Practical Radiation Oncology® (2026) **16**, e210–e218

practical radiation oncology
pro
www.practicalradonc.org

Basic Original Report

Mapping Patterns of Pelvic Lymph Node Metastasis in Bladder Urothelial Carcinoma: Implications for Personalized Pelvic Radiation Therapy

Tian Cheng, MD,[a,1] Han Hao, MD,[b,1] Chao Liu, MD,[a] Xiaoying Li, MD,[a] Xianshu Gao, MD, PhD,[a,*] and Shangbin Qin, MD[a,*]

[a]*Department of Radiation Oncology, Peking University First Hospital, Beijing, P.R. China; and* [b]*Department of Urology, Peking University First Hospital, Beijing, P.R. China*

Received 24 July 2025; accepted 2 October 2025

Purpose: This study aimed to evaluate the association between primary bladder urothelial carcinoma T-stage, G-grade, and pelvic lymph node metastasis (PLNM), and to delineate the location of metastatic pelvic lymph nodes across different T-stage and G-grade combinations.

Methods and Materials: Surgical and pathologic data from 1555 patients who underwent radical cystectomy with pelvic lymph node dissection for bladder urothelial carcinoma at our hospital between October 2014 and September 2024 were collected and analyzed. Pelvic lymph nodes were anatomically classified into 6 regions: peri-vesical, internal iliac/obturator, external iliac, presacral, common iliac, and paraortic. Descriptive statistics were used to quantify PLNM rates and distribution patterns by T-stage and G-grade. Multivariate logistic regression identified independent predictors of PLNM.

Results: Of the 1555 patients analyzed, 297 (19.1%) exhibited pathologically confirmed PLNM. Stratified by T-stage, PLNM rates progressively increased from 2.6% in Ta/Tis/T1 patients to 11.0% in T2, 29.8% in T3, and 50.0% in T4. Similarly, G-grade stratification revealed no lymph node involvement in G1 patients (0%), whereas PLNM rates rose to 2.9% in G2 and 23.9% in G3. Notably, among T2G3, T3G3, and T4G3 patients with lymph node metastasis, 96.9%, 93.6%, and 84.9% of patients had metastases exclusively below the iliac bifurcation, whereas 100%, 95.7%, and 95.9% had metastases exclusively below the aortic bifurcation, respectively. Multivariate logistic regression confirmed T-stage (odds ratio, 2.766; 95% CI, 2.347-3.259; $P < .001$) and G-grade (odds ratio, 3.794; 95% CI, 1.874-7.681; $P < .001$) as independent predictors of PLNM, with no significant associations observed for age, sex, or tumor size.

Conclusions: We present a detailed map of PLNM in patients with bladder urothelial carcinoma with different T-stages and G-grades. The internal iliac/obturator packages appear to be most commonly involved. These findings demonstrate the significant impact of T-stage and G-grade on both the incidence and extent of PLNM. Collectively, these results may support future personalized treatment tailored to tumor stage and grade.

Sources of support: This work was supported by the Peking University First Hospital Domestic Multicenter Clinical Research Program, Grant number: 22CZ020301-4810005.

Research data are stored in an institutional repository and will be shared on request to the corresponding author.

*Corresponding authors: Shangbin Qin and Xianshu Gao; Emails: doctorgaoxs@126.com champion_qin@hotmail.com

[1]T.C. and H.H. contributed equally to this work.

https://doi.org/10.1016/j.prro.2025.10.002

Introduction

Pelvic lymph node metastasis (PLNM) is a common and prognostically critical event in the progression of bladder cancer. Despite its clinical significance, current guidelines—including the National Comprehensive Cancer Network (version 1.2025)[1] and European Association of Urology (2025)[2]—provide no detailed recommendations for pelvic nodal target volumes in bladder-preserving radiation therapy. This ambiguity perpetuates heterogeneous practices.

