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Impact of pelvic lymph node dissection on oncological outcomes in patients with clinically staged non-muscle-invasive bladder cancer undergoing radical cystectomy: A systematic review

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ABSTRACT

Introduction: In the majority of very high-risk and selected high-risk cases of clinically non-muscle-invasive bladder cancer (NMIBC), radical cystectomy (RC) may be performed. However, the necessity of pelvic lymph node dissection (PLND) in this clinical scenario is debated. The aim of this review was to evaluate how the presence and extent of PLND influence survival outcomes.

Materials and methods: A systematic literature search was performed on July 6th, 2025, without language or time restrictions. Studies were considered eligible if they compared oncological outcomes between various extents of PLND during RC for NMIBC. The primary endpoint was overall survival (OS); secondary endpoints included cancer-specific survival (CSS) and recurrence-free survival (RFS).

Results: Nine retrospective studies comprising 20,806 patients were included. Pathological upstaging to muscle-invasive disease was observed in 19.1 %–42.0 % of patients. Seven studies evaluated OS, three CSS, and four RFS. Most studies demonstrated OS benefit associated with PLND, particularly in patients with cT1 tumors. Greater lymph node yield - especially the removal of ≥ 10 or > 20 nodes - was consistently associated with improved OS. Extended PLND was linked to better CSS and RFS in several studies. However, findings for recurrence-related outcomes were heterogeneous and endpoint definitions varied.

Conclusions: PLND during RC for clinically NMIBC may be associated with improved survival, especially in patients with cT1 disease. Higher lymph node yield may further enhance oncologic benefit. These findings support the consideration of at least limited PLND during RC for clinically NMIBC. Prospective randomized studies are needed to establish definitive recommendations.

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1. Introduction

Bladder cancer (BC) is a common malignancy with the incidence of approximately 500,000 cases each year. The most frequent risk factors of BC development are age, male sex, and tobacco smoking (Lenis et al., 2020; Lenis, 2020). Non-muscle-invasive bladder cancer (NMIBC) accounts for approximately 70–75 % of newly diagnosed BC cases (EAU Guidelines, 2025; Kaufman et al., 2009; Lenis et al., 2020; Lenis, 2020). The standard initial treatment for NMIBC consists of transurethral resection of the bladder tumor (TURBT), often followed by risk-adapted intravesical therapies (EAU 2025, (Holzbeierlein, 2024). While the majority of patients can be successfully managed with bladder-sparing approaches, a clinically meaningful subset is at substantial risk of progression to muscle-invasive bladder cancer (MIBC) (EAU 2025, (Krajewski, 2022; Holzbeierlein, 2024; Brouzes, 2025). According to contemporary international guidelines, including those from the European Association of Urology (EAU) and American Urological Association (AUA), early radical cystectomy (RC) should be considered for patients with very high-risk NMIBC and for selected patients with high-risk disease who are unlikely to benefit from or have failed intravesical therapy (EAU 2025; Holzbeierlein, 2024). This recommendation is supported by evidence demonstrating inferior oncologic outcomes of delayed RC in these groups (Jäger, 2011; Pang and Noon, 2019).

Pelvic lymph node dissection (PLND) during radical cystectomy (RC) is a well-established standard of care for MIBC, where lymph node metastases are common and PLND provides crucial staging information and a potential therapeutic benefit (EAU 2025; Katims and Bochner, 2023). In contrast, the role of PLND in the context of NMIBC remains far less defined. Patients with NMIBC are generally presumed to have organ-confined disease, and the prevalence of lymph node metastases at the time of radical cystectomy is substantially lower than that observed in patients with MIBC (EAU 2025; Bruins, 2014; Singh et al., 2024). As a result, the necessity and optimal extent of PLND in this population are debated, with practice patterns varying widely.

An additional source of uncertainty in this setting is the well-documented clinical under-staging that might occur at the pathologic examination of the TURBT specimen. Several studies have reported substantial rates of pathological upstaging to muscle-invasive disease at radical cystectomy, underscoring the challenges inherent to preoperative risk stratification in this population (Ark, 2014; Shariat, 2007).

Given the absence of randomized controlled trials, the available evidence regarding PLND in NMIBC largely derives from retrospective single-center series and large administrative databases, each with inherent methodological limitations. Consequently, the true oncologic value of PLND - and the impact of its extent - in patients undergoing RC for NMIBC is not well elucidated.

That is why, we performed the first systematic review of the literature to critically assess the available evidence on the impact of PLND on survival outcomes in patients undergoing RC for clinically NMIBC. The aim of this review was to evaluate how the presence and extent PLND influences overall survival, cancer-specific survival, and recurrence-free survival in these patients.

2. Materials and methods

The review was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Page, 2021).

2.1. Evidence acquisition

We performed a systematic literature search of PubMed, Embase, and Scopus databases on July 6th, 2025, without language or time restrictions. Search terms included, but were not limited to: (radical cystectomy OR cystectomy, radical OR total cystectomy OR complete cystectomy) AND (pelvic lymph node dissection OR pelvic lymphadenectomy OR lymphadenectomy OR lymph node dissection OR PLND OR nodal dissection) AND ("non-muscle-invasive bladder cancer" OR NMIBC OR carcinoma in situ OR CIS). Only original articles were included and assessed. Case reports, abstracts and meeting reports were excluded from the analysis. The reference lists of the studies selected for full-text review were also screened for relevant articles.

