniques in urologic surgery, particularly for renal surgery and PN.¹ Whether surgical modality is related to PSMs after PNs remains controversial, as there are contradicting studies both demonstrating and refuting the relationship.^{13,17–19} Using contemporary data from the NCDB, we demonstrate that surgical approach is not independently associated with increased risk of PSMs in patients undergoing PN

for large (>4 cm), cT_{1b} and cT_{2a} masses. This is in contrast to the recent study by Tabayoyong and colleagues, which looked at patients undergoing PN for clinical T_{1a} RCC and concluded that minimally invasive surgical approaches were associated with higher rates of PSMs.¹⁸ In support of our findings, Ficarra and coworkers demonstrated in a large retrospective matched-pair analysis that the rate of PSM after an OPN was comparable to that of RAPN, 5.5% and 5.7%, respectively.²⁰ Similarly, Porpiglia and colleagues found no significant differences in rates of PSM as dictated by surgical approach when looking at data from patients undergoing PN for cT_{1b} tumors.¹⁹

Another important finding was that PN performed at an academic facility was independently associated with lower rates of PSMs. Since we were unable to account for individual surgeon characteristics or volume, the reason behind the protective effect against PSM afforded by an academic center is speculative. However, it is possible that a more experienced cohort of surgeons is operating in these settings. As a result, these surgeons may be better equipped to handle the greater technical difficulty of performing a PN in large masses, resulting in a different rate of observed PSM. The implication from this hypothesis makes a compelling argument for the consolidation of care at academic centers, especially for the more technically challenging cases, thereby allowing for better quality of oncologic care.

In addition, we found that increasing tumor size (T_{1b} vs T_{2a}) did not confer increased risk of having a PSM on multivariable analysis. Although current guidelines advocate for the management of T₁ masses with PN when amenable,^{6,7} several studies have demonstrated the technical feasibility, oncologic efficacy, and safety for performing PN on larger tumors.^{8–10} A study by Benoit and coworkers showed that PN on tumors >7 cm had similar outcomes to tumors 4 to 7 cm with respect to Trifecta attainment (a combination of negative surgical margins, functional preservation, and complication-free

TABLE 2. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH POSITIVE SURGICAL MARGIN

Variable	OR (95% CI)	p
Age		
<50	Reference	
50–59	1.14 (0.70–1.77)	0.65
60–79	1.57 (1.01–2.44)	0.05
80+	1.99 (1.05–3.77)	0.04
Sex		
Male	Reference	
Female	0.87 (0.67–1.14)	0.31
Race		
White	Reference	
African American	1.52 (1.06–2.17)	0.02
Other	1.07 (0.54–2.10)	0.85
Income		
63,00+	Reference	
<38,000	0.93 (0.59–1.47)	0.76
38,000–62,999	0.74 (0.53–1.03)	0.07
Education		
<7%	Reference	
7–20%	1.48 (1.03–2.14)	0.03
≥21%	1.52 (0.92–2.52)	0.10
Geography		
Metro	Reference	
Rural	4.82 (2.45–9.46)	<0.001
Urban	1.26 (0.85–1.87)	0.24
CCI (0)		
0	Reference	
1	0.86 (0.64–1.15)	0.31
2	1.30 (0.89–1.91)	0.18
Insurance		
Private	Reference	
Government	1.09 (0.83–1.45)	0.54
Uninsured	0.48 (0.17–1.31)	0.15
Facility distance		
<10 miles	Reference	
10–25	0.90 (0.65–1.24)	0.52
25+	0.93 (0.65–1.34)	0.71
Center volume		
High	Reference	
Intermediate	1.08 (0.77–1.50)	0.67
Low	1.25 (0.86–1.82)	0.24
Facility location		
Northeast	Reference	
Midwest	1.26 (0.87–1.81)	0.22
South	0.98 (0.69–1.40)	0.92
West	1.21 (0.79–1.86)	0.38
Facility type		
Academic/research	Reference	
Nonacademic	1.57 (1.15–2.15)	0.004
Year of diagnosis		
2010	Reference	
2011	1.25 (0.87–1.79)	0.23
2012	1.11 (0.77–1.60)	0.59
2013	1.23 (0.85–1.76)	0.27
Surgical approach		
OPN	Reference	
LPN	0.71 (0.46–1.10)	0.12
RAPN	1.11 (0.85–1.44)	0.44

