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Accuracy of clinical nodal staging and factors associated with receipt of lymph node dissection at the time of surgery for nonmetastatic renal cell carcinoma

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Abstract

Introduction: The benefit of lymph node dissection (LND) in renal cell carcinoma (RCC) remains poorly defined. Despite this uncertainty, the American Urological Association (AUA) guideline on localized renal cancer recommends that LND be performed for staging purposes when there is suspicion of regional lymphadenopathy on imaging. Using the National Cancer Database (NCDB), we sought to determine how much of a departure the new AUA guideline is from current practice. We hypothesized that practice patterns would reflect the "Expert Opinion" recommendation and that patients who are clinical lymph node (cLN) positive would receive a LND more often than those who are cLN negative. Additionally, we sought to determine factors that would trigger a LND as well the accuracy of clinical staging by examining the relationship between cLN and pathologic lymph node (pLN) status of patients who received a LND.

Materials and methods: The NCDB was queried for patients with nonmetastatic RCC who underwent partial nephrectomy or nephrectomy from 2010 to 2014. Patient sociodemographic and clinical characteristics were extracted. Frequency distributions were calculated for patients with both cLN and pLN status available. Of patients who received a LND, sensitivity, specificity, and positive/negative predictive values (PPV/NPV) of cLN status for pLN positivity were calculated. Logistic regression models were used to examine association between clinical and socioeconomic factors and receipt of LND. Propensity score matching was used in sensitivity analyses to examine potential for reporting bias in NCDB data.

Results: We identified 110,963 patients who underwent surgery for RCC, of whom 11,867 (11%) had LND performed at the time of surgery. cLN and pLN information were available in 11,300 patients, of which 1,725 were preoperatively staged as having positive cLN. More LNDs were performed per year for patients who were cLN negative than cLN positive. Of patients who received a LND, the majority of patients were cLN negative across all clinical T (cT) stages. Multivariable analysis showed that all patients who had care at an academic/research institution (odds ratio [OR]: 1.58, 95% confidence interval [CI]: 1.43−1.74) and had to travel >12.5 to 31.0 miles and >31.0 miles to a treatment center (OR: 1.08, 95%CI: 1.01−1.15 and OR: 1.28, 95%CI: 1.20−1.36, respectively) were more likely to get a LND. As cT stage increased from cT2-4, the risk of LND increased (OR range: 4.7−7.90, respectively). Patients who were cLN positive were more likely to receive a LND at the time of surgery (OR: 18.68, 95%CI: 16.62−21.00). Of the patients who received a LND, clinical staging was more specific than sensitive.

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Conclusion: More patients received a LND who were cLN negative compared to patients who were cLN positive. Patients who were cLN positive were more likely to receive a LND. Treatment center type, distance to treatment center, cT stage, and cLN positivity were factors associated with LND receipt.

Keywords: National Cancer Database; Renal cell carcinoma; Lymphadenectomy; Lymph node yield; Clinical nodal status; Pathological nodal status; NDCB

1. Introduction

Lymph node involvement is associated with a poor prognosis for patients with renal cell carcinoma (RCC) [1−3]. Despite this, the utility of lymph node dissection (LND) during the surgical management of RCC remains controversial [4−7]. This stems from the lack of strong evidence of improved survival outcomes in those receiving LND, the lack of a uniform surgical template due to the unpredictability of lymphatic spread, and the low incidence of lymph node metastases in the absence of clinical suspicion [4,8,9].

Despite this uncertainty, AUA published new guidelines on the treatment of renal masses last year stating that LND should be performed for staging purposes when there is suspicion of regional lymphadenopathy (strength of recommendation = Expert Opinion) [10]. Recent studies also suggest that LND should be used in patients with certain disease characteristics for a potential benefit in cancer control and staging. These features include histologic subtype by biopsy and preoperative imaging revealing tumor size/stage and lymphadenopathy [11−14].