2.2. Criteria of inclusion and selection of the studies

Studies were assessed for eligibility using the PICO (population, intervention, comparison, outcomes) approach. The inclusion criteria were as follows:

(P)opulation: Patients with clinically staged NMIBC who underwent RC (final pathological staging may differ).

(I)ntervention/(C)omparison: Various extents of PLND (including no PLND).

(O)utcomes: Primary - overall survival (OS). Secondary - cancer-specific survival (CSS), recurrence-free survival (RFS).

Two authors independently screened the titles and abstracts of all articles using the predefined inclusion criteria. Full-text articles were assessed by two authors to determine whether they met the inclusion criteria. Final inclusion of the studies had to be agreed to by all of the investigators. Lastly, a critical analysis and data synthesis of the selected articles has been performed.

2.3. Data extraction

A standardized data extraction form was created and used to collect: study-related data (first author, publication year, country, study design, study duration, number of patients, extent of LND, follow up period), clinicopathological data (sex, age, tumor stage and grade, lymph node yield, number of patients with pathologically confirmed positive lymph nodes, proportion of patients who received neoadjuvant (NAC) and adjuvant chemotherapy (AC)), and survival data (including 5-year OS, CSS, and RFS rates, as well as their corresponding unadjusted or adjusted hazard ratios (HRs) with 95 % confidence intervals (CIs)). For papers that did not provide HRs and 95 % CIs, data were extracted from any Kaplan-Meier curves for calculation of the HR and CI using methods described by Tierney et al. (2007).

2.4. Assessment of quality for studies included

Two reviewers independently assessed the quality of the included studies using the "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies" provided by the National Institute of Health (National Heart, nd).

The potential risk of bias, measurement bias, and others as presented in Supplementary Table 1. Studies were rated as good and poor quality, where high risk of bias translated to a rating of poor quality ("−") and low risk of bias translated to a rating of good quality ("+").

3. Results

3.1. Search results

The initial search yielded 788 records (Pubmed: 196; Embase: 533; Scopus: 59). 219 were duplicates and were removed. Next, 569 articles were screened by title and abstract analysis to identify potentially relevant articles. 555 records were excluded and the remaining 14 were sought for retrieval. All 14 full-text reports were assessed for eligibility. After an in-depth analysis, 5 more articles did not meet the inclusion criteria. Finally, 9 studies were included in this review (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025) (Fig. 1).