(continued)

TABLE 2. (CONTINUED)

Variable	OR (95% CI)	p
Side		
Left	Reference	
Right	0.93 (0.73–1.19)	0.57
Histology		
Clear cell/cstic	Reference	
Papillary	0.80 (0.58–1.10)	0.17
Chromophobe	0.73 (0.39–1.40)	0.35
Mixed	1.84 (1.04–3.24)	0.04
Grade		
Well differentiated	Reference	
Moderately differentiated	1.13 (0.58–1.10)	0.57
Poorly differentiated	1.36 (0.87–2.13)	0.18
Undifferentiated	2.42 (1.26–4.65)	0.008
Size		
pT _{1b}	Reference	
pT _{2a}	0.72 (0.45–1.16)	0.18
LVI		
Negative	Reference	
Present	1.35 (0.77–2.37)	0.30

CI = confidence interval; OR = odds ratio.

recovery).²¹ Conversely, in a recent population-based report using data from the Ontario Cancer Registry, it was found that tumor stage was significantly associated with PSM when comparing pT_{1b} to pT_{1a} masses.¹³ However, no significant association was found when looking solely at tumor size per 1-cm increments.¹³ Our study failed to find any relationship between

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH POSITIVE SURGICAL MARGIN IN PATIENTS WITH STAGE cT_{1b} AND cT_{2a}

Variable	OR (95% CI)	p
Year of diagnosis		
2010	Reference	
2011	1.18 (0.82–1.71)	0.37
2012	1.15 (0.79–1.66)	0.46
2013	1.15 (0.80–1.67)	0.45
Surgical approach		
OPN	Reference	
LPN	0.79 (0.52–1.22)	0.28
RAPN	1.09 (0.83–1.43)	0.54
Side		
Left	Reference	
Right	0.90 (0.70–1.15)	0.40
Histology		
Clear cell/cystic	Reference	
Papillary	0.79 (0.56–1.12)	0.19
Chromophobe	1.84 (1.12–3.02)	0.02
Mixed	1.71 (0.94–3.11)	0.08
Grade		
Well differentiated	Reference	
Moderately differentiated	0.89 (0.59–1.36)	0.60
Poorly differentiated	1.09 (0.70–1.70)	0.69
Undifferentiated	1.90 (1.00–3.62)	0.05
Size		
cT _{1b}	Reference	
cT _{2a}	0.94 (0.59–1.49)	0.78

TABLE 4. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH POSITIVE SURGICAL MARGIN IN PATIENTS WITH STAGE cT_{1b} AND cT_{2a} (INCLUDING CONVERSION-TO-OPEN PARTIAL NEPHRECTOMY)

Variable	OR (95% CI)	p
Year of diagnosis		
2010	Reference	
2011	1.19 (0.83–1.72)	0.35
2012	1.21 (0.84–1.75)	0.30
2013	1.21 (0.84–1.76)	0.30
Surgical approach		
OPN	Reference	
LPN	0.79 (0.52–1.22)	0.29
RAPN	1.08 (0.83–1.42)	0.57
CPN	1.01 (0.42–2.43)	0.98
Side		
Left	Reference	
Right	0.91 (0.72–1.16)	0.46
Histology		
Clear cell/cystic	Reference	
Papillary	0.77 (0.54–1.09)	0.14
Chromophobe	1.84 (1.13–2.99)	0.01
Mixed	1.69 (0.93–3.08)	0.09
Grade		
Well differentiated	Reference	
Moderately differentiated	0.92 (0.60–1.40)	0.69
Poorly differentiated	1.09 (0.70–1.70)	0.70
Undifferentiated	2.01 (1.06–3.78)	0.03
Size		
cT _{1b}	Reference	
cT _{2a}	0.96 (0.61–1.51)	0.84

CPN = conversion-to-open partial nephrectomy.

categorical tumor size and rates of PSM, suggesting that size alone should not alter surgical approach, and should rather be dictated by surgeon comfort level with an individual tumor.