We sought to determine how much of a departure the new LND guideline recommendation is from contemporary practice patterns seen in the National Cancer Database (NCDB), a hospital registry database that captures both clinical and pathologic nodal information from centers with oncology expertise. We hypothesized that recent practice patterns would follow the new guideline in that (1) among patients receiving LND, more would have a positive cLN status than those with negative cLN status and (2) patients with lower clinical tumor stage (cT) would undergo fewer LNDs compared to those with higher cT stage. We also sought to determine factors that increase the odds of receiving a LND and the accuracy of clinical staging by examining the correlation between cLN and pLN status in those patients who received a LND.

2. Materials and methods

2.1. Data source

The NCDB is a national, hospital registry database developed in 1988 and administered by both the American College of Surgeons Commission on Cancer and the American Cancer Society as a quality improvement project. Having over 34 million records of patients with cancer, this is the largest hospital-based clinical cancer registry in the world [15]. The database includes demographic information including aggregate measures on education attainment and income as well as individual diagnosis and treatment information. This study was institutional review board exempt since the data set did not include any protected health information. The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

2.2. Study population

The NCDB was queried for patients with RCC. A total of 173,834 patients diagnosed from 2010 to 2014 were included in the kidney cancer data set. We excluded patients with metastasis ($n = 36,870$), nonsurgical treatment ($n = 24,001$), and patients with missing or inconsistent other critical information ($n = 2,000$). We captured all nonmetastatic patients who underwent surgical treatment (whether partial nephrectomy or radical nephrectomy) for RCC. The study population was then stratified by receipt of LND at the time of surgery. The final sample size for main analyses was 110,963, including 11,867 patients who underwent LND.

2.3. Study variables

Patient's age, sex, race, ethnicity (Hispanic yes/no), Charlson Deyo Comorbidity Index, distance from treatment center, education attainment, household income, type of health insurance, hospital type, clinical primary tumor stage, clinical lymph node positivity, surgical modality, and year of diagnosis were extracted. NCDB defines education attainment as the proportion of adults in the patient's zip code who did not graduate from high school. NCDB determines household income by matching patient's zip code at diagnosis against the 2012 American Community Survey Data (US Census Bureau).

2.4. Statistical analysis

Frequencies and proportions were calculated for all sociodemographic and clinical categorical variables. Chi-square and Kruskal-Wallis tests were used to compare proportions and medians. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95%CI) for receiving LND. All available sociodemographic and clinical variables were examined in

univariate models. Variables demonstrating significance of $P < 0.05$ on univariate analyses were included in the multivariable model. Final multivariable logistic regression model included: sex, race, Charlson Deyo comorbidity score, distance from treatment center, education attainment, household income, type of health insurance, type of hospital, clinical primary tumor stage, clinical lymph node positivity, and surgical modality. Linear regression was used to estimate the change in mean distance from treatment facility relative to hospital type. To compare the proportions of patients who were staged preoperatively as having cLN positive to those who were staged pLN positive, we restricted subanalyses to the LND population. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using clinical and pathologic lymph node variables restricted to the LND population. Additionally, a separate logistic regression analysis was conducted to examine only negative cLN patients. Variables included in this additional model were: sex, race, Charlson Deyo comorbidity score, distance from treatment center, type of health insurance, type of hospital, clinical primary tumor stage, and surgical modality.

2.5. Sensitivity analysis

We conducted 2 different sensitivity analyses to examine the potential for reporting bias in the NCDB data. First, a 1-to-1 propensity score matching by cLN status was performed to examine if the reporting of cLN status varied among treatment facilities. Propensity scores were computed by modeling individual logistic regressions using clinical node status as dependent variable with independent variables including age, sex, race/ethnicity, distance from treatment center and type of hospital. Covariate balance between matched groups was examined after propensity scores were computed (Supplemental Table 1). Afterwards, we used logistic regression to examine the receipt of LND. Second, we built a logistic regression model where clinical node status was the outcome and hospital type was the independent variable. This model was further adjusted for 2 main confounders: histology (i.e., clear cell and non-clear cell) and clinical stage. An alpha level of 0.05 was used to determine statistical significance. All statistical analyses were performed using SAS Version 9.4 (SAS Institute Inc. Cary, NC).