No study was considered fatally flawed as per the "Quality

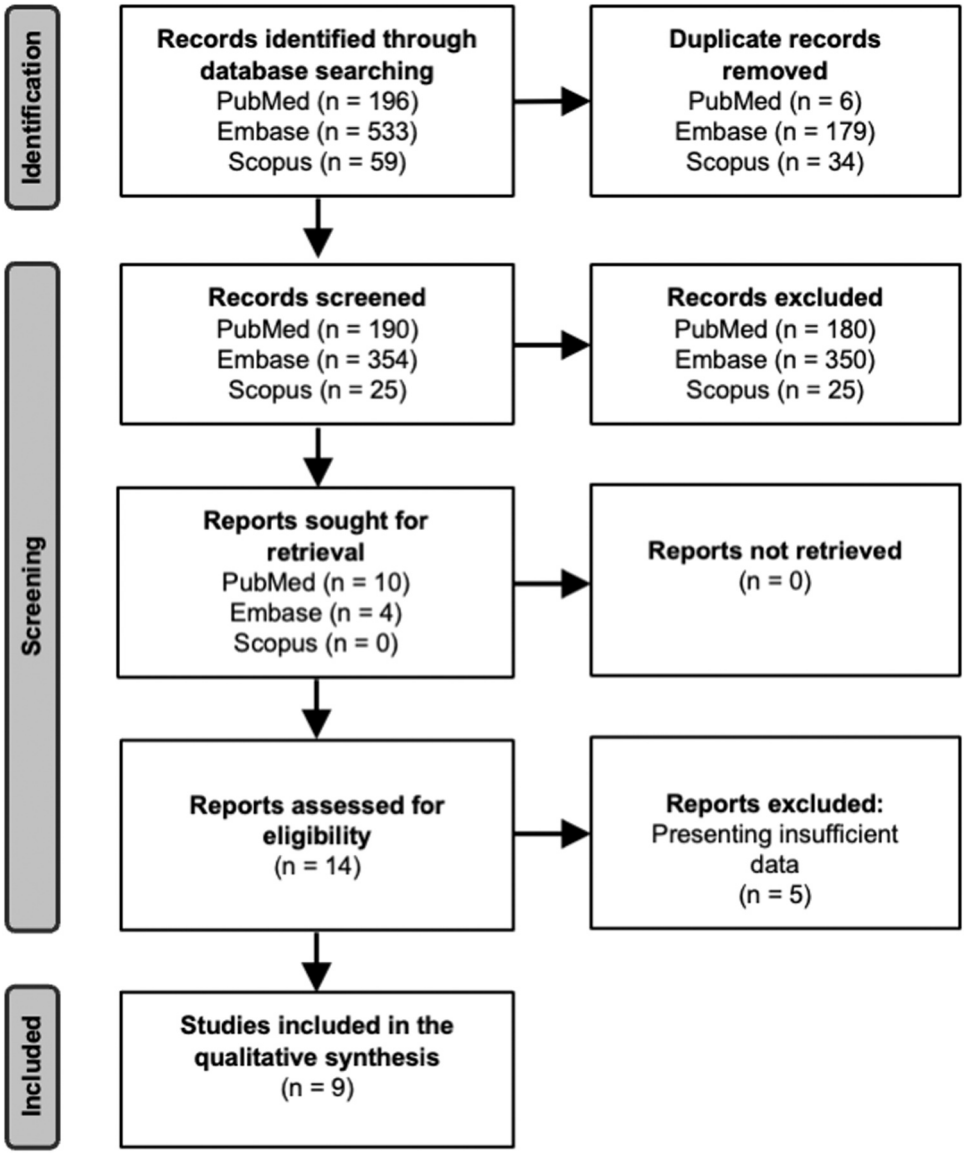

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses flowchart of the study selection process.

Assessment Tool for Observational Cohort and Cross-Sectional Studies". Studies' risk to performance bias was moderately low across all the 9 studies (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025). The risk of attrition bias due to incomplete outcome data was absent across all the studies (Supplementary Table 1).

3.2. Study locations and types

Baseline characteristics of the included studies are presented in Table 1 (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025). Six out of 9 studies were conducted in the USA (Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024), 1 in Japan (Sazuka, 2025), and 2 in China (Hao, 2016; Huang, 2025). All of the included studies were retrospective (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025). Only 2 studies were conducted in a single-center (Hao, 2016; Lin et al., 2014), 3 implemented data from National Cancer Database (Lenis, 2020; von Landenberg, 2018; Moldovan et al., 2024) and 1 used Surveillance, Epidemiology, and End Results Program database (Tang et al., 2022). In addition, propensity score matching was performed in 2 papers (Lenis, 2020; Sazuka, 2025) and inverse probability of treatment weighted - in 1 (von Landenberg, 2018).

3.3. Study sample sizes, follow-up, reported outcomes, and clinical characteristics

Overall, 20,806 patients with clinically NMIBC undergoing RC with various extents of PLND were included. The study groups varied in size: from 52 to 9399 patients. Mean/median follow-up time reported in the included papers was between 37.5 and 84 months. Regarding the outcomes, 7 studies assessed the influence of PLND on OS (Hao, 2016; Khanna, 2022; Lenis, 2020; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Sazuka, 2025. CSS was evaluated in 3 papers (Hao, 2016; Huang, 2025; Khanna, 2022) and RFS - in 4 (Huang, 2025; Khanna, 2022; Lin et al., 2014; Sazuka, 2025).

Clinical and pathological characteristics of main cohorts in the included studies are presented in Table 2 (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025). Collectively, the

Table 1
Baseline characteristics of the included studies.

Study	Country	Study design	Study duration	Patients, number	Extent of LND	Follow-up, months	Reported outcomes of interest
(Hao, 2016)	China	Retrospective, single center	2006–2012	164	Group 1: 0 nodes Group 2: > 0 nodes	Median: 46.5	OS, CSS
(Huang, 2025)	China	Retrospective, multicenter	2019–2024	544	Group 1: 0 nodes Group 2: > 0 nodes	Group 1: median 69 Group 2: median 69	CSS, RFS
(Khanna, 2022)	USA	Retrospective, multicenter	1980–2018	1647	Group 1: ≤ 10 nodes Group 2: > 10 nodes AND Group 1: ≤ 20 nodes Group 2: > 20 nodes	Median: 49.2	OS, CSS, RFS
(Lenis, 2020)	USA	Retrospective, multicenter (NCDB), PSM	2004–2013	2691	Group 1: < 10 nodes Group 2: ≥ 10 nodes	Group 1: mean 37.5 Group 2: mean 38.7	OS
(Lin et al., 2014)	USA	Retrospective, single center	1990–2010	196	Group 1: < 10 nodes Group 2: ≥ 10 nodes	Group 1: median 75 Group 2: median 54.6	RFS
(Moldovan et al., 2024)	USA	Retrospective, multicenter (NCDB)	2004–2019	9399	Group 1: 0 nodes Group 2: > 0 nodes	Mean: 64	OS
(Sazuka, 2025)	Japan	Retrospective, multicenter, PSM	2013–2019	52 (after PSM)	Group 1: 0 nodes Group 2: > 0 nodes	NR	OS, RFS (after PSM)
(Tang et al., 2022)	USA	Retrospective, multicenter (SEER)	2004–2015	1701	Group 1: 0 nodes Group 2: > 0 nodes	Group 1: 67 Group 2: 84	OS
(von Landenberg et al., 2017)	USA	Retrospective, multicenter (NCDB), IPTW	2004–2013	4412	Group 1: < 10 nodes Group 2: ≥ 10 nodes	NR	OS