The debate over pelvic nodal irradiation (PLN-RT) is epitomized by conflicting trial outcomes. Seminal Radiation Therapy Oncology Group (RTOG) protocols in the United States (including RTOG 9506, 9706, 9906, and 0233) mandated comprehensive PLN-RT during bladder-preserving radiation therapy.[3-6] A large multicenter study[7] also demonstrated through inverse probability treatment weighted analysis that whole-pelvic radiation therapy significantly improved overall and cancer-specific survival compared with bladder-only irradiation in patients with muscle-invasive bladder cancer (MIBC). In contrast, the BC2001 trial reported a mere 5% pelvic nodal recurrence rate at 5 years with bladder-only radiation therapy, without compromising survival or organ preservation.[8,9] Recent expert consensus guideline[10] also reflected ongoing lack of agreement regarding PLN-RT. These conflicting findings underscore the need to reassess the risk of pelvic nodal metastases and their stratification based on clinicopathological features.

A PLNM map for patients with bladder cancer helps to clarify metastatic spread patterns and define the reasonable limits of pelvic nodal target volumes. While existing research focuses on T-stage influence in PLNM of bladder cancer,[11] histologic grading (G-grade)—a key indicator of biological aggressiveness—has not been adequately incorporated into quantitative metastasis risk stratification. To address these concerns, we analyzed pathologic data from a consecutive radical cystectomy cohort at our institution (2014-2024). This study aimed to: (1) quantify PLNM rates across pathologic T-stages (American Joint Committee on Cancer 8th edition) and G-grades (World Health Organization 2016 classification); (2) map pelvic nodal spread patterns stratified by pathologic T-stage and G-grade, elucidating their synergistic impact on metastatic topography.

Methods and Materials

Study population

A retrospective review was conducted on our computerized cystectomy database, which contains comprehensive clinical and pathologic data for all patients undergoing radical cystectomy between October 2014 and September 2024. The database includes details on patient demographics, treatment modalities, pathologic findings, and follow-up data. The study cohort comprised patients meeting the following criteria: (1) successful completion of radical cystectomy with pelvic lymph node dissection; (2) postoperative pathologic confirmation of urothelial carcinoma; (3) surgical dissection encompassing at least bilateral external iliac lymph nodes and internal iliac/obturator lymph nodes, with extension determined at the surgeon's discretion based on intraoperative findings and imaging, and not exceeding the inferior mesenteric artery; and (4) complete pathologic Tumor-Node-Metastasis staging documentation. Ultimately, 1555 patients who met all inclusion criteria were included in the analysis.

This study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Peking University First Hospital (2025-111). Informed consent was waived for this retrospective study.

Treatment protocol and pathologic assessment

All patients underwent a standard surgical procedure, which included radical cystectomy with meticulous pelvic lymphadenectomy and urinary diversion. Lymph nodes were categorized into the following regions for separate histopathologic examination: peri-vesical lymph nodes; internal iliac/obturator lymph nodes; external iliac lymph nodes; common iliac vessels lymph nodes; presacral lymph nodes (defined as the nodal tissue anterior to the sacrum between the aortic bifurcation and sacral promontory, medial to the internal iliac vessels and ureters); and paraortic lymph nodes (all groups above the aortic bifurcation defined as paraortic lymph nodes).

All cystectomy specimens were examined following a uniform pathologic protocol by the uropathology laboratory at our institution. Pathologic assessment included multiple sections of tumors, bladder walls, and regional lymph nodes. Tumor size was determined from the pathologic specimen and was defined as the largest tumor diameter based on combined gross and microscopic examination. Pathologic staging and grading were performed according to the American Joint Committee on Cancer bladder cancer staging criteria[12] and the World Health Organization 1973 grading classification,[13] respectively.

Statistical analysis

Statistical analysis was performed using SPSS 24.0. Continuous data were expressed as mean and range, whereas categorical data were expressed as number and percentage. All tests were 2-tailed. Univariate logistic regression analysis was initially conducted with PLNM as the dependent variable, and age, sex, tumor size, stage, and grade as independent variables. Variables

demonstrating statistical significance were subsequently included in multivariate logistic regression analysis. A P value of <.05 was considered statistically significant.