3. Results

A total of 110,963 nonmetastatic patients were found to have undergone surgery for RCC. Of those patients, only 11% received a LND at the time of surgery. Sociodemographic and clinical characteristics of the study population are shown in Table 1. LND at time of surgery is more frequent in academic or research hospital compared to other types of hospitals ($P < 0.01$). LNDs are also more frequently performed during open surgery and in patients who are cLN positive.

Per year from 2010 to 2014, the majority of patients who received a LND were cLN negative each year (Fig. 1). When the cohort was stratified by cT stage, the majority of patients who received a LND were cLN negative across all cT stages compared to those who were cLN positive (Table 2). From the 1,725 patients clinically staged as cLN positive, 74% were found to have positive pLN. Among all patients who received a LND, nodal yield was available for 11,551 patients. Median nodal yield for these patients was 3.0 (Interquartile Range [IQR] = 6.0) nodes. For those who were cLN positive, nodal yield was 4.0 (IQR = 7.0) while for those cLN negative it was 2.0 (IQR = 5.0). This difference in nodal yield between the 2 cLN groups was statistically significant ($P < 0.0001$).

In our main model, patients enrolled in Medicaid (OR: 0.87, 95%CI: 0.83–0.91) and other government insurance (OR: 0.79, 95%CI: 0.64–0.97) were less likely to have a LND compared to patients with private insurance (Table 3). Patients having robotic or laparoscopic surgery were less likely to have a LND compared to open surgery (OR: 0.73, 95%CI: 0.69–0.77 and OR: 0.63, 95%CI: 0.60–0.66, respectively). Patients with higher cT2-4 stage were more likely to have a LND compared to patients who were cT1 and the magnitude of the risk increased as cT stage increased (OR range: 4.70–7.90 respectively). Patients who were cLN positive were more likely to have a LND compared to patients who were cLN negative (OR: 18.68, 95%CI: 16.62–21.00).

Patients having care at academic/research hospitals had a significantly higher likelihood of having a LND compared to patients receiving care at a community cancer hospitals (OR: 1.58, 95%CI: 1.43–1.74). Patients who had to travel longer distance to a treatment center were more likely to receive a LND, specifically those who had to travel >12.5 to 31.0 miles and >31.0 miles (OR: 1.08, 95%CI: 1.01–1.15 and OR: 1.28, 95%CI: 1.20–1.36, respectively). Patients also traveled farther to receive care at academic/research hospitals (Table 4).

Results from the analysis including only the cLN negative population ($n = 106,370$) were comparable to our main model (Table 5). Patients who received care at an academic/research institution (OR: 1.58, 95%CI: 1.43–1.74), traveled farther (>31 miles) to a treatment center (OR: 1.22, 95%CI: 1.14–1.30), and had a higher cT stage (cT2-4, OR range: 4.87–11.10) were more likely to receive LND. Patients were less likely to receive a LND if they received a robotic or laparoscopic surgery compared to open surgery (OR: 0.73, 95%CI: 0.69–0.78 and OR: 0.60, 95%CI: 0.59–0.66, respectively).

Clinical LN and pLN information was available for 11,300 patients who received LND. Of those patients who received a LND, 1,725 were clinically staged as having positive cLN. Ultimately, 1,895 patients were found to have positive pLN after surgical intervention. The sensitivity of clinical staging to detect positive pLN in patients who received a LND was

Table 1
Socio-demographic and clinical characteristics of the study population by LND receipt for patients with non-metastatic RCC, NCDB 2010-2014