LND - lymph node dissection; NCDB - National Cancer Database; OS - overall survival; CSS - cancer-specific survival; RFS - recurrence-free survival; PSM - propensity score matching; NR - not reported; SEER - Surveillance, Epidemiology, and End Results Program; IPTW - inverse probability of treatment weighted

included studies demonstrated significant variability in clinical characteristics. The extent of PLND differed between the articles and included 0 nodes, > 0 nodes, < 10 nodes, ≤ 10 nodes, ≥ 10 nodes, > 10 nodes, ≤ 20 nodes, and > 20 nodes dissected. Male sex was predominant in all of the studies and men constituted 79.5 % (n = 12,984/16,342) of the included cohort (where data on sex were available). The median/-mean age ranged from 67 to 79 years. In terms of clinical tumor stage, cT1 was the most common and accounted for 42.3 % - 94.2 %, depending on the study. Also, the vast majority of the tumors were high-grade. Importantly, substantial pathological upstaging was observed across the included studies, with 19.1 %–42.0 % of patients found to harbor muscle-invasive disease (pT2 or higher) at final pathology after RC. Positive lymph node status was reported in 3.7–13.6 % of patients who underwent PLND. Utilization of NAC and AC was generally rare across studies, with NAC administered in 0 % - 6.3 % of cases and AC in 0 % - 11.7 %.

3.4. Results of the systematic review

Oncological outcomes of interest reported in the included studies are presented in Table 3 (Hao, 2016; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022; von Landenberg, 2018; Moldovan et al., 2024; Huang, 2025; Sazuka, 2025).

3.4.1. Overall survival

Four studies compared OS between patients who underwent no pelvic lymph node dissection and those who had any PLND (0 nodes vs. >0 nodes dissected) (Hao, 2016; Tang et al., 2022; Moldovan et al., 2024; Sazuka, 2025). In a univariable analysis, Sazuka et al. found no statistically significant difference in OS between the matched groups (HR: 1.52, 95 % CI: 0.51–4.58) (Sazuka, 2025). In contrast, Tang, Wu, and Li reported significantly improved OS among patients who underwent PLND (estimated HR: 0.70, 95 % CI: 0.60–0.81), noting an increase in median survival time (139 vs. 89 months, $p < 0.001$) (Tang et al., 2022). This survival benefit was observed only in patients with T1 tumors, with no significant OS differences for Ta or Tis tumors (Tang et al., 2022). Similarly, Hao et al. reported improved 5-year OS in patients who underwent PLND during RC (66 % without PLND vs. 89 % with PLND, $p = 0.012$) and a reduced risk of mortality in univariate analysis (estimated HR: 0.42, 95 %CI: 0.18–0.97) (Hao, 2016). Moldovan et al. also confirmed an OS benefit, demonstrating that PLND was associated with a lower hazard of death in multivariate analysis (aHR: 0.68, 95 %CI: 0.62–0.74) (Moldovan et al., 2024).

Two studies investigated whether the removal of ≥ 10 lymph nodes impacted OS compared to < 10 nodes. Lenis et al. found that dissecting ≥ 10 nodes significantly improved 5-year OS (68.7 % vs. 60.6 %, $p < 0.01$) and reduced the risk of death by 25 % (aHR: 0.75, 95 %CI: 0.64–0.88) (Lenis, 2020). Similarly, von Landenberg et al. observed improved survival in patients with ≥ 10 nodes removed, regardless of NAC administration (No NAC: HR: 0.85, 95 %CI: 0.76–0.95; NAC: HR: 0.49, 95 %CI: 0.28–0.83) (von Landenberg, 2018).

Lastly, Khanna et al. demonstrated that removal of > 20 lymph nodes was associated with improved 5-year OS (75.4 % vs. 65.3 %, $p < 0.001$) and a lower risk of death (aHR: 0.75, 95 % CI: 0.64–0.88), compared to

Table 2
Clinical and pathological characteristics of main cohorts in the included studies.