Results

Clinical characteristics

Table 1 summarizes the baseline characteristics of the study cohort. The median age was 67 years (IQR, 60-73; range, 22-92 years), with a 4.6:1 male-to-female ratio. Of the cases, 70.7% (1099/1555) were MIBC (pT2-T4), whereas 29.3% (456/1555) were nonmuscle-invasive bladder disease (NMIBC, pT1/Ta/Tis). Histologic grading included 0.3% (4/1555) G1, 20.3% (307/1555) G2, and 79.5% (1205/1555) G3 tumors. The median tumor size was 3.0 cm (IQR, 2.5-4.5 cm; range, 0.2-12.0 cm). The median number of lymph nodes retrieved per patient was 9 (IQR, 6-13; range, 1-52), which meets the benchmark for accurate nodal staging as established by Herr et al.[14]

Table 1 Patients' characteristics

Patient characteristic	Total cohort (N = 1555)
Age	
Mean (SD)	65.8 (9.69)
Median (range)	67 (22-92)
Gender, n (%)	
Male	1275 (82.0%)
Female	280 (18.0%)
T-stage	
pT1/Ta/Tis	456 (29.3%)
pT2	453 (29.1%)
pT3	436 (28.0%)
pT4	210 (13.5%)
N-stage	
pN0	1258 (80.9%)
pN1	137 (8.8%)
pN2	142 (9.1%)
pN3	18 (1.2%)
G-grade	
G1	4 (0.3%)
G2	307 (20.3%)
G3	1205 (79.5%)
Tumor size	
<3.0 cm	390 (37.5%)
≥3.0 cm but <6.0 cm	545 (52.4%)
≥6.0 cm	105 (10.1%)

Probability of PLNM in patients with different T-stages and G-grades

Lymph node metastasis was pathologically confirmed in 19.1% of patients (297/1,555). Among node-positive cases, the median number of metastatic pelvic lymph nodes was 2 (IQR, 1-3, range, 1-40), with 46.5% of these patients (137/297) demonstrating only 1 pelvic lymph node involvement (Table 1).

The lymph node metastasis rate demonstrated incremental escalation with advancing T-stage and G-grade (Fig. 1). Stratified by T-stage, PLNM rates increased progressively from 2.6% in pTa/Tis/T1 tumors to 11.0% in pT2, 29.8% in pT3, and 50.0% in pT4 tumors. Similarly, G-grade stratification revealed no lymph node involvement in G1 tumors (0%), while PLNM rates rose to 2.9% in G2 and 23.9% in G3 tumors. Notably, among advanced pT-stage tumors (pT3-4), G2 tumors exhibited a significantly lower nodal metastasis rate than G3 tumors (17.2% vs 37.3%; $P = .03$).

The mean number of metastatic lymph nodes per node-positive patient also increased with advancing T-stage and G-grade: pTa/Tis/T1, pT2, pT3, and pT4 cases exhibited averages of 2.17, 2.34, 2.88, and 4.08 positive nodes, respectively, while G1, G2, and G3 tumors showed averages of 0, 1.11, and 3.25 nodes.

Among node-positive patients, 79.1% (235/297) had pT3/T4 disease and 97.0% (288/297) exhibited G3 histology, with 98.7% (293/297) harboring at least 1 high-risk feature (pT3/T4 and/or G3). Univariate logistic regression identified significant positive correlations between PLNM and tumor T-stage/G-grade (both $P < .001$), whereas age, sex, or tumor size showed no statistical relevance. Multivariate logistic regression with backward stepwise variable selection confirmed pathological T-stage (odds ratio, 2.766; 95% CI, 2.347-3.259; $P < .001$) and G-grade (odds ratio, 3.794; 95% CI, 1.874-7.681; $P < .001$) as independent predictors of PLNM (Table 2).

Distribution pattern of pelvic metastatic lymph nodes of patients with different T-stages and G-grades

Among the 297 node-positive patients, a total of 946 metastatic lymph nodes were identified, indicating a mean of 3.19 positive nodes per patient. Within this PLNM cohort, 210 patients (731 metastatic lymph nodes) had documented lymph node locations. As detailed in Table 3, analysis of lymph node distribution revealed that the internal iliac/obturator nodes were the most frequently involved site (83.8%, 176/210), followed by the external iliac nodes (33.3%, 70/210). This distribution pattern was consistent across all T-stage and G-grade subgroups (Fig. 2).

