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Factors and Outcomes Contributing to Pelvic Lymph Node Dissection in Non-Muscle Invasive Bladder Cancer

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Background

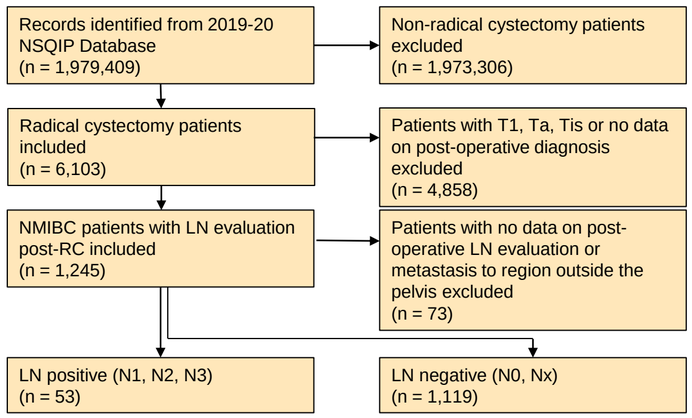
Bladder cancer represents the 6th most common for men and is classified into muscle-invasive bladder cancer (MIBC) and non-muscle-invasive bladder cancer (NMIBC).[1] NMIBC (T1, Ta, Tis), accounting for approximately 75% of new bladder cancer diagnoses, is limited to the mucosa, submucosa, and lamina propria.[2] Studies have approximated the rate of recurrence in NMIBC between 50 - 70%, which sometimes progresses to muscle invasive disease.[3]

Management of NMIBC ranges from surveillance, intravesical chemotherapy to radical cystectomy (RC) and is dependent upon the TNM staging and grading of the tumor.[4] Clinically, staging is determined via imaging, physical exam, and histology on transurethral resection of bladder tumor (TURBT), while pathologic grading is determined via radical cystectomy and pelvic lymph node dissection (PLND).[5]

PLND has been shown to have a therapeutic benefit in localized bladder cancer when done in conjunction with RC, in addition to diagnostic and therapeutic elements.[6] While the relationship between PLND and MIBC has been studied extensively, the role of lymph node (LN) dissection during RC for NMIBC remains unclear, with few studies and conflicting results.[6,7,8] Furthermore, although lymph node metastasis has been found to occur in up to 16.2% of NMIBC patients, its reported that nearly half have insufficient PLND during RC and 16.6% have no PLND done at all.[9,7] The aim of this data analysis is to determine the predictive factors and outcomes for LN positive patients undergoing PLND with RC in NMIBC.

Methods

Our data source was the National Surgical Quality Improvement Program (NSQIP), a HIPAA compliant database which consists of de-identified patient data from 706 participating hospital institutions including 273 variables on 1,076,441 cases in 2019 and variables on 902,968 cases in 2020 based on Current Procedural Terminology (CPT) code.



The data was analyzed using MedCalc® statistical software. For continuous variables, t-test was used to find significant differences. For categorical variables, Chi Square test was used to find significant differences. Statistical significance was set at P-value < 0.05. Patient characteristics and postoperative outcomes are outlined in Table 1. Receiver operating characteristic (ROC) analysis was performed to determine optimal number of lymph nodes (Figure 1).

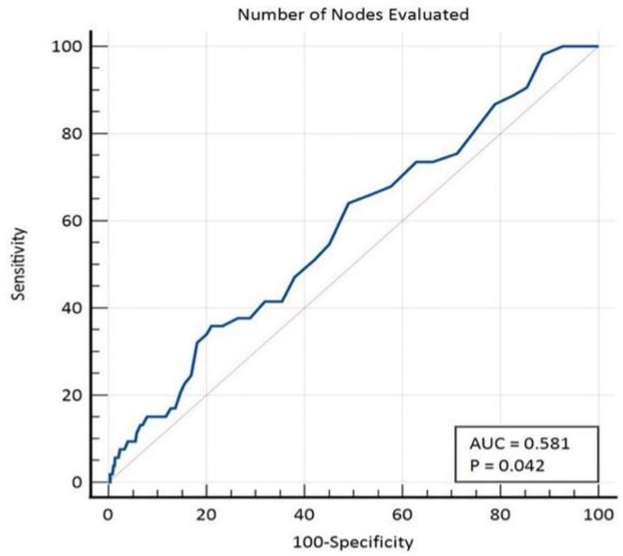
Results

Table 1. *Patient Characteristics and Postoperative Outcomes, Lymph Node Positive vs. Lymph Node Negative*