Currently, the relationship between PSM and age at the time of surgery remains unclear. Findings from our analysis indicate that increasing age beyond 60 was associated with an

increased risk for PSM, which is in contrast to findings demonstrated in a recent study by Ani and coworkers.¹³ Schiavina and colleagues hypothesize that the independent predictive value of age at the time of surgery for PSM after a PN largely revolves around the idea of increased renal and cardiovascular comorbidities that most commonly exist in older patients.²² As renal function deterioration and rate of end-stage renal disease correlate with increasing age,^{23,24} urologists may be more inclined to preserve as much parenchyma as possible, which as a result may lead to an increased risk of PSM.²² Furthermore, the age-associated anesthesia mortality risk with elderly patients²⁵ could serve as an impetus for a more expeditious surgery.

While the significance of obtaining negative surgical margins as a surrogate for complete tumor removal has been shown in studies involving bladder, prostate, and breast cancer,^{26–28} the consequences are less clearly defined for renal masses and remain controversial.^{12–17} The main limitations of the various studies looking at the oncologic impact of PSMs in PNs are the short- to intermediate-term follow-up and small sample sizes.¹⁷ It has also been argued that the clinical relevance of PSM after a PN stems largely from the intrinsic histopathological properties of the primary renal lesion with regard to the tumor grade and stage.¹⁶ In this study, undifferentiated tumor grade was significantly associated with PSM. However, margin status did not affect OS ($p=0.88$). This is not surprising, given our short follow-up period, which was dictated by the fact that 2010 marked the first year that data regarding surgical approach were available in NCDB. Longer follow-up is needed to fully understand the survival implication of PSMs, especially in larger or more complex masses.

The findings of our study must be interpreted within the context of the study design. The retrospective nature of the study and lack of standardization of surgical modalities is a limitation. We could not account for individual surgeon volume, and instead used center volume. This may be a reason for why center volume was not predictive of PSM, but the type of center (academic vs nonacademic) was. Furthermore, because of limitation of the database, we were unable to account for cancer-specific or recurrence-free survival. We were also not able to

FIG. 1. Kaplan-Meier estimates of overall survival based on margin status.

account for tumor complexity such as nephrometry score²⁹; however, with our analysis, we were able maintain a relatively homogenous cohort of patients with large, noninvasive tumors. Finally, we were unable to account for margin length, which some have speculated to have important implications.

Conclusions

In a contemporary national cohort, surgical approach was not associated with increased risk of PSM for large, noninvasive renal masses. Furthermore, increased size from T_{1b} to T_{2a} was also not associated with increased risk. These data suggest that surgical approach should be dictated by surgeon comfort level with an individual tumor, and not by size criteria alone.

Acknowledgment

X.W. was partially supported by the following grant: Clinical and Translational Science Center at Weill Cornell Medical College (UL-TR000457-06).

Author Disclosure Statement

No competing financial interests exist.