Study	Group: number of patients	Male sex, n (%)	Age	Pre-RC tumor stage, n (%)	Tumor grade, n (%)	Post-RC Tumor stage	LN yield	Positive LN status, n (%)	NAC, n (%)	AC, n (%)
(Hao, 2016)	0 nodes: n = 23 > 0 nodes: n = 141	134 (81.7)	< 40: 3 (1.8) 40–49: 17 (10.4) 50–59: 42 (25.6) 60–69: 59 (25.6) 70–79: 38 (23.2) ≥ 80: 5 (3.0)	NR	G1: 1 (0.6) G2: 65 (39.6) G3: 98 (59.8)	Tis: 5 (3.0) Ta: 0 (0.0) T1: 159 (97.0)	NA NR	6 (3.7)	0 (0.0)	NR
(Huang, 2025)	0 nodes: n = 132	109 (82.6)	Median: 69	Tis: 6 (4.5) Ta: 5 (3.8) T1: 121 (91.7)	LG: 12 (9.1) HG: 120 (90.9)	T0: 6 (4.5) Tis: 8 (6.1) Ta: 1 (0.8) T1: 82 (62.1) ≥T2: 35 (26.5)	NA	NA	0 (0.0)	NR
	> 0 nodes: n = 412	337 (81.8)	Median: 69	Tis: 13 (3.2) Ta: 11 (2.7) T1: 388 (94.2)	LG: 49 (11.9) HG: 363 (88.1)	T0: 38 (9.2) Tis: 24 (5.8) Ta: 2 (0.5) T1: 190 (46.1) ≥T2: 158 (38.3)	Median: 14	29 (7.0)	0 (0.0)	NR
(Khanna, 2022)	≤ 10 nodes n = NR > 10 nodes n = NR ≤ 20 nodes n = NR > 20 nodes n = NR	1366 (82.9)	Median: 68	Tis: 366 (22.2) Ta: 307 (18.6) T1: 974 (59.1)	HG: 1267 (76.9)	<T2: 1333 (80.9) ≥T2: 314 (19.1)	Median: 15	98 (6.0)	0 (0.0)	57 (3.5)
(Lenis, 2020)	< 10 nodes: n = 918	641 (69.8)	< 65: 367 (40 %) 65–79: 445 (48.5 %) > 79: 106 (11.5 %)	Tis: 46 (5.0) Ta: 101 (11.0) T1: 771 (84.0)	LG: 97 (10.6) HG: 689 (75.1) Unknown: 132 (14.4)	<T2: 517 (56.3) ≥T2: 386 (42.0) Unknown: 15 (1.6)	Mean: 5 Median: 5	101 (11.0)	42 (4.6)	79 (8.6)
	≥ 10 nodes: n = 1773	1269 (71.6)	< 65: 884 (49.9 %) 65–79: 771 (43.5 %) > 79: 118 (6.7 %)	Tis: 99 (5.6) Ta: 173 (9.8) T1: 1501 (84.7)	LG: 146 (8.2) HG: 1395 (78.7) Unknown: 232 (13.1)	<T1: 1035 (58.4) ≥T2: 708 (39.9) Unknown: 30 (1.7)	Mean: 22 Median: 11	241 (13.6)	112 (6.3)	189 (10.7)
(Lin et al., 2014)	< 10 nodes: n = 109	84 (77.1)	Mean: 68	Tis: 16 (14.7) Ta: 20 (18.3) T1: 73 (67.0)	NR	<T2: 143 (73.0) ≥T2: 53 (27.0)	Median: 8	13 (6.6)	2 (1.0)	23 (11.7)
	≥ 10 nodes: n = 87	70 (80.5)	Mean: 68	Tis: 17 (19.5) Ta: 12 (13.8) T1: 58 (66.7)	NR					
(Moldovan et al., 2024)	0 nodes: n = 380 > 0 nodes: n = 7483	7449 (79.3)	< 65: 3511 (37.4) ≥ 65: 5888 (62.6)	Tis: 25 (6.6) Ta: 78 (20.5) T1: 277 (72.9) Tis: 482 (6.4) Ta: 941 (12.6) T1: 6060 (81.0)	NR	NR	NR	NR	NR	NR
(Sazuka, 2025)	0 nodes: n = 26	NR	Median: 79	<T1: 15 (57.7) T1: 11 (42.3) Concomitant Tis: 15 (57.7)	NR	NR	NA	NA	0 (0.0)	0 (0.0)
	> 0 nodes: n = 26	NR	Median: 75	<T1: 15 (57.7) T1: 11 (42.3) Concomitant Tis: 16 (61.5)	NR	NR	NR	NR	0 (0.0)	NR
(Tang et al., 2022)	0 nodes: n = 609	526 (86.4)	Median: 70	Tis: 62 (10.2) Ta: 127 (20.9) T1: 420 (68.9)	LG: 124 (20.4) HG: 374 (61.4) Unknown: 111 (18.2)	NR	NA	NA	NR	NR

(*continued on next page*)

Table 2 (*continued*)

Study	Group: number of patients	Male sex, n (%)	Age	Pre-RC tumor stage, n (%)	Tumor grade, n (%)	Post-RC Tumor stage	LN yield	Positive LN status, n (%)	NAC, n (%)	AC, n (%)
	> 0 nodes: n = 1092	999 (91.5)	Median: 67	Tis: 62 (5.7) Ta: 109 (10.0) T1: 921 (84.3)	LG: 109 (10.0) HG: 865 (79.2) Unknown: 118 (10.8)	NR	Median: 14	44 (4.0)	NR	NR
(von Landenberg et al., 2017)	< 10 nodes: n = 2139	NR	NR	NR	NR	NR	NR	NR	200 (4.5)	NR
	≥ 10 nodes: n = 2273	NR	NR	NR	NR	NR	NR	NR		NR

n - number; RC - radical cystectomy; LN - lymph node; NAC - neoadjuvant chemotherapy; AC - adjuvant chemotherapy; LG - low-grade; HG - high-grade; NR - not reported; NA - not applicable

Table 3
Oncological outcomes of interest reported in the included studies.

