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Impact of pelvic lymph node dissection on survival outcomes in non-muscle invasive bladder cancer: a multicenter retrospective study

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This multicenter, retrospective study evaluated the impact of pelvic lymph node dissection (PLND) on survival outcomes in non-muscle invasive bladder cancer (NMIBC) patients undergoing radical cystectomy (RC) and identified factors associated with upstaging. A total of 544 NMIBC patients who underwent RC with or without PLND between 2019 and 2024 were analyzed. Survival outcomes, including cancer-specific survival (CSS) and recurrence-free survival (RFS), were compared using Kaplan-Meier analysis and Cox proportional hazards models, while factors associated with upstaging were examined through logistic regression. Of the 544 patients, 509 (93.6%) were staged as cT1, and 412 (75.7%) underwent PLND. Upstaging occurred in 193 patients (35.5%), with pathological stages distributed as pT1 (50.0%), pT2 (20.8%), pT3 (11.2%), and pT4 (3.5%). Among patients who underwent PLND, 29 (7.0%) had positive lymph nodes. PLND was associated with improved RFS (5-year: 84.3% vs. 71.5%; adjusted hazard ratio [HR] = 0.33, 95% confidence interval [CI]: 0.20–0.56, $p < 0.001$) but did not significantly impact CSS (5-year: 86.5% vs. 81.6%; adjusted HR = 0.57, 95% CI: 0.32–1.02, $p = 0.06$). Lymph node positivity was linked to the worst prognosis. cT1 tumors, histological subtypes, and PLND were significant predictors of upstaging. In patients with cT1 tumors or histological subtypes, repeat transurethral resection is recommended to obtain more precise staging, which may inform further therapeutic decisions. While PLND is not routinely recommended for all NMIBC patients, it may be considered in those with high-risk features, particularly cT1 tumors or histological subtypes.

Keywords Non-muscle invasive bladder cancer, Pelvic lymph node dissection, Radical cystectomy, Outcomes, Upstaging

Non-muscle invasive bladder cancer (NMIBC) accounts for approximately 75% of all newly diagnosed bladder cancer cases[1]. Despite its relatively favorable prognosis compared to muscle-invasive bladder cancer (MIBC), NMIBC presents significant challenges due to its high recurrence and progression rates. Intravesical Bacillus Calmette-Guérin (BCG) therapy has been shown to reduce recurrence rates by approximately 30% compared to transurethral resection (TUR) alone, and also delays disease progression[2]. However, up to 30% of patients with clinical T1 stage disease ultimately experience disease progression to muscle-invasive stages, necessitating radical cystectomy (RC)[3].

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Bilateral pelvic lymph node dissection (PLND) during RC has long been considered a standard practice for patients with MIBC, providing essential information on lymph node involvement (pN stage) and offering potential therapeutic benefits through the removal of micrometastases[1]. Landmark studies have shown that extending the PLND template increases nodal-positivity detection by approximately 33% compared to limited dissection and doubles the detection rate of occult metastases (26% vs. 13%), translating into a 10–20% absolute improvement in 5-year recurrence-free survival (RFS) among patients with pT2–pT3 MIBC[4,5]. However, the role of PLND in NMIBC remains controversial. A retrospective cohort study suggested that adequate PLND, defined by the authors as removal of at least 10 lymph nodes, may improve overall survival (OS)[6], although this was not supported by Lin et al., who found no RFS benefit[7]. Another study reported that this potential survival benefit was particularly evident in patients with cT1 disease[8]. In contrast, recent prospective data have shown no clear oncologic advantage and have highlighted increased postoperative morbidity[9]. The role of PLND and the clinical significance of lymph node yield in NMIBC remain to be clarified.

In this multicenter study, we aim to evaluate the impact of PLND on cancer-specific survival (CSS) and RFS, as well as to identify key factors associated with upstaging in NMIBC patients undergoing RC.