References

1. Bjurlin MA, Walter D, Taksler GB, et al. National trends in the utilization of partial nephrectomy before and after the establishment of AUA guidelines for the management of renal masses. *Urology* 2013;82:1283–1289.
2. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: A retrospective cohort study. *Lancet Oncol* 2006;7:735–740.
3. Kim SP, Thompson RH, Boorjian SA, et al. Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: A systematic review and meta-analysis. *J Urol* 2012;188:51–57.
4. Weight CJ, Larson BT, Fergany AF, et al. Nephrectomy induced chronic renal insufficiency is associated with increased risk of cardiovascular death and death from any cause in patients with localized cT1b renal masses. *J Urol* 2010;183:1317–1323.
5. Van Poppel H, Da Pozzo L, Albrecht W, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011;59:543–552.
6. Finelli A, Ismaili N, Bro B, et al. Management of small renal masses: American Society of Clinical Oncology Clinical Practice guideline. *J Clin Oncol* 2017;13:276–278.
7. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. *J Urol* 2009;182:1271–1279.
8. Breau RH, Crispen PL, Jimenez RE, et al. Outcome of stage T2 or greater renal cell cancer treated with partial nephrectomy. *J Urol* 2010;183:903–908.
9. Brewer K, O'Malley RL, Hayn M, et al. Perioperative and renal function outcomes of minimally invasive partial nephrectomy for T1b and T2a kidney tumors. *J Endourol* 2012;26:244–248.
10. Long CJ, Canter DJ, Kutikov A, et al. Partial nephrectomy for renal masses ≥ 7 cm: Technical, oncological and functional outcomes. *BJU Int* 2012;109:1450–1456.
11. Hung AJ, Cai J, Simmons MN, et al. “Trifecta” in partial nephrectomy. *J Urol* 2013;189:36–42.
12. Bensalah K, Pantuck AJ, Rioux-Leclercq N, et al. Positive surgical margin appears to have negligible impact on survival of renal cell carcinomas treated by nephron-sparing surgery. *Eur Urol* 2010;57:466–471.
13. Ani I, Finelli A, Alibhai SMH, et al. Prevalence and impact on survival of positive surgical margins in partial nephrectomy for renal cell carcinoma: A population-based study. *BJU Int* 2013;111:E300–E305.
14. Yossepowitch O, Thompson RH, Leibovich BC, et al. Positive surgical margins at partial nephrectomy: Predictors and oncological outcomes. *J Urol* 2008;179:2158–2163.
15. Khalifeh A, Kaouk JH, Bhayani S, et al. Positive surgical margins in robot-assisted partial nephrectomy: A multi-institutional analysis of oncologic outcomes (leave no tumor behind). *J Urol* 2013;190:1674–1679.
16. Shah PH, Moreira DM, Okhunov Z, et al. Positive surgical margins increase risk of recurrence after partial nephrectomy for high risk renal tumors. *J Urol* 2016;196:327–334.
17. Maurice MJ, Zhu H, Kim SP, et al. Reexamining the association between positive surgical margins and survival after partial nephrectomy in a large American cohort. *J Endourol* 2016;30:698–703.
18. Tabayoyong W, Abouassaly R, Kiechle JE, et al. Variation in surgical margin status by surgical approach among patients undergoing partial nephrectomy for small renal masses. *J Urol* 2015;194:1548–1553.
19. Porpiglia F, Mari A, Bertolo R, et al. Partial nephrectomy in clinical T1b renal tumors: Multicenter comparative study of open, laparoscopic and robot-assisted approach (the RECORD project). *Urology* 2016;89:45–51.
20. Ficarra V, Minervini A, Antonelli A, et al. A multicentre matched-pair analysis comparing robot-assisted versus open partial nephrectomy. *BJU Int* 2014;113:936–941.
21. Benoit T, Nouhaud FX, Roumigué M, et al. Does a tumor size higher than 7cm impact partial nephrectomy outcomes for the treatment of renal cancer? *Prog Urol* 2015;25:138–144.
22. Schiavina R, Borghesi M, Chessa F, et al. Predictors of positive surgical margins after nephron-sparing surgery for renal cell carcinoma: Retrospective analysis on 298 consecutive patients. *Urologia* 2014;81:40–45.
23. Weinstein JR, Anderson S. The aging kidney: Physiological changes. *Adv Chronic Kidney Dis* 2010;17:302–307.
24. Capitanio U, Larcher A, Terrone C, et al. End-stage renal disease after renal surgery in patients with normal preoperative kidney function: Balancing surgical strategy and individual disorders at baseline. *Eur Urol* 2016;70:558–561.
25. Li G, Warner M, Lang BH, et al. Epidemiology of anesthesia-related mortality in the United States, 1999–2005. *Anesthesiology* 2009;110:759–765.
26. Ohori M, Wheeler TM, Kattan MW, et al. Prognostic significance of positive surgical margins in radical prostatectomy specimens. *J Urol* 1995;154:1818–1824.
27. Dotan ZA, Kavanagh K, Yossepowitch O, et al. Positive surgical margins in soft tissue following radical cystectomy for bladder cancer and cancer specific survival. *J Urol* 2007;178: 2308–2312; discussion:2313.
28. Houssami N, Macaskill P, Marinovich ML, et al. The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: A meta-analysis. *Ann Surg Oncol* 2014;21:717–730.

29. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: A comprehensive standardized system for quantitating renal tumor size, location and depth. *J Urol* 2009;182:844–853.