Study	Group	5-year OS	p-value	Multivariable Cox Regression Analysis - OS, HR (95 % CI)	5-year CSS	p-value	Multivariable Cox Regression Analysis - CSS, HR (95 % CI)	5-year RFS	p-value	Multivariable Cox Regression Analysis - RFS, HR (95 % CI)
(Hao, 2016)	0 nodes	66 %	0.012	Ref.	73 %	0.011	Ref.	NR	NR	NR
	> 0 nodes	89 %		Univariable: 0.42 (0.18–0.97)	95 %		Univariable: 0.34 (0.14–0.82)	NR		NR
(Huang, 2025)	0 nodes	NR	NR	NR	81.6 %	0.13	Ref.	71.5 %	0.015	Ref.
	> 0 nodes	NR		NR	86.5 %		0.57 (0.32–1.02)	84.3 %		0.33 (0.20–0.56)
(Khanna, 2022) (10 nodes threshold)	≤ 10 nodes	NR	NR	NR	NR	NR	NR	LPRFS: 91.0 %	0.003	Ref.
	> 10 nodes	NR		NR	NR		NR	LPRFS: 93.7 %		LPRFS: 0.63 (0.42–0.93)
(Khanna, 2022) (20 nodes threshold)	≤ 20 nodes	65.3 %	< 0.001	Ref.	78.4 %	0.002	Ref.	NR	NR	NR
	> 20 nodes	75.4 %		0.75 (0.64–0.88)	86.7 %		0.67 (0.52–0.87)	NR		NR
(Lenis, 2020)	< 10 nodes	60.6 %	< 0.01	Ref.	NR	NR	NR	NR	NR	NR
	≥ 10 nodes	68.7 %		0.75 (0.64 −0.88)	NR		NR	NR		NR
(Lin et al., 2014)	< 10 nodes	NR	NR	NR	NR	NR	NR	NR	NR	Ref.
	≥ 10 nodes	NR		NR	NR		NR	NR		1.00 (0.51–1.95)
(Moldovan et al., 2024)	0 nodes	NR	NR	Ref.	NR	NR	NR	NR	NR	NR
	> 0 nodes	NR		0.68 (0.62–0.74)	NR		NR	NR		NR
(Sazuka, 2025)	0 nodes	NR	NR	Ref.	NR	NR	NR	NR	NR	Ref.
	> 0 nodes	NR		Univariable: 1.52 (0.51–4.58)	NR		NR	NR		NUTRFS Univariable: 2.21 (0.83–5.83)
(Tang et al., 2022)	0 nodes	NR	NR	Ref.	NR	NR	NR	NR	NR	NR
	> 0 nodes	NR		Univariable: 0.70 (0.60–0.81)	NR		NR	NR		NR
(von Landenberg et al., 2017)	< 10 nodes	NR	NR	Ref.	NR	NR	NR	NR	NR	NR
	≥ 10 nodes	NR		Univariable: No NAC: 0.85 (0.76–0.95) NAC: 0.49 (0.28–0.83)	NR		NR	NR		NR

OS - overall survival; CSS - cancer-specific survival; RFS - recurrence-free survival; HR - hazard ratio; CI - confidence interval; Ref. - reference; NR - not reported; NUTRFS - non-urothelial tract recurrence-free survival; NAC - neoadjuvant chemotherapy; LPRFS - local pelvic recurrence-free survival

dissection of ≤ 20 nodes (Khanna, 2022).

3.4.2. *Cancer-specific survival*

Two studies compared CSS between patients who underwent no PLND and those who had any PLND (0 nodes vs. >0 nodes dissected) (Hao, 2016; Huang, 2025). In the study by Huang *et al.*, 5-year CSS rates were 86.5 % in the PLND group and 81.6 % in the no-PLND group; however, this difference was not statistically significant (p = 0.13). Multivariable analysis also showed no significant difference in cancer-related mortality between groups (aHR: 0.57, 95 %CI: 0.32–1.02) (Huang, 2025). Conversely, Hao et al. reported a significantly improved 5-year CSS in patients who underwent PLND (95 % vs. 73 %, p = 0.011). In univariate analysis, PLND was associated with a 66 % reduction in the risk of death due to bladder cancer (HR: 0.34, 95 %CI: 0.14–0.82) (Hao, 2016).

Additionally, one study by Khanna *et al.* examined the effect of extended PLND, comparing dissection of ≤ 20 vs. > 20 lymph nodes. Patients who had over 20 nodes removed during RC experienced significantly better CSS (86.7 % vs. 78.4 %, p = 0.002), a finding supported by multivariate analysis (aHR: 0.67, 95 % CI: 0.52–0.87)

(Khanna, 2022).

3.4.3. Recurrence-free survival

Huang *et al.* evaluated the impact of any PLND on 5-year RFS. They found that patients who did not undergo PLND had significantly lower 5-year RFS compared to those who did (71.5 % vs. 84.3 %, $p = 0.015$). PLND was independently associated with a 67 % reduction in the risk of recurrence (aHR: 0.33, 95 % CI: 0.20–0.56) (Huang, 2025). A second study by Sazuka *et al.* assessed non-urinary-tract recurrence-free survival (NUTRFS) as an endpoint when comparing no PLND vs. any PLND. No statistically significant difference was found between the groups in terms of recurrence outside the urinary tract (HR: 2.21, 95 %CI: 0.83–5.83) (Sazuka, 2025).