	Total Cohort N = 1171		Lymph Node Positive N = 53		Lymph Node Negative N = 1118		P Value
Patient Demographics:							
Mean Age in Years (Range)	67.6	(30–89)	67.6	(37–79)	68.8	(30–89)	
Male Gender (%)	919	(78.5%)	40	(75.5%)	879	(78.6%)	
Non-Caucasian Race (%)	294	(25.1%)	18	(34.0%)	276	(24.7%)	
Hispanic Ethnicity (%)	36	(3.1%)	1	(1.9%)	35	(3.1%)	
Preoperative Considerations:							
Pre-op ASA Classification Greater than 3 (%)	903	(76.7%)	47	(88.7%)	856	(76.6%)	
Preoperative Non-Functional Health Status (%)	14	(1.2%)	0	(0.0%)	14	(1.3%)	
Prior Pelvic Surgery (%)	569	(48.6%)	29	(54.7%)	540	(48.3%)	
Prior Pelvic Radiotherapy (%)	80	(6.8%)	3	(5.7%)	77	(6.9%)	
Chemotherapy (within 90 days of surgery) (%)	380	(32.5%)	31	(58.5%)	349	(31.2%)	P<0.01
Comorbidities:							
Current Smoker (within past year) (%)	228	(19.5%)	11	(20.8%)	217	(19.4%)	
Diabetes Mellitus Treated with Insulin (%)	946	(80.8%)	44	(83.0%)	902	(80.7%)	
Hypertension (Treated with Medication) (%)	697	(59.5%)	28	(52.8%)	669	(59.8%)	
Dyspnea (%)	64	(5.5%)	5	(9.4%)	58	(5.2%)	
Bleeding Disorder (%)	31	(2.6%)	3	(5.7%)	28	(2.5%)	
Outcome Variable:							
Total Operation Time (Minutes) (Range)	332.6	(90–765)	351.4	(172–603)	331.7	(90–765)	
Length of Hospital Stay (Days) (Range)	7.0	(0–29)	7.3	(2–25)	7.0	(0–29)	
Patient Requiring Bleeding Transfusion (%)	250	(21.3%)	16	(30.2%)	234	(20.9%)	
Organ Space Incisional Surgical Site Infection (%)	85	(7.3%)	3	(5.7%)	82	(7.2%)	
Rectal Injury (%)	10	(0.8%)	1	(1.9%)	9	(0.8%)	P=0.02
Return to Operating Room (%)	50	(4.3%)	6	(11.3%)	44	(3.9%)	P<0.01
Sepsis (%)	98	(8.4%)	4	(7.5%)	94	(8.4%)	
Urinary Tract Infection (%)	108	(9.2%)	7	(13.2%)	101	(9.0%)	
Wound Disruption (%)	23	(2.0%)	3	(5.7%)	20	(1.8%)	P=0.04

P Value represents T-Test for continuous variables and Chi-Square for categorical variables.
ASA = American Society of Anesthesiologists

Figure 1*. ROC curve associated with criteria of >16 lymph nodes dissected. Area under curve (AUC) = 0.581 (95% CI = 0.553 – 0.610) and P Value = 0.04.*



The total rate of LN involvement was 4.53%. In the LN positive group, N1, N2, N3 groups were distributed, 54.7%, 30.2%, 15.1%. The average number of LNs evaluated were 22.8 (LN positive) vs.18.9 (LN negative). Although not statistically significant, the LN positive group was younger (67.6 vs. 68.8), more likely to be a current smoker (20.8% vs. 19.4%), and diagnosed with diabetes mellitus treated with insulin (83.0% vs. 80.7%), dyspnea (9.4% vs. 5.2%), and a bleeding disorder (5.7% vs. 2.5%).