Address correspondence to:
Douglas S. Scherr, MD
Department of Urology
Weill Cornell Medicine
New York Presbyterian Hospital
525 East 68th Street
Sarr Pavilion, 9th Floor
New York, NY 10065
E-mail: dss2001@med.cornell.edu

Abbreviations Used

CI = confidence interval
 CPN = conversion-to-open partial nephrectomy
 HR = hazard ratio
 LPN = laparoscopic partial nephrectomy
 NCDB = National Cancer Database
 OPN = open partial nephrectomy
 OR = odds ratio
 OS = overall survival
 PN = partial nephrectomy
 PSM = positive surgical margin
 RAPN = robot-assisted partial nephrectomy
 RCC = renal-cell carcinoma

APPENDIX

APPENDIX TABLE A1. DEMOGRAPHICS AND BASELINE CHARACTERISTICS OF PATIENTS WITH cT_{1B} AND cT_{2A} UNDERGOING PARTIAL NEPHRECTOMY (INCLUDING CONVERSION-TO-OPEN PARTIAL NEPHRECTOMY) FROM 2010 TO 2013 STRATIFIED BY SURGICAL APPROACH

Variable	No. of RAPN (%)	No. of LPN (%)	No. of OPN (%)	No. of CPN (%)	p
Overall	2399 (35.9)	795 (11.9)	3361 (50.3)	122 (1.8)	
Age					0.04
<50	502 (20.9)	155 (19.5)	591 (17.6)	25 (20.5)	
50–59	665 (27.7)	208 (26.2)	927 (27.6)	39 (32.0)	
60–79	1140 (47.5)	390 (49.1)	1703 (50.7)	56 (45.9)	
80+	92 (3.8)	42 (5.3)	140 (4.2)	2 (1.6)	
Sex					0.04
Male	1589 (66.2)	534 (67.2)	2255 (67.1)	96 (78.7)	
Female	810 (33.8)	261 (32.8)	1106 (32.9)	26 (21.3)	
Race					0.09
White	1995 (83.2)	656 (82.5)	2764 (82.2)	103 (84.4)	
African American	313 (13.1)	98 (12.3)	434 (12.9)	19 (15.6)	
Other	91 (3.8)	41 (5.2)	163 (4.9)	0 (0)	
Income					<0.001
<38,000	410 (17.2)	130 (16.5)	607 (18.1)	26 (21.3)	
38,000–62,999	1171 (49.0)	333 (42.2)	1650 (49.3)	58 (47.5)	
63,000+	808 (33.8)	326 (41.3)	1090 (32.6)	38 (31.2)	
Education					0.06
<7%	580 (24.3)	214 (27.1)	767 (22.9)	29 (23.8)	
7–20%	1407 (58.8)	421 (53.4)	1956 (58.4)	74 (60.7)	
≥21%	405 (16.9)	154 (19.5)	625 (18.7)	19 (15.6)	
Geography					<0.001
Metro	1951 (83.7)	678 (88.5)	2699 (82.5)	93 (76.2)	
Rural	39 (1.7)	17 (2.2)	57 (1.7)	2 (1.6)	
Urban	340 (14.6)	71 (9.3)	517 (15.8)	27 (22.1)	
CCI					0.05
0	1609 (67.1)	551 (69.3)	2193 (65.3)	78 (63.9)	
1	612 (25.5)	175 (22.0)	849 (25.3)	34 (27.9)	
2+	178 (7.4)	69 (8.7)	319 (9.5)	10 (8.2)	
Insurance					<0.001
Private	1249 (52.5)	392 (49.9)	1635 (49.3)	55 (45.1)	
Government	1078 (45.3)	366 (46.6)	1536 (46.3)	62 (50.8)	
Uninsured	52 (2.2)	28 (3.6)	144 (4.3)	5 (4.1)	

(continued)

APPENDIX TABLE A1. (CONTINUED)