Materials and methods

Ethics statement

This multicenter study was approved by the Medical Ethics Committee of the Second Hospital of Tianjin Medical University (Approval No. Kesh[2024] No. 066). Data-sharing agreements were established with all participating institutions prior to the initiation of the study. All data were de-identified before analysis, and strict protocols for patient confidentiality and data protection were followed throughout the study. As a retrospective analysis, written informed consent was waived by the Medical Ethics Committee of the Second Hospital of Tianjin Medical University. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Study population

This multicenter retrospective study included 544 patients from three participating centers. Inclusion criteria were: (1) a clinical diagnosis of NMIBC (cTa, Tis, or cT1) based on TUR pathology, with confirmation of the presence of muscularis propria in the specimen; (2) available re-TUR results when indicated, with clinical staging determined by the highest pathological stage; (3) preoperative imaging excluding muscle-invasive or metastatic disease; and (4) subsequent treatment with RC. Exclusion criteria were: (1) prior neoadjuvant therapy; (2) non-urothelial carcinoma; (3) metastatic disease; (4) failure to undergo RC or RC performed more than 3 months after TUR; and (5) incomplete medical records. The choice of surgical approach (laparoscopic or robotic) was made based on patient and surgeon preferences. PLND was performed in cases with radiologically suspicious nodes on preoperative imaging or when palpable nodal abnormalities were encountered intraoperatively. In the absence of such findings, the decision to proceed with lymph node dissection was based on the operating surgeon's discretion, taking into account institutional practices, imaging results, and patient-specific risk factors. Adjuvant chemotherapy with a platinum-based regimen was administered to patients with pT ≥ 3 or pN + disease.

Clinicopathologic data and survival outcomes

Clinicopathologic data, oncological follow-up, and survival status, including the underlying cause of death, were collected. All surgical specimens were processed according to standard pathological procedures. Tumor staging was performed based on the 2017 American Joint Committee on Cancer (AJCC) TNM staging system[10]. Tumor grading followed the 2022 World Health Organization (WHO) grading system[11]. Histological subtypes were defined as UC exhibiting any variant differentiation (e.g., squamous, glandular, micropapillary) according to the 2022 WHO classification[11]. Histological subtypes were determined by the TUR pathology.

CSS was defined as the time from RC to either cancer-specific death or the date of the last follow-up. The cause of death was determined by the attending physician based on medical chart review and death certificates[12]. RFS was defined as the time from RC to the first occurrence of recurrence (locoregional or distant) or the date of the last follow-up. Upstaging was defined as the transition from clinical Ta/Tis/T1 to pathological T ≥ 2 or N+.

The primary endpoint was CSS, comparing patients who underwent RC with PLND versus those who did not (no-PLND). The secondary endpoints included RFS, the upstaging rate, and factors associated with upstaging prior to RC.

Follow-up protocol

Patients were followed according to institutional protocols. Typically, postoperative surveillance included physical examination, laboratory tests, and radiographic evaluation (chest and abdominal CT scans). Surveillance was conducted at 3- to 4-month intervals during the first year, semiannually for the next 4 years, and annually thereafter.

Statistical analyses

The clinicopathological characteristics were compared using the chi-squared or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Kaplan-Meier curves were used to estimate survival outcomes for CSS and RFS, with differences between groups compared using the log-rank test. Cox proportional hazards models were employed to evaluate associations between clinicopathological variables and survival outcomes. Logistic regression was utilized to identify factors associated with upstaging prior to RC. Variables with statistical significance in univariate analysis were included in the multivariable models. In addition, gender was included in the multivariable logistic regression model for upstaging due to its borderline significance in univariate analysis. All statistical analyses were performed using R version 4.2.2. A two-sided p-value of less than 0.05 was considered statistically significant.

Results

Clinical and pathological characteristics

The clinical and pathological characteristics of the 544 patients included in the study are summarized in Table 1. The median age was 69 years (interquartile range [IQR]: 63–75), with 82% of patients being male, and 93.6% classified as cT1 stage. The median number of days from TUR to RC was 38 days (IQR: 26–55). A total of 75.7% of patients underwent PLND. There were no significant differences in baseline characteristics between the PLND and no-PLND groups prior to RC ($p > 0.05$). The pathological T-stages were as follows: pT1 in 50.0%, pT2 in 20.8%, pT3 in 11.2%, and pT4 in 3.5%. A significant difference was observed between the PLND and no-PLND groups in terms of pT stage ($p = 0.017$). In the PLND group, the median number of lymph nodes dissected was 14 (IQR: 8–21), with 7.0% of patients having positive lymph nodes (pN+). (Table 1).