LN positive patients were significantly more likely to have undergone chemotherapy within 90 days of surgery (58.55% vs. 31.2%, p < 0.01). LN positive patients were more likely to undergo rectal injury (1.9% vs. 0.8%, p = 0.02), return to the operating room (11.3% vs. 3.9%, p < 0.01), and experience wound disruption (5.7% vs. 1.8%, p = 0.04). Other postoperative outcomes were not statistically significant. ROC analysis demonstrates that 50% of lymph node diagnoses were made with a PLND of at least 16 LNs.

Discussion

- While PLND for MIBC has shown accurate nodal staging, decreased local recurrence, and higher survival rates, the role of PLND in NMIBC is typically more diagnostic; yet given the frequency of LN metastasis in NMIBC, this role should be reconsidered.[10,11,8]
- 29% of patients diagnosed with MIBC or NMIBC have pathologically node confirmed metastasis.[12] Staging for NMIBC is important for predicting morbidity and mortality, and thus sufficient PLND is essential for prognosis.
- Our findings of statistically significantly higher rates of rectal injury, wound disruption, and return to the operating room in LN positive patients may be explained by the increase in operating time needed to complete a more thorough PLND and the increased risks of complications that arise such as lymphocele formation, thromboembolic events and direct injury to surrounding structures.[13]
- There remains disagreement as to the ideal anatomical template and number of nodes needed in PLND.[14] Some surgeons take only internal and external iliac LNs, while others dissect all nodes between the aortic bifurcation, common iliac vessels, genitofemoral nerves, circumflex iliac veins, and internal iliac vessels, and sometimes even beyond.[15-19]
- In MIBC, ≥9 LNs were required to increase likelihood of accurate staging and improve patient outcomes.[20] Our findings suggest that in NMIBC, at least 16 LNs should be sampled.
- Even if templates are followed precisely, the potential of unidentified LN outsides the defined region exists.[21-23] Ultimately, consistency in dissection technique is likely more important than total LN count in achieving improved outcomes.[17]

Conclusion

Recent research demonstrates survival benefit in LN dissection in patients with NMIBC, particularly for patients with cTis or T1 staging. Nearly half of NMIBC patients undergoing RC do not receive an adequate PLND, despite an association with increased overall survival. The present study investigates predictive factors and outcomes for LN positive patients with NMIBC. Further research is needed to advance our understanding of PLND's role in the management of NMIBC.

References

1. International Agency for Research on Cancer. Global Cancer Observatory. Accessed 3/8/22.
2. Cumberbatch MGK et. al. (2018) Eur Urol. 74 (6):784-795.
3. Sylvester RJ et. al. (2006) Eur Urol. 49:466-5.
4. Slovacek H et. al. (2021) Curr Oncol Rep. 23(9):105.
5. Chang SS et. al. (2016). J Urol. 196(4)1021-1029.
6. Perera M et. al. (2018). Nat Rev Urol. 15(11):686-692.
7. Lenis AT et. al. (2020). Urol Oncol. 38(10)796.e7-796.e14
8. Khanna A et. al. (2022). J Urol. 20(3):551-558.
9. Fritsche HM et. al. (2009). Eur Urol. 57(2):300-309.
10. Dat A et. al. (2019). Trans Cancer Res. 8(Suppl2):S180-S182.
11. Nakagawa T. (2020). Int J Urol. 28(1):7-15
12. Moschini M et al. (2018). Urol Oncol. 36(6):307.e9-307.e14.
13. Herr HW et. al. (2002). J Urol. 167(3):1295-1298.
14. Packiam VT et. al. (2020) Transl Androl Urol. 9(6):3082-3093.
15. Bruins HM et. al. (2014) Eur Urol. 66(6):1065-1067.
16. Herr H. et. al. (2004). J Urol. 171(5):1823-1828.
17. Dorin RP et. al. (2011). Eur Urol. 60(5):946-52.
18. Bi L et. al. (2014). BJU Int. 113(5b):E39-48.
19. Stein JP. (2006). Urol Oncol. 24(4):349-55.
20. Loeb S et. al. (2010). Rev Urol. 12(1):20-24.
21. Leissner J et. al. (2004) J Urol. 171(1):139-144.
22. Steven K et. al. (2007) J Urol. 178(4 pt1):1218-1224.
23. Dangle PP et. al. (2010). J Urol. 183(2):449-503.