<i>Variable</i>	<i>No. of RAPN (%)</i>	<i>No. of LPN (%)</i>	<i>No. of OPN (%)</i>	<i>No. of CPN (%)</i>	<i>p</i>
Facility distance					<0.001
<10	886 (37.1)	335 (42.5)	1238 (37.0)	50 (41.0)	
10–25	672 (28.1)	236 (29.9)	845 (25.2)	30 (24.6)	
25+	833 (34.8)	218 (27.6)	1265 (37.8)	42 (34.4)	
Center volume					<0.001
High	743 (31.0)	266 (33.5)	1238 (36.8)	22 (18.0)	
Intermediate	924 (38.5)	259 (32.6)	985 (29.3)	56 (45.9)	
Low	732 (30.5)	270 (34.0)	1138 (33.9)	44 (36.1)	
Facility location					<0.001
Northeast	524 (23.5)	271 (36.0)	848 (26.7)	43 (37.1)	
Midwest	614 (27.5)	131 (17.4)	760 (23.9)	29 (25.0)	
South	759 (34.0)	249 (33.1)	1208 (38.0)	35 (30.2)	
West	338 (15.1)	101 (13.4)	366 (11.5)	9 (7.8)	
Facility type					<0.001
Academic/research	1212 (54.2)	443 (58.9)	1908 (60.0)	70 (60.3)	
Nonacademic	1023 (45.8)	309 (41.1)	1274 (40.0)	46 (39.7)	
Year of diagnosis					<0.001
2010	306 (12.8)	167 (21.0)	763 (22.7)	31 (25.4)	
2011	510 (21.3)	223 (28.1)	916 (27.3)	25 (20.5)	
2012	697 (29.1)	209 (26.3)	898 (26.7)	31 (25.4)	
2013	886 (36.9)	196 (24.7)	784 (23.3)	35 (28.7)	
Side					0.39
Left	1221 (50.9)	408 (51.3)	1669 (49.7)	54 (44.3)	
Right	1178 (49.1)	387 (48.7)	1692 (50.3)	68 (55.7)	
Histology					0.04
Clear cell	1639 (68.3)	546 (68.7)	2449 (72.9)	83 (68.0)	
Papillary	506 (21.1)	160 (20.1)	593 (17.6)	25 (20.5)	
Chromophobe	172 (7.2)	60 (7.6)	225 (6.7)	11 (9.0)	
Mixed	72 (3.0)	27 (3.4)	77 (2.3)	2 (1.6)	
Cystic	10 (0.4)	2 (0.3)	17 (0.5)	1 (0.8)	
Grade					0.51
Well differentiated	191 (10.3)	61 (9.8)	278 (10.5)	8 (8.3)	
Moderately differentiated	1040 (56.0)	360 (58.1)	1453 (54.7)	46 (47.4)	
Poorly differentiated	565 (30.4)	176 (28.4)	841 (31.7)	38 (39.2)	
Undifferentiated	61 (3.3)	23 (3.7)	85 (3.2)	5 (5.2)	
Size					<0.001
cT _{1b}	2258 (94.1)	720 (90.6)	3038 (90.4)	111 (91.0)	
cT _{2a}	141 (5.9)	75 (9.4)	323 (9.6)	11 (9.0)	
LVI					0.32
Negative	1859 (95.6)	623 (94.4)	2556 (95.4)	84 (92.3)	
Present	86 (4.4)	37 (5.6)	122 (4.6)	7 (7.7)	
Margin status					0.006
Positive	209 (8.7)	46 (5.8)	222 (6.6)	8 (6.6)	
Negative	2190 (91.3)	749 (94.2)	3139 (93.4)	114 (93.4)	

CCI=Charlson comorbidity index; CPN=conversion-to-open partial nephrectomy; LPN=laparoscopic partial nephrectomy; LVI=lymphovascular invasion; OPN=open partial nephrectomy; RAPN=robot-assisted partial nephrectomy.