Patient characteristics	No LND N (%)	LND N (%)	*P* value
All patients	99,096 (89)	11,867 (11)	
Age (years)			
≤50	26,088 (26)	3,033 (24)	0.18
>50–60	25,347 (26)	3,125 (26)	
>60–70	24,036 (24)	2,867 (24)	
>70	23,625 (24)	2,842 (24)	
Sex			
Male	61,372 (62)	7,562 (64)	<0.01
Female	37,724 (38)	4,305 (36)	
Race			
White	83,001 (85)	10,082 (86)	<0.01
Black	11,827 (12)	1,284 (11)	
American Indian	509 (0.5)	43 (0.4)	
Asian	1,933 (2)	224 (2)	
Other	843 (1)	114 (1)	
Hispanic ethnicity			
Yes	6,201 (7)	705 (6)	0.15
No	89,156 (93)	10,749 (94)	
Charlson comorbidity index			
0	677,388 (68)	8,307 (70)	<0.01
1	23,581 (24)	2,687 (23)	
2	8,127 (8)	873 (7)	
Distance from treatment center (miles)			
≤5.4	25,496 (26)	2,710 (23)	<0.01
>5.4–12.5	24,944 (25)	2,691 (23)	
>12.5–31.0	24,615 (25)	2,878 (24)	
>31.0	24,041 (24)	3,588 (30)	
Income 2008–12 ($)			
≥62,000	17,474 (18)	1,962 (17)	0.02
≥47,999–62,999	23,279 (23)	2,771 (23)	
≥38,000–47,999	23,279 (23)	2,771 (24)	
<38,000	17,474 (18)	1,962 (17)	
Education attainment[a]			
<7%	22,695 (23)	2,771 (23)	0.13
7–12.9%	32,676 (33)	3,967 (33)	
13–20.9%	26,345 (27)	3,124 (26)	
>21%	17,099 (17)	1,955 (17)	
Insurance			
Private insurance	45,671 (47)	5,578 (48)	<0.01
Not insured	3,200 (3)	476 (4)	
Medicaid	5,606 (6)	710 (6)	
Medicare	42,051 (43)	4,789 (41)	
Other government	1337 (1)	130 (1)	
Hospital type			
Academic/Research Cancer Program	38,378 (41)	5,927 (52)	<0.01
Community Cancer Program	6403 (7)	678 (6)	
Comprehensive Community Cancer Program	38,934 (41)	3,660 (32)	
Integrated Network Cancer Program	10,218 (11)	1,085 (10)	
Clinical primary tumor			
1a	42,677 (49)	1,366 (13)	<0.01
1b	23,555 (27)	2,096 (20)	
2	12,269 (14)	3,625 (34)	
3	7,460 (9)	3,280 (31)	
4	366 (0.4)	321 (3)	
Clinical lymph node positive			
No	96,442 (99.5)	9,928 (85.2)	<0.01
Yes	496 (0.5)	1,725 (14.8)	
Surgical modality			
Robotic	30,124 (30)	2,345 (20)	<0.01
Laparoscopic	30,625 (31)	2,941 (25)	
Open	38,347 (39)	6,581 (55)	
Year of diagnosis			
2010	18,649 (19)	2,209 (19)	
2011	19,099 (19)	2,264 (19)	
2012	19,913 (20)	2,381 (20)	
2013	20,428 (21)	2,448 (21)	
2014	21,007 (21)	2,565 (22)	

[a] Number of adults in the patient's zip code who did not graduate from high school; *Chi-square test *P* value.LND = lymph node dissection.

67% while the specificity of clinical staging to detect positive pLN in patients who received a LND was 95%. Among all cLN negative patients who received a LND, the NPV of LND was 94%. Among all cLN positive patients who received a LND, the PPV of LND was 74%.

We performed PSM analysis of clinical node status as described in the methods with a final sample size of 4,228 (n = 2,114 per group). We found very similar results in the PSM population compared to our original analysis (Supplemental Table 2). Therefore, potential reporting bias had a minimal effect in our main results. Similarly, minimal differences were seen in diagnosing cLN positive patients between 4 different hospital types before and after adjustment (Supplemental Table 3).