Predictors of upstaging

A total of 193 patients (35.5%) experienced upstaging. Multivariable logistic regression analysis revealed that cT1 stage (OR: 2.74, 95% CI: 1.03–7.26, $p = 0.026$), the presence of histological subtypes (OR: 1.90, 95% CI: 1.23–2.93, $p = 0.004$), and PLND (OR: 1.67, 95% CI: 1.07–2.61, $p = 0.021$) were significantly associated with upstaging to pT ≥ 2 or pN + status at the time of RC (Table 2). Model calibration was assessed using a calibration plot, which demonstrated good agreement between predicted and observed probabilities (Fig. S1).

Variable	Total ($n = 544$)	No-PLND ($n = 132$)	PLND ($n = 412$)	*p* value
Median age, yr (IQR)	69 (63–75)	69 (64–74)	69 (63–75)	0.760
Gender, n (%)				0.942
Female	98 (18.0)	23 (17.4)	75 (18.2)	
Male	446 (82.0)	109 (82.6)	337 (81.8)	
Clinical T-stage, n (%)				0.593
cTa	16 (2.9)	5 (3.8)	11 (2.7)	
cTis	19 (3.5)	6 (4.5)	13 (3.2)	
cT1	509 (93.6)	121 (91.7)	388 (94.2)	
Tumor grade, n (%)				0.466
Low	61 (11.2)	12 (9.1)	49 (11.9)	
High	483 (88.8)	120 (90.9)	363 (88.1)	
Concomitant CIS, n (%)				0.439
Absent	447 (82.2)	105 (79.5)	342 (83.0)	
Pesent	97 (17.8)	27 (20.5)	70 (17.0)	
Lymphovascular invasion, n (%)				0.084
Absent	463 (85.1)	119 (90.2)	344 (83.5)	
Present	81 (14.9)	13 (9.8)	68 (16.5)	
Histological subtypes, n (%)				0.928
Absent	425 (78.1)	104 (78.8)	321 (77.9)	
Present	119 (21.9)	28 (21.2)	91 (22.1)	
Pathological T-stage, n (%)				**0.017***
pT0	44 (8.1)	6 (4.5)	38 (9.2)	
pTa	3 (0.6)	1 (0.8)	2 (0.5)	
pTis	32 (5.9)	8 (6.1)	24 (5.8)	
pT1	272 (50.0)	82 (62.1)	190 (46.1)	
pT2	113 (20.8)	24 (18.2)	89 (21.6)	
pT3	61 (11.2)	6 (4.5)	55 (13.3)	
pT4	19 (3.5)	5 (3.8)	14 (3.4)	
Median removed lymph nodes (IQR)	-	-	14 (8–21)	-
Pathological N-stage, n (%)				-
pN0	383 (70.4)	-	383 (93.0)	
pN1	19 (3.5)	-	19 (4.6)	
pN2	10 (1.8)	-	10 (2.4)	
pNx	132 (24.3)	132 (100.0)	-	

Table 1. Clinicopathological characteristics of NMIBC patients who underwent RC, stratified by PLND and No-PLND. PLND = Pelvic lymph node dissection; CIS = Carcinoma in situ; * $p < 0.05$; No p-values were calculated for Pathological N-stage due to the absence of pNx cases in the PLND group and pN0, pN1, pN2 cases in the No-PLND group.