Lin *et al.* investigated whether the removal of at least 10 lymph nodes influenced RFS. Both univariate ($p = 0.63$) and multivariate analyses showed no significant association between the excision of ≥ 10 nodes and RFS (aHR: 1.00, 95 %CI: 0.51–1.95) (Lin et al., 2014). Finally, a study by Khanna et al. demonstrated that the dissection of > 10 lymph nodes was associated with significantly improved 5-year local-pelvic recurrence-free survival (LPRFS) (93.7 % vs. 91 %, $p = 0.003$). This association remained significant in multivariate analysis, with a lymph node yield > 10 linked to a reduced risk of local recurrence of bladder cancer (aHR: 0.63, 95 %CI: 0.42–0.93) (Khanna, 2022).

4. Discussion

To our knowledge, this is the first systematic review to comprehensively synthesize available evidence regarding the oncological impact of PLND in patients undergoing RC for clinically staged NMIBC. The present analysis is focused on outcomes of patients selected for RC based on preoperative staging. This reflects real-world clinical practice, where decisions regarding the performance and extent of PLND must be made at the time of surgery without definitive pathological staging.

Across 9 retrospective studies encompassing more than 20,000 patients, the cumulative data suggest that performing PLND, may be associated with meaningful oncologic benefits, including improvements in OS, CSS, and selected recurrence related-related outcomes. Importantly, a higher lymph node yield - particularly ≥ 10 or > 20 nodes - was consistently associated with improved survival across multiple studies. This suggests that not only the presence of PLND but also its adequacy in terms of nodal dissection may be crucial in achieving better survival in clinically staged NMIBC.

Several studies demonstrated a consistent association between the presence of any PLND and improved OS (Hao, 2016; Tang et al., 2022; Moldovan et al., 2024). Only Sazuka *et al.* reported that PLND during RC had no significant effect on OS (Sazuka, 2025). In other included papers, extended lymphadenectomy was linked to a better OS, when compared to a lower lymph-node yield (Khanna, 2022; Lenis, 2020; von Landenberg, 2018). Importantly, subgroup analyses by Tang, Wu, Li, and Moldovan *et al.* suggested that the survival benefit of PLND may be limited to patients with cT1 tumors (Tang et al., 2022; Moldovan et al., 2024).

CSS was also improved with PLND in the majority of studies evaluating this endpoint, particularly when the lymph node yield exceeded 20 nodes (Hao, 2016; Khanna, 2022). Even though Huang *et al.* did not observe a statistically significant difference between the “no PLND” and “PLND” groups, their multivariate analysis trended toward a protective effect of PLND on CSS (Huang, 2025).

RFS was not a homogeneous endpoint in our review, as Khanna et al. analyzed LPRFS and Sazuka et al. researched NUTRFS (Khanna, 2022; Sazuka, 2025). Therefore, the direct comparison of all the included studies is not possible. Nonetheless, any PLND during RC improved RFS (Huang, 2025), but had no impact on NUTRFS (Sazuka, 2025). Also, the dissection of at least 10 lymph nodes had no additional effect on RFS (Lin et al., 2014), but was protective of local-pelvic recurrences (Khanna, 2022).

From an oncological standpoint, several mechanisms may explain the observed association between PLND and improved survival outcomes in the included group. Although NMIBC is traditionally considered organ-confined, it has been demonstrated that lymph node metastases are not negligible in this population. In the included studies positive lymph-nodes were found in 3.7–13.6 % of cases (Hao, 2016; Huang, 2025; Khanna, 2022; Lenis, 2020; Lin et al., 2014; Tang et al., 2022). In addition, a prospective study by Bruins *et al.* reported lymph node metastases in 9 % of patients undergoing RC for clinically staged NMIBC (Bruins, 2014). Crucially, the authors found that only 1.1 % of patients had lymph node involvement after final pathological confirmation of non-muscle invasive disease (Bruins, 2014). These results highlight a significant risk of occult muscle-invasive disease, particularly among patients with cT1 tumors. In these cases, PLND does not only serve as a staging procedure, but also as a therapeutic intervention. In addition, higher lymph node yield may contribute to improved oncological outcomes through more accurate pathological staging and a stage-migration effect, allowing more appropriate postoperative management, such as adjuvant chemotherapy or immunotherapy.

Interestingly, the literature regarding the extent of PLND in bladder cancer remains contradictory. A meta-analysis from 2014 has shown that extended PLND provided better RFS, even for patients with negative lymph-nodes (Bi, 2014). However, a recent meta-analysis of randomized controlled trials demonstrated that the extended PLND was not associated with improved RFS, nor OS (Ślusarczyk, 2025).

The potential therapeutic benefit of PLND must be balanced against the risk of perioperative morbidity. Extended PLND is often associated with a longer operative time and hospital stay, as well as an increased incidence of complications, such as vascular injury or lymphocele (Perera et al., 2018). In a randomized trial comparing extended versus limited PLND, Gschwend *et al.* reported higher rates of lymphocele in the extended dissection group (Gschwend, 2019). More recently, a meta-analysis of randomized controlled trials has confirmed that extended PLND was associated with a higher risk of postoperative complications and mortality (Ślusarczyk, 2025). Nonetheless, in patients with clinically high-risk or very high-risk NMIBC, the potential oncologic benefit of extended PLND—especially in terms of accurate staging and removal of occult nodal disease—may outweigh the incremental surgical risk. These considerations further support an individualized approach to PLND, taking into account patient comorbidity, tumor risk profile, and surgical expertise.