4. Discussion

While it remains controversial if there is any benefit of performing a LND during RCC, these findings from the NCDB offer a basis for future studies investigating the utility of clinical staging as a trigger for LND in patients with nonmetastatic RCC. In contrast to what we expected, the majority of patients receiving an LND were cLN negative. When patients who received a LND were stratified by cT stage, the majority of patients across all cT stages were cLN negative. It is difficult to discern why the majority of patients who were cLN negative received LND. While the overall incidence of lymph node metastasis in RCC is relatively low, it is especially low in low-stage tumors without clinical evidence of lymphadenopathy [16,17]. It is possible that suspicious regional lymphadenopathy was found intraoperatively leading to a LND especially robotically with its stereoscopic, magnified vision. Of the patients who received a LND, preoperative clinical staging was more specific than sensitive for determining pLN status (95% vs. 67%, respectively). Of the patients who received a LND, those who were cLN negative were highly likely to be pLN

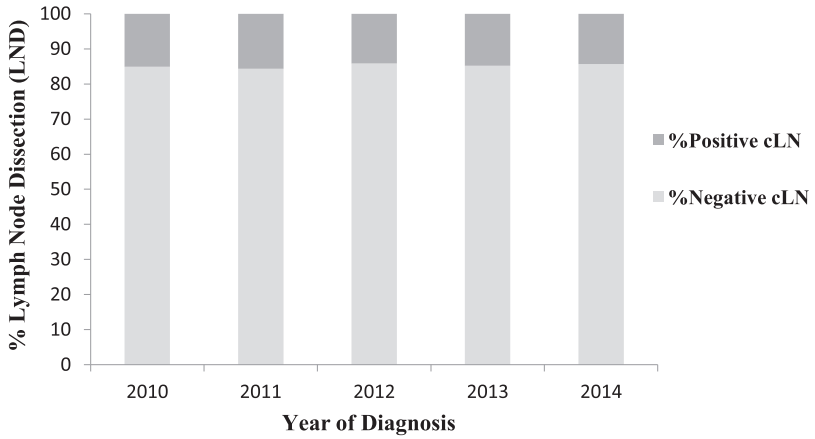

Fig. 1. Distribution of lymph node dissection by clinical lymph node status in renal cell carcinoma patients, NCDB 2010-2014.

Table 2
Clinical lymph node status for patients who received a lymph node dissection stratified by clinical stage

cT stage	cLN positive *n* (%)	cLN negative *n* (%)
1	359 (8%)	4,096 (92%)
2	457 (13%)	3,110 (87%)
3	713 (22%)	2,515 (78%)
4	130 (41%)	185 (59%)

cLN = clinical lymph node; cT = clinical tumor stage.

negative with a NPV of 94% while the PPV of cLN was 74%. Nevertheless, these results and practice patterns are not in alignment with the newest AUA guideline as well as recent studies arguing against LND at the time of radical nephrectomy since there was no therapeutic benefit in low cT stage patients [9,18].

Patients found to have cLN positive were more likely to receive a LND than those who are not (OR: 18.68 95%CI: 16.62−21.00). The magnitude of risk of having a LND was widely higher for cLN positive patients compared to patients with other risk factors such as hospital type, distance traveled to a treatment center, or cT stage. This illustrates the importance of cLN staging and the need for improved imaging for RCC. To assess factors associated to LND that were not driven by cLN positivity, analysis was performed for those who were specifically cLN negative. The results demonstrated that the strongest risk factor for LND in patients who were cLN negative was cT stage. In both cohorts, the magnitude of risk of LND increases as cT stage increases. This correlates with the belief that higher risk patients (higher cT stage) may benefit from LND due to higher risk of microscopic nodal disease [9].