Univariate analysis	OR	95% CI	*p* value
Age (continuously coded)	0.99	0.98–1.01	0.514
Gender			
Female versus male	1.54	0.99–2.41	0.056
Clinical T-stage			
cT1 versus cTa/cTis	3.51	1.34–9.21	**0.011***
Tumor grade			
High versus low	1.48	0.82–2.68	0.19
Concomitant CIS			
Present versus absent	0.69	0.43–1.12	0.135
Lymphovascular invasion			
Present versus absent	1.98	1.23–3.18	**0.005****
Histological subtypes			
Present versus absent	2.14	1.41–3.23	< **0.001*****
PLND			
Present versus absent	1.72	1.12–2.66	**0.014***

Multivariate analysis	OR	95% CI	*p* value
Gender			
Male	Reference		
Female	1.47	0.93–2.33	0.099
Clinical T-stage			
cTa/cTis	Reference		
cT1	2.74	1.03–7.26	**0.026***
Lymphovascular invasion			
Absent	Reference		
Present	1.43	0.87–2.37	0.164
Histological subtypes			
Absent	Reference		
Present	1.90	1.23–2.93	**0.004****
PLND			
Absent	Reference		
Present	1.67	1.07–2.61	**0.021***

Table 2. Univariate and multivariate logistic regression analysis of upstaging during radical cystectomy. OR = Odds ratio; CI = Confidence interval; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Predictors of cancer-specific survival and recurrence-free survival

The median follow-up time was 32.2 months (range: 1.4–64.2). A total of 37 patients (9.0%) in the PLND group and 17 patients (12.8%) in the no-PLND group died from bladder cancer ($p = 0.241$), while recurrence occurred in 44 patients (10.7%) and 23 patients (17.4%), respectively ($p = 0.048$). Patterns of recurrence are detailed in Table S1. Kaplan-Meier curves showed that the 5-year CSS rates for the PLND and no-PLND groups were 86.5% and 81.6%, respectively (adjusted HR = 0.57, 95% CI: 0.32–1.02, $p = 0.06$), while the 5-year RFS rates were 84.3% versus 71.5% (adjusted HR = 0.33, 95% CI: 0.20–0.56, $p < 0.001$) (Fig. 1A and B). The pNx stage exhibited CSS and RFS outcomes slightly worse than pN0, while pN + patients had the worst CSS and RFS (Fig. 1C and D). Similarly, pT2 patients had CSS and RFS rates comparable to those with pT ≤ 1, whereas patients with pT ≥ 3 had the worst CSS and RFS outcomes (Fig. 1E and F).

In univariate Cox regression analysis, pathological T-stage and N-stage were significantly associated with CSS (Table 3). Multivariable analysis demonstrated that pN0 (HR: 0.47, 95% CI: 0.25–0.86, $p = 0.015$) was associated with better CSS, while pN+ (HR: 2.82, 95% CI: 1.04–7.62, $p = 0.041$) was associated with poorer CSS (Table 3).

For RFS, univariate Cox regression analysis identified the presence of histological subtypes, pathological T-stage, and N-stage as significant predictors (Table 4). Multivariable analysis showed that compared to pT ≤ 1, pT2 (HR: 2.08, 95% CI: 1.02–4.25, $p = 0.044$) and pT ≥ 3 (HR: 9.37, 95% CI: 4.85–18.10, $p < 0.001$) were associated with poorer RFS (Table 4).

In the PLND group, the number of lymph nodes dissected (greater than 10 versus 10 or fewer) was not significantly associated with either CSS (HR: 0.98, 95% CI: 0.51–1.90, $p = 0.954$) or RFS (HR: 1.23, 95% CI: 0.65–2.33, $p = 0.517$).

Sensitivity analyses

Sensitivity analyses restricted to patients with histological subtypes ($n = 119$) showed findings consistent with the overall cohort, with PLND significantly improving RFS and no significant impact on CSS (Table S2 and Fig. S2).