Crucially, the interpretation of the findings of the present systematic review requires careful consideration of several important methodological and clinical limitations.

A key methodological issue that warrants particular emphasis is the substantial rate of pathological upstaging observed among patients undergoing RC for clinically staged NMIBC (Huang, 2025; Khanna, 2022; Lenis et al., 2020; Lenis, 2020; Lin et al., 2014). This is a clinically meaningful finding, as patients with MIBC represent a biologically and prognostically distinct subgroup for whom PLND is an established component of standard surgical management. Consequently, pooling patients with occult muscle-invasive disease together with those with pathologically confirmed NMIBC may introduce bias and potentially overestimate the oncologic benefit of PLND, when such benefit is attributed exclusively to true NMIBC. However, the inclusion of patients who were subsequently up-staged to MIBC reflects real-world clinical practice, in which decisions regarding the performance and extent of PLND are made based on preoperative clinical staging rather than final pathological findings. From a practical standpoint, surgeons must determine the extent of lymphadenectomy at the time of RC without definitive knowledge of final tumor stage. Therefore, the risk of pathological up-staging represents an inherent limitation of current clinical risk stratification and a critical consideration when planning RC with or without PLND in patients with high- and very high-risk NMIBC. Furthermore, cT1 high-grade tumors are associated with a significant risk of progression, and the interval between TURBT and RC may allow

progression to MIBC. Highlighting these issues underscores the clinical relevance of PLND decision-making in this population and supports the rationale for evaluating outcomes based on clinical staging. That is why, the findings of this review should not be construed as definitive evidence supporting PLND in patients with pathologically confirmed NMIBC, but rather as an evaluation of PLND in patients undergoing RC based on a preoperative diagnosis of NMIBC.

It is worth mentioning that the advancements in imaging, risk stratification, and molecular classification of NMIBC will likely allow for a more precise clinical staging and better patient selection for RC with PLND. For example, wide implementation of MRI-based protocols, may improve the detection of muscle-invasive, locally advanced, or nodal disease. Integration of refined clinical risk models and emerging molecular markers may ultimately enable a more individualized, risk-adapted approach to PLND, helping identify patients most likely to benefit, while minimizing unnecessary surgical complications.

Beyond pathological up-staging, interpretation of the available literature is further limited by the retrospective design of all included studies and the heavy reliance on large administrative databases, including the National Cancer Database and the Surveillance, Epidemiology, and End Results Program. While these databases provide large sample sizes and substantial statistical power, they lack granularity in several clinically relevant domains. Important factors such as completeness and quality of transurethral resection, presence of concomitant carcinoma in situ, tumor size, multifocality, lymphovascular invasion, and surgeon experience are either inconsistently recorded or entirely unavailable. These limitations restrict the ability to adequately adjust for confounding variables and may influence observed survival associations.

Another important limitation is our inability to perform meaningful subgroup or sensitivity analyses that excluded patients with MIBC on final pathology. Among the included studies, just one reported survival outcomes of patients with pathologically confirmed NMIBC only (Hao, 2016). As a result, the core question of whether PLND confers a survival benefit in patients with strictly pathologically confirmed NMIBC remains unanswered. This represents a critical gap in the existing literature and highlights the need for future prospective studies or high-quality registries designed to stratify outcomes according to both clinical and pathological staging.

Finally, the included studies varied significantly in terms of PLND extent and patient selection. Utilization of neoadjuvant and adjuvant chemotherapy was rare, and the impact of these therapies on outcomes could not be reliably assessed. Furthermore, the lack of standardized templates for PLND and the variability in surgical technique likely contributed to the heterogeneity of results.

5. Conclusions

This systematic review indicates that pelvic lymph node dissection during radical cystectomy for clinical NMIBC may be associated with improved OS, CSS, and RFS, especially in cT1 disease. Evidence suggests that a more extensive PLND might offer the greatest benefit. Therefore, consideration should be given to performing at least a limited PLND during RC for clinical NMIBC, especially in patients with high-risk pathological features. However, these findings are influenced by substantial pathological upstaging, retrospective study designs, and limitations inherent to large database analyses. Standardization of PLND templates and further prospective randomized trials with detailed pathological assessment are essential to clarify the oncologic value and define the optimal extent of lymphadenectomy in this patient population.

CRediT authorship contribution statement

YAG: Investigation, methodology, writing – original draft. JŁ: Investigation, methodology, writing – original draft. HTC: Data curation. WK: Supervision. BIC: Supervision. RC: Methodology. VS: Data curation. AK: Visualization. FC: Visualization. YI: Methodology. MG: Writing – review and editing. SGAK: Supervision. KS: Conceptualization. BC: writing – review and editing. RN: Supervision. EM: Conceptualization. RT: Conceptualization. MSK: Supervision. FDG: Conceptualization, supervision, writing – review and editing. All authors read and approved the final manuscript.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.critrevonc.2026.105192.

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