APPENDIX TABLE A2. PROPENSITY SCORE-MATCHED ANALYSIS

Characteristic	Before propensity score matching				After propensity score matching			
	Positive margin (%)	Negative margin (%)	Standardized difference (%)	p	Positive margin (%)	Negative margin (%)	Standardized difference (%)	p
Overall	263 (6.5)	3762 (93.5)			243 (50.0)	243 (50.0)		
Surgical Approach				0.02				0.76
RAPN	112 (42.6)	1293 (34.4)	16.9		104 (42.8)	98 (40.3)	5.0	
LPN	32 (12.2)	490 (13.0)	-2.6		31 (12.8)	36 (14.8)	-6.0	
OPN or unspecified	119 (45.3)	1979 (52.6)	-14.8		108 (44.4)	109 (44.9)	-0.8	
Age				0.002				0.99
<50	37 (14.1)	838 (22.3)	-21.4		26 (10.7)	25 (10.3)	1.3	
50-59	70 (26.6)	1118 (29.7)	-6.9		68 (28.0)	71 (29.2)	-2.7	
60-79	143 (54.4)	1681 (44.7)	19.5		136 (56.0)	134 (55.1)	1.7	
80+	13 (4.9)	125 (3.3)	8.1		13 (5.4)	13 (5.4)	0.0	
Sex				0.97				0.46
Male	168 (63.9)	2408 (64.0)	-0.3		154 (63.4)	146 (60.1)	6.8	
Female	95 (36.1)	1354 (36.0)	0.3		89 (36.6)	97 (39.9)	-6.8	
Race				0.06				0.38
White	202 (76.8)	3106 (82.6)	-14.3		188 (77.4)	191 (78.6)	-3.0	
African American	45 (17.1)	484 (12.9)	11.9		42 (17.3)	42 (18.5)	-3.2	
Other	16 (6.1)	172 (4.6)	6.7		13 (5.4)	7 (2.9)	12.5	
Income				0.43				0.90
<38,000	53 (20.2)	639 (17.0)	8.1		49 (20.2)	45 (18.5)	4.2	
38,000-62,999	125 (47.5)	1850 (49.2)	-3.3		118 (48.6)	120 (49.4)	-1.6	
63,000+	85 (32.3)	1257 (33.4)	-2.3		76 (31.3)	78 (32.1)	-1.8	
Unknown	0 (0)	16 (0.4)	-9.2		—	—	—	
Education				0.15				0.93
≥21	52 (19.8)	651 (17.3)	6.4		49 (20.2)	52 (21.4)	-3.0	
7-20	164 (62.4)	2226 (59.2)	6.5		151 (62.1)	147 (60.5)	3.4	
<7	47 (17.9)	870 (23.1)	-13.0		43 (17.7)	44 (18.1)	-1.1	
Unknown	0 (0)	15 (0.4)	-8.9		—	—	—	
Geography				0.06				0.74
Metro	206 (78.3)	3036 (80.7)	-5.9		192 (79.0)	189 (77.8)	3.0	
Urban	44 (16.7)	572 (15.2)	4.2		41 (16.9)	41 (16.9)	-6.4	
Rural	9 (3.4)	56 (1.5)	12.5		7 (2.9)	7 (2.9)	8.3	
Unknown	4 (1.5)	98 (2.6)	-7.6		3 (1.2)	3 (1.2)	0	
CCI				0.09				0.56
0	167 (63.5)	2522 (67.0)	-7.4		152 (62.6)	145 (59.7)	5.9	
1	63 (24.0)	918 (24.4)	-1.0		63 (25.9)	62 (25.5)	0.9	
2+	33 (12.6)	322 (8.6)	13.0		28 (11.5)	36 (14.8)	-9.7	
Insurance				0.01				0.75
Government	135 (51.3)	1545 (41.1)	20.7		129 (53.1)	128 (52.7)	0.8	
Private	115 (43.7)	2021 (53.7)	-20.1		103 (42.4)	103 (42.4)	0	
Uninsured	9 (3.4)	146 (3.9)	-2.4		7 (2.9)	10 (4.1)	-6.7	
Unknown	4 (1.5)	50 (1.3)	1.6		4 (1.7)	2 (0.8)	7.5	
Facility distance				0.58				0.72
≤10	103 (39.2)	1355 (36.0)	6.5		93 (38.3)	86 (35.4)	6.0	
10-25	67 (25.5)	987 (26.2)	-1.7		61 (25.1)	68 (28.0)	-6.5	
25+	93 (35.4)	1406 (37.4)	-4.2		89 (36.6)	89 (36.6)	0	
Unknown	0 (0)	14 (0.4)	-8.6		—	—	—	
Center volume				<0.001				0.92
High	69 (26.2)	1305 (34.7)	-18.4		65 (26.8)	66 (27.2)	-0.9	
Intermediate	75 (28.5)	1257 (33.4)	-10.6		66 (27.2)	62 (25.5)	3.7	
Low	119 (45.3)	1200 (31.9)	27.7		112 (46.1)	115 (47.3)	-2.5	
Facility location				0.09				0.94
Midwest	74 (28.1)	901 (24.0)	9.6		70 (28.8)	66 (27.2)	3.7	
Northeast	57 (21.7)	943 (25.1)	-8.0		53 (21.8)	58 (23.9)	-4.9	
South	89 (33.8)	1195 (31.8)	4.4		86 (35.4)	87 (35.8)	-0.9	
West	34 (12.9)	457 (12.2)	2.4		34 (14.0)	32 (13.2)	2.4	
Unknown	9 (3.4)	266 (7.1)	-16.4		—	—	—	