Interestingly, patients who traveled farther distances to treatment center were more likely to receive a LND than those who received treatment closer to their residential zip code in the entire patient population as well as the those patients who were cLN negative. Patients may potentially be traveling farther distances, especially in rural areas, to receive care. Receiving care at an academic or research institution also resulted in a high risk of receiving a LND compared to care at a community cancer hospital in the entire patient population as well as those who were cLN negative. It is possible that patients who travel farther are traveling to more specialized centers like academic/research centers to receive care. Compared to an academic/research hospital, patients traveled less to have surgery in hospitals that were not academic/research hospital (Table 4). When analyzing the distance traveled to a treatment center with respect to the hospital type, the distribution of patients who traveled further occurred more frequently with patients who received care at an academic/research center.

Patients in our main analysis who had minimally invasive surgery (robotic and laparoscopic approach) were less likely to have a LND at the time of surgery (OR: 0.73, 95%CI: 0.69−0.77 and OR: 0.63, 95%CI: 0.60−0.66, respectively). Patients who were cLN negative and had minimally invasive surgery were also less likely to have a LND at the time of surgery (OR: 0.73, 95%CI: 0.69−0.78 and OR: 0.60, 95%CI: 0.59−0.66, respectively). This may be because minimally invasive surgery for RCC is more often utilized for lower cT stage/lower risk disease compared to open surgery for larger masses and those patients who have lower risk disease have a lower risk of microscopic nodal disease.

While our study shows evidence that patients with negative cLN are receiving LND and patients who were cLN positive were more likely to receive a LND, additional work is needed to determine the optimal clinical staging evaluation and triggers for LND. Studer et al. determined that cLN status by preoperative CT imaging may not correlate with pLN status [19]. While they showed that preoperative CT imaging is 95% sensitive in detecting enlarged lymph nodes, these findings may not correlate with pLN. Approximately 60% of their patients with enlarged lymph nodes on preoperative imaging had findings of inflammatory changes and not disease [19]. While the size of lymph

Table 3
Multivariable logistic regression model for the associations between socio-demographic and clinical variables with lymph node dissection receipt in patients with non-metastatic RCC, NCDB 2010−2014

Variable	OR (95% CI) LND	*P* value
Sex		
Female	Ref	
Male	0.97 (0.93−1.02)	0.22
Race		
White	Ref	
Black	0.97 (0.79−1.05)	0.43
Native American	0.61 (0.42−0.90)	0.01
Asian	0.93 (0.79−1.09)	0.38
Other	1.13 (0.90−1.42)	0.30
Charlson comorbidity index		
0	Ref	
1	0.98 (0.93−1.03)	0.47
2	0.94 (0.87−1.02)	0.16
Distance from treatment center (miles)		
≤5.4	Ref	
>5.4−12.5	1.09 (0.98−1.11)	0.22
>12.5−31.0	1.08 (1.01−1.15)	0.03
>31.0	1.28 (1.20−1.36)	<0.01
Income 2008−12		
≥63,000	Ref	
≥47,999−62,999	0.98 (0.92−1.04)	0.49
≥38,000−47,999	0.91 (0.85−0.98)	0.02
<38,000	0.87 (0.80−0.96)	<0.01
Education attainment[a]		
<7%	Ref	
7−12.9%	1.03 (0.97−1.10)	0.34
13−20.9%	1.02 (0.95−1.11)	0.57
>21%	0.99 (0.91−1.09)	0.90
Insurance		
Private insurance	Ref	
Not insured	1.05 (0.93−1.18)	0.46
Medicaid	1.06 (0.96−1.17)	0.24
Medicare	0.87 (0.83−0.91)	<0.01
Other government	0.79 (0.64−0.97)	0.03
Hospital type		
Community Cancer Program	Ref	
Academic/Research Program	1.58 (1.43−1.74)	<0.01
Comprehensive Community Cancer Program	0.96 (0.87−1.05)	0.36
Integrated Network Cancer Program	1.11 (0.99−1.24)	0.08
Surgical modality		
Open	Ref	
Robotic	0.73 (0.69−0.77)	<0.01
Laparoscopic	0.63 (0.60−0.66)	<0.01
Clinical stage T		
1	Ref	
2	4.70 (4.45−4.96)	<0.01
3	5.93 (5.60−6.26)	<0.01
4	7.90 (6.53−9.56)	<0.01
Clinical positive lymph node		
cLN-	1.00	
cLN+	18.68 (16.62−21.00)	<0.01

[a] Number of adults in the patient's zip code who did not graduate from high school.
CI = confidence interval; cLN- = clinical negative lymph node; cLN+ = clinical positive lymph node; OR = odds ratio.