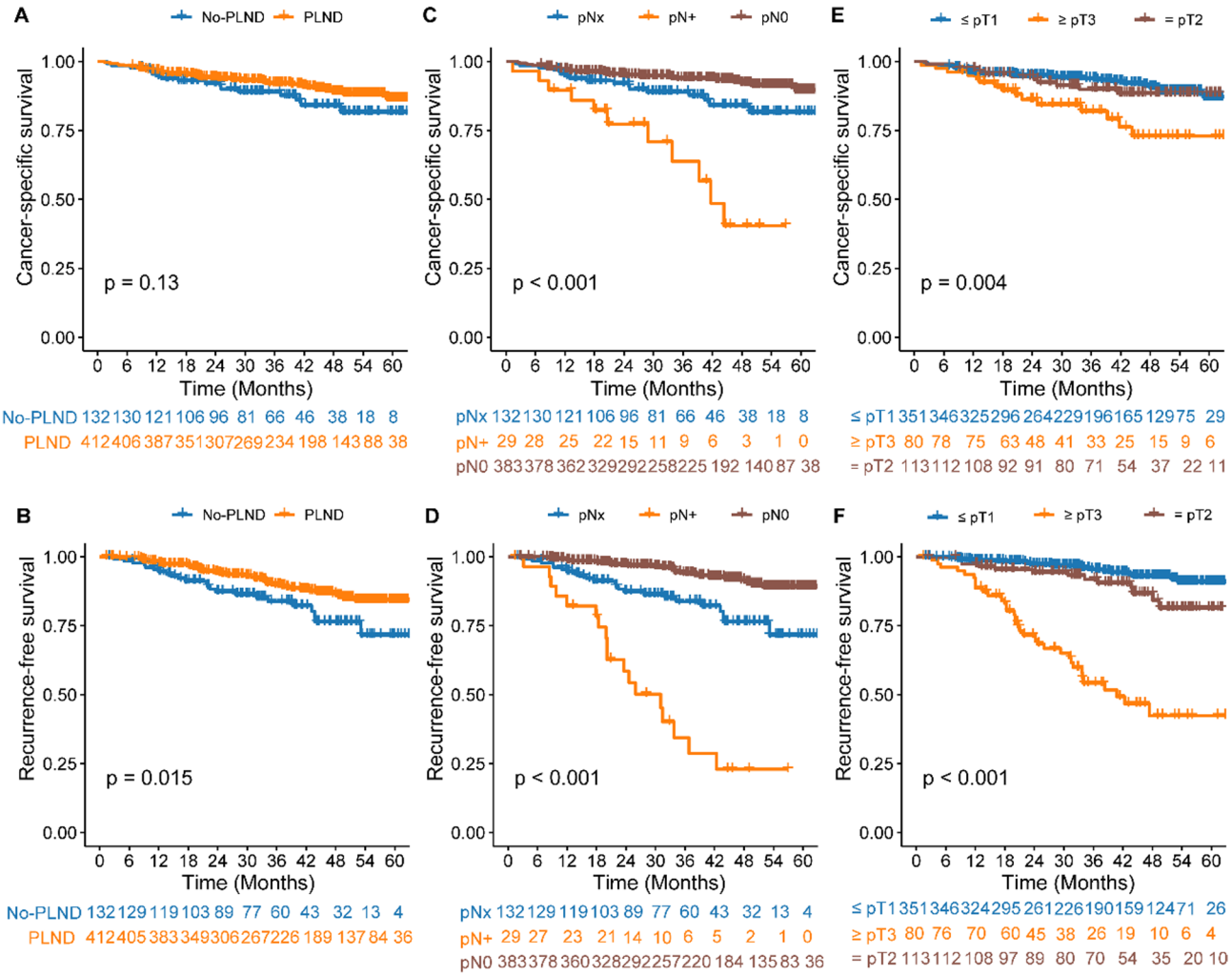

Fig. 1. Kaplan-Meier Survival Curves. **(A)** CSS by PLND status; **(B)** RFS by PLND status; **(C)** CSS by pathological N-status; **(D)** RFS by pathological N-status; **(E)** CSS by pathological T-stage; **(F)** RFS by pathological T-stage.

Discussion

In this multicenter study, we evaluated the impact of PLND on cancer-specific survival and recurrence-free survival in patients with NMIBC undergoing RC. Our findings showed that, although PLND did not significantly improve 5- year CSS (86.5% vs. 81.6%), it was associated with a significant improvement in 5- year RFS (84.3% vs. 71.5%) when compared to the non-PLND group. Further analysis revealed that patients with positive lymph nodes (pN+) had the worst CSS and RFS, whereas those with pN0 had significantly better survival, underscoring the critical role of lymph node status in prognostic assessment of bladder cancer[13]. Furthermore, PLND plays a critical role in accurately assessing lymph node status, which is essential for prognosis and guiding postoperative treatment.