(continued)

APPENDIX TABLE A2. (CONTINUED)

<i>Characteristic</i>	<i>Before propensity score matching</i>				<i>After propensity score matching</i>			
	<i>Positive margin (%)</i>	<i>Negative margin (%)</i>	<i>Standardized difference (%)</i>	<i>p</i>	<i>Positive margin (%)</i>	<i>Negative margin (%)</i>	<i>Standardized difference (%)</i>	<i>p</i>
Facility type				<0.001				0.86
Academic/research	114 (43.4)	2074 (55.1)	−23.7		110 (45.3)	108 (44.4)	1.7	
Nonacademic	140 (53.2)	1422 (37.8)	31.4		133 (54.7)	135 (55.6)	−1.7	
Unknown	9 (3.4)	266 (7.1)	−16.4		—	—	—	
Year of diagnosis				0.41				0.83
2010	60 (22.8)	991 (26.3)	−8.2		53 (21.8)	57 (23.5)	−3.9	
2011	99 (37.6)	1309 (34.8)	5.9		94 (38.7)	88 (36.2)	5.1	
2012	104 (39.5)	1462 (38.9)	1.4		96 (39.5)	98 (40.3)	−1.7	
Side				0.13				0.78
Left	142 (54.0)	1849 (49.2)	9.7		135 (55.6)	132 (54.3)	2.5	
Right	121 (46.0)	1913 (50.9)	−9.7		108 (44.4)	111 (45.7)	−2.5	
Histology				0.002				0.81
Clear cell	162 (61.6)	2609 (69.4)	−16.4		151 (62.1)	161 (66.3)	−8.6	
Papillary	60 (22.8)	770 (20.5)	5.7		58 (23.9)	50 (20.6)	7.9	
Cystic	1 (0.4)	24 (0.6)	−3.6		—	—	—	
Chromophobe	26 (9.9)	283 (7.5)	8.4		23 (9.5)	22 (9.1)	1.4	
Mixed	14 (5.3)	76 (2.0)	17.6		11 (4.5)	10 (4.1)	2.0	
Grade (differentiated)				0.02				0.92
Well	15 (5.7)	365 (9.7)	−15.0		14 (5.8)	13 (5.4)	1.8	
Moderately	119 (45.3)	1723 (45.8)	−1.1		109 (44.9)	118 (48.6)	−7.4	
Poorly	56 (21.3)	879 (23.4)	−5.0		53 (21.8)	48 (19.8)	5.1	
Undifferentiated	11 (4.2)	85 (2.3)	10.9		9 (3.7)	7 (2.9)	4.6	
Unknown	62 (23.6)	710 (18.9)	11.5		58 (23.9)	57 (23.5)	1.0	
Size				0.31				0.15
pT _{1b}	245 (93.2)	3437 (91.4)	6.7		226 (93.0)	217 (89.3)	13.1	
pT _{2a}	18 (6.8)	325 (8.6)	−6.7		17 (7.0)	26 (10.7)	−13.1	
LVI				0.06				0.62
Present	13 (4.9)	98 (2.6)	12.3		10 (4.1)	13 (5.4)	−5.8	
Negative	196 (74.5)	2942 (78.2)	−8.7		181 (74.5)	185 (76.1)	−3.8	
Unknown	54 (20.5)	722 (19.2)	3.4		52 (21.4)	45 (18.5)	7.2	