Table 4
Linear model for the association between great circle distance in miles and hospital type in the lymph node dissection population

Hospital type	β (95%CI) miles
Academic/Research	0
Community Center Program	38.0 (46.0, 30.0)
Comprehensive Community Center	29.9 (34.0, 25.8)
Integrated Network	26.0 (32.4., 19.5)

CI = confidence interval.

nodes on preoperative imaging is the most commonly used surrogate physicians have in determining cLN status, Capitano et al. investigated factors related to the correlation between cLN and pLN status [13]. They showed that as clinical tumor size increases, the probability of correlation between cLN and pLN status increases. It also demonstrated that patients with positive cLN and metastasis at the time of diagnosis were predictors of positive pLN [13]. Gershman et al. expanded on these findings and explored the predictive value of features from radiographic images in order to identify pN1 disease at the time of LND [20]. The study found that factors predictive of pN1 disease included the size of the retroperitoneal lymph nodes and evidence of perinephric/sinus fat invasion on CT imaging. Babaian et al. looked at other preoperative clinical factors that can predict positive pLN via a nomogram including lactate dehydrogenase, cLN status, local symptoms, and performance status [21]. Our results echoed similar trends by Connolly et al. who explored the relationship between preoperative CT imaging with pLN status [22]. They found preoperative CT imaging to have a higher NPV than PPV regarding pLN status. However, their study categorized lymph node status subjectively instead of objectively [22].

The reason why more patients in our cohort across all cT stages with no evidence of lymphadenopathy received LND compared to those with evidence of LND remains unclear. One possible explanation is that the LND is performed for financial benefit to the surgeon and that a "regional" LND is performed for staging as well as billing purposes [23]. An analysis of billing codes for LND is needed to see if there is a RVU/dollar benefit for the procedure. Other potential explanations include surgeon preference or habit (LND is routinely done during prostatectomy or radical cystectomy). The most recent AUA guideline for LND indications is based on expert opinion, which might not be shared by the majority practitioners across country. Another possible explanation is a selection bias inherent to retrospective data where the number of patients who received a LND and were cLN positive were smaller compared to the patients who did not receive a LND [6].

Prospective studies are needed to determine the appropriate triggers for LND. Other studies have also had substantial proportions of patients receiving LND at the time of surgery ranging from 24%−34% [18,24,25]. While

Table 5
Multivariable logistic regression model for the association between lymph node dissection receipt in patients with nonmetastatic RCC who were cLN negative (n = 106,370)