The incidence of lymph node metastasis in MIBC during RC ranges from 24–43%[14–16], and PLND is considered a standard procedure in MIBC to provide more accurate pN staging and improve prognosis[1]. However, the lymph node metastasis rate in NMIBC is also non-negligible, with previous studies reporting a range of 6–19%[17]. In our study, the lymph node metastasis rate was 7%, which is consistent with prior reports. The prognosis of NMIBC with positive lymph nodes is significantly worse[18], highlighting the potential necessity of PLND in this patient population. However, the role of PLND in NMIBC prognosis remains under-researched, and results from existing studies are inconsistent. Lyu et al.[9] reported a prospective randomized controlled trial of 101 NMIBC patients, finding no survival benefit of PLND but an increased incidence of complications. In contrast, Kitamura et al.[19] suggested that PLND might offer survival benefits by removing undetected micrometastases. Similarly, Moldovan et al.[8], based on an NCDB cohort of 9,399 NMIBC patients, and Tang et al.[20], using a SEER analysis of 1,701 patients, both found that PLND improved OS in T1 but not in Ta/Tis disease.

One potential reason for these differing results could be the number of lymph nodes removed. Khanna et al.[21] found that removing more than 10 lymph nodes was associated with improved RFS, and removing more than 20 lymph nodes correlated with improved CSS and OS in NMIBC patients. Similarly, Lenis et al.[6] demonstrated that removal of ≥ 10 lymph nodes significantly improved OS in NMIBC patients. However, conflicting findings

Univariate analysis	HR	95% CI	*p* value
Age (continuously coded)	1.02	0.99–1.05	0.111
Gender			
Female versus male	0.86	0.42–1.76	0.676
Clinical T-stage			
cT1 versus cTa/cTis	1.15	0.43–3.07	0.778
Tumor grade			
High versus low	2.29	0.71–1.40	0.164
Concomitant CIS			
Present versus absent	0.92	0.45–1.89	0.826
Lymphovascular invasion			
Present versus absent	1.44	0.74–2.78	0.285
Histological subtypes			
Present versus absent	1.57	0.87–2.81	0.132
Pathological T-stage			
pT ≤ 1	Reference		
pT = 2	1.2	0.60–2.41	0.606
pT ≥ 3	2.74	1.46–5.14	**0.002****
Pathological N-status			
pNx	Reference		
pN0	0.48	0.26–0.88	**0.017***
pN+	3.73	1.74–8.00	**<0.001*****
Multivariate analysis	**HR**	**95% CI**	***p* value**
Pathological T-stage			
pT ≤ 1	Reference		
pT = 2	1.12	0.55–2.28	0.752
pT ≥ 3	1.46	0.62-0.42	0.389
Pathological N-status			
pNx	Reference		
pN0	0.47	0.25–0.86	**0.015***
pN+	2.82	1.04–7.62	**0.041***

Table 3. Univariate and multivariate cox regression analyses for prediction of CSS. CSS = Cancer-specific survival; HR = Hazard ratio; CI = Confidence interval; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

have been reported. A study spanning over 20 years found no difference in RFS between patients with ≥ 10 or < 10 lymph nodes removed[7]. In our study, the median number of lymph nodes removed in the PLND group was 14 (IQR: 8–21), and no significant correlation was found between the number of lymph nodes removed and either CSS or RFS. Some researchers argue that adherence to meticulous dissection techniques within an extended template is more critical for achieving optimal oncologic outcomes than the total number of lymph nodes removed[22].

Another factor contributing to the variation in results could be population heterogeneity. Previous studies have reported upstaging rates of 26–78% in NMIBC patients undergoing RC[17,23,24]. In our study, 193 patients (35.5%) experienced upstaging, defined as the progression from NMIBC to pT ≥ 2 or pN+. In contrast, in the randomized study by Lyu et al.[9], patients found to have MIBC at RC were excluded, and no lymph node metastases were detected in the PLND group, resulting in a more selected and lower-risk NMIBC cohort. It is well established that MIBC differs significantly from NMIBC in terms of RFS and CSS[17]. Therefore, the varying proportions of pT stages in different studies could potentially explain the divergent outcomes. Our study found that both cT1 stage and the presence of histological subtypes were significantly associated with upstaging. These findings suggest that NMIBC patients with histological subtypes may be at a higher risk of understaging during TUR and, in accordance with current guidelines[25], should be managed similarly to cT1 patients, including consideration for repeat TUR.