Variable	n (%)	OR (95% CI) LND	P value
Sex			
Female	40,351 (38)	Ref	0.31
Male	66,019 (62)	0.97 (0.93−1.02)	
Race			
White	89,193 (85)	Ref	
African American	12,600 (12)	0.92 (0.85−0.99)	0.06
Native American	531 (0.5)	0.59 (0.40−0.87)	0.02
Asian	2,080 (2)	0.95 (0.81−1.11)	0.34
Other	922 (0.9)	1.16 (0.92−1.46)	0.38
Charlson comorbidity index			
0	72,512 (68)	Ref	
1	25,228 (24)	0.98 (0.93−1.04)	0.51
2	8,630 (8)	0.97 (0.89−1.05)	0.11
Distance from treatment center (miles)			
≤5.4	27,018 (25)	Ref	
>5.4−12.5	26,512 (25)	1.04 (0.98−1.11)	0.28
>12.5−31.0	26,417 (25)	1.07 (1.00−1.14)	0.05
>31.0	26,423 (25)	1.22 (1.14−1.30)	<0.01
Insurance			
Private insurance	49,206 (47)	Ref	
Not insured	3,498 (3)	1.05 (0.93−1.18)	0.42
Medicaid	6,066 (6)	1.05 (0.95−1.16)	0.17
Medicare	44,869 (43)	0.92 (0.87−0.98)	0.03
Other government	1,404 (1)	0.78 (0.63−0.97)	0.04
Hospital type			
Community Cancer Program	6,802 (7)	Ref	
Academic/Research Program	42,573 (42)	1.58 (1.43−1.74)	<0.01
Comprehensive Community Cancer Program	40,620 (40)	0.95 (0.86−1.05)	0.51
Integrated Network Cancer Program	10,915 (11)	1.10 (0.98−1.24)	0.88
Surgical modality			
Open	42,465 (40)	Ref	
Robotic	32,436 (30)	0.73 (0.69−0.78)	<0.01
Laparoscopic	31,469 (30)	0.60 (0.59−0.66)	<0.01
Clinical stage T			
1	80,707 (76)	Ref	
2	15,013 (14)	4.87 (4.61−5.14)	<0.01
3	9,572 (9)	6.33 (5.97−6.72)	<0.01
4	485 (0.5)	11.10 (9.13−13.49)	<0.01

CI = confidence interval; OR = odds ratio.

conventional imaging techniques continue to improve and novel modalities are developed, additional exploration will be needed to determine the optimal method for RCC clinical staging. As our data illustrates, cLN staging plays an important factor in receiving a LND. Improvement in imaging for RCC will help decide which patients need a LND and those who do not. Prospective trials will also need to evaluate the impact of LND on staging and survival now that adjuvant therapy has been approved for RCC [26−28]. To date there is only one randomized trial examining the impact of LND on survival which showed no benefit [4]. Finally, in this cohort, a median of 3.0 (IQR = 6.0) nodes were extracted during LND. However, it is unknown what template was used for LND. Prospective studies need to address a consensus on a template for LND. Various templates have been described, but a standardized LND would allow consistency in surgical technique and allow for comparisons of nodal yield and impact of LND across institutions [17].

This study has several limitations inherent to the NCDB, a hospital registry database. First, it is difficult to elucidate what approach was used to identify cLN status in patients captured by the NCDB. The NCDB does not identify the imaging modality used by physicians in the database. Additionally, while the NCDB captures approximately 70% of patients with cancer across various hospital environments, it may not represent all patients with RCC across the country [15]. Similarly, residual error in our estimates may still exist due to unavailable and unmeasured confounders. For example, coding errors may be possible within the NCDB

in terms of cLN and pLN status. The source documents for determining these classifications are different, which should minimize this type of error. Lastly, the NCDB cannot elucidate the extent of LND performed at the time of surgery for RCC as it captures patients from a wide array hospital environments and surgeons. In spite of these limitations, the NCDB still provides very useful information because it represents a large cancer patient population from a wide geographic area across multiple institutions. Therefore, findings from our study are more likely to reflect contemporary practice. In order to examine reporting bias and present stronger results, a 1-to-1 propensity score matching was performed revealing minimal differences in those patients who would receive a LND. Further studies will need to answer the "who, when, and how much" for LND in the management of RCC. Our results provide a foundation for future endeavors to determine the utility of LND for clinical staging and survival in patients with nonmetastatic RCC.

5. Conclusions

Within the NCDB, current practice patterns show more patients received a LND who were cLN negative compared to patients who were cLN positive, which is incongruous with the most recent AUA guideline. A follow-up study will be needed to see if future practice patterns are influenced by this most recent "expert opinion" guidance. Amongst the patients who received a LND, those who were cLN negative were highly likely to be pLN negative (94%), while those who are cLN positive had a 74% likelihood of being pLN positive. Nevertheless, treatment center type, distance to treatment center, cLN status, and cT stage were important factors for LND receipt in this NCDB cohort. Additional investigation is needed to determine how clinical staging can best select the RCC patient population most likely to benefit from LND.

Disclosure of interest

No potential conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2019.06.003.

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