This study has several limitations. First, as a retrospective study, it is subject to inherent selection bias, particularly in the decision-making process for PLND, which was based on preoperative imaging findings, intraoperative assessment, and surgeon discretion rather than a standardized protocol. Second, although the study included a large multicenter cohort, variations in the quality of TUR and RC procedures across centers may have introduced confounding factors. Third, the absence of a central pathology review could have led to inter-institutional variability in pathological assessments, potentially affecting the consistency and accuracy of staging. This limitation reflects the real-world practice across different centers but may reduce uniformity. Fourth, molecular subtyping was not performed in this cohort, which may limit more refined risk stratification and prognostic evaluation. Fifth, while this study provides important real-world evidence, prospective validation

Univariate analysis	HR	95% CI	*p* value
Age (continuously coded)	1.01	0.98–1.03	0.788
Gender			
Female versus male	0.74	0.38–1.46	0.388
Clinical T-stage			
cT1 versus cTa/cTis	1.37	0.57–3.019	0.469
Tumor grade			
High versus low	1.75	0.70–4.36	0.229
Concomitant CIS			
Present versus absent	0.81	0.41–1.59	0.541
Lymphovascular invasion			
Present versus absent	1.08	0.56–2.05	0.824
Histological subtypes			
Present versus absent	1.88	1.13–3.14	**0.015***
Pathological T-stage			
pT ≤ 1	Reference		
pT = 2	2.08	1.03–4.21	**0.043***
pT ≥ 3	11	6.27–19.31	**<0.001*****
Pathological N-status			
pNx	Reference		
pN0	0.33	0.17–0.57	**<0.001*****
pN+	5.21	2.79–9.70	**<0.001*****
Multivariate analysis	**HR**	**95% CI**	***p* value**
Histological subtypes			
Absent	Reference		
Present	1.21	0.71–2.05	0.489
Pathological T-stage			
pT ≤ 1	Reference		
pT = 2	2.08	1.02–4.25	**0.044***
pT ≥ 3	9.37	4.85–18.10	**<0.001*****
Pathological N-status			
pNx	Reference		
pN0	0.25	0.14–0.44	**<0.001*****
pN+	1.03	0.49–2.16	0.929

Table 4. Univariate and multivariate cox regression analyses for prediction of RFS. RFS = Recurrence-free survival; HR = Hazard ratio. CI = Confidence interval; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

in a randomized controlled setting would be valuable to confirm these findings and minimize potential biases. Finally, the potential role of sentinel lymph node mapping[26], as a less invasive alternative to standard or extensive PLND, warrants further investigation in future studies.

Conclusions

In this multicenter cohort, PLND was significantly associated with improved RFS (HR 0.33, 95% CI 0.20–0.56, $p < 0.001$), but had no significant impact on CSS (HR 0.57, 95% CI 0.32–1.02, $p = 0.06$) in NMIBC patients undergoing RC. pN + disease was identified as an independent poor prognostic factor, highlighting the importance of accurate lymph node staging. Both cT1 stage and histological subtypes were significantly associated with upstaging, suggesting that repeat TUR may benefit selected patients. These findings indicate that PLND should be selectively considered based on patient risk profiles, particularly in those with high-risk features such as cT1 stage or histological subtypes.

Data availability

De-identified raw data are available upon reasonable request from the corresponding author.

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H.H., Z.L.W., and Y.K.Q.: Conception and design of the study, data acquisition, manuscript writing; S.W.H., K.P.J., J.M.C., J.F.D., W.C., S.L., and J.W.H.: Data acquisition, analysis, manuscript writing; J.N.G. and H.T.C.: Data acquisition, manuscript editing; C.S., Z.Z., and X.S.L.: Study support, manuscript revision.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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