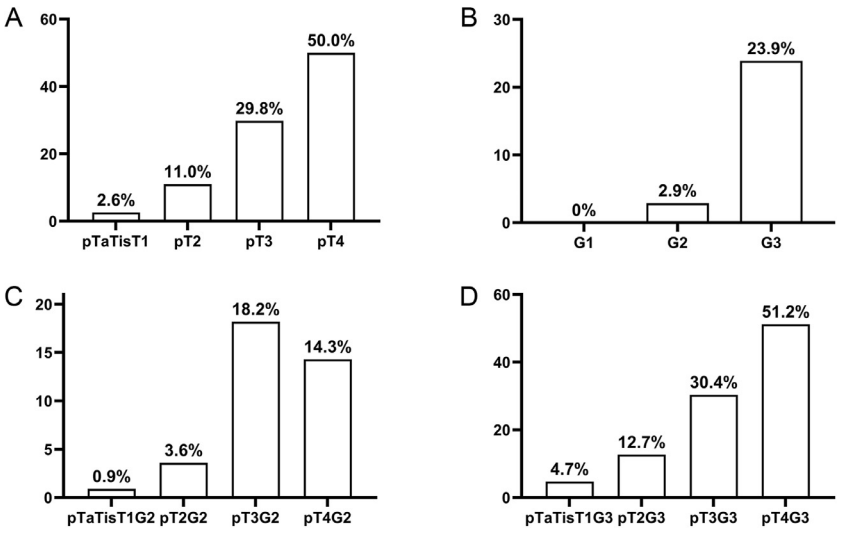

Figure 1 Probability of pelvic lymph node metastasis (PLNM) in patients across pathological T-stages and G-grades.

Table 2 Univariate and multivariate logistic regression analysis of factors associated with pelvic lymph node metastasis in bladder urothelial carcinoma

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
pT-stage	3.123 (2.671-3.650)	<.001	2.766 (2.347-3.259)	<.001
G-grade	10.427 (5.307-20.484)	<.001	3.794 (1.874-7.681)	<.001
Age	0.999 (0.986-1.012)	.894	–	–
Sex	0.755 (0.552-1.032)	.078	–	–
Tumor size	1.002 (1.000-1.004)	.076	–	–

Abbreviations: CI = confidence interval; pT-stage = pathological T-stage; OR = odds ratio.

Table 3 Distribution of pelvic lymph node metastases by anatomic zone in documented PLNM patients

Anatomic zones	Patients with PLNM*	Metastatic lymph nodes (%)
Peri-vesical	9	13 (1.8)
Internal iliac/obturator	176	467 (63.9)
Right	117	230 (31.5)
Left	114	237 (32.4)
External iliac	70	153 (20.9)
Right	41	78 (10.7)
Left	40	75 (10.3)
Presacral	12	25 (3.4)
Common iliac	17	44 (6.0)
Right	12	34 (4.7)
Left	7	10 (1.4)
Paraortic	7	29 (4.0)

Abbreviation: PLNM = pelvic lymph node metastasis.
*Individual patients may have nodal deposits in multiple zones; therefore, the sum of patients may exceed.

To establish comprehensive metastatic mapping across all T-stage/G-grade combinations, we analyzed the anatomic distribution patterns of lymph node metastases in the 210 patients with documented nodal locations. The distribution of pelvic metastatic lymph nodes varied by tumor stage and grade: No metastatic nodes were observed in G1 patients. In G2 patients, metastases were confined to the internal iliac/obturator and external iliac lymph node regions regardless of pathologic T-stage. G3 NMIBC cases involved internal iliac/obturator, external iliac, and presacral nodes, whereas pT2G3 tumors additionally involved peri-vesical and common iliac nodes. Advanced pT3G3 and pT4G3 patients showed metastatic spread extending to paraortic lymph nodes (Fig. 1).

Metastasis prevalence in specific anatomic zones correlated strongly with advancing pathological T-stage and G-grade, demonstrating progressive anatomic spread: metastases extended stepwise from proximal sites (internal iliac/obturator regions) to distal regions (common iliac and paraortic areas) with disease progression. For example, common iliac node involvement increased from 1.2% of all metastases in pT2G3 to 5.8% in pT3G3 and 7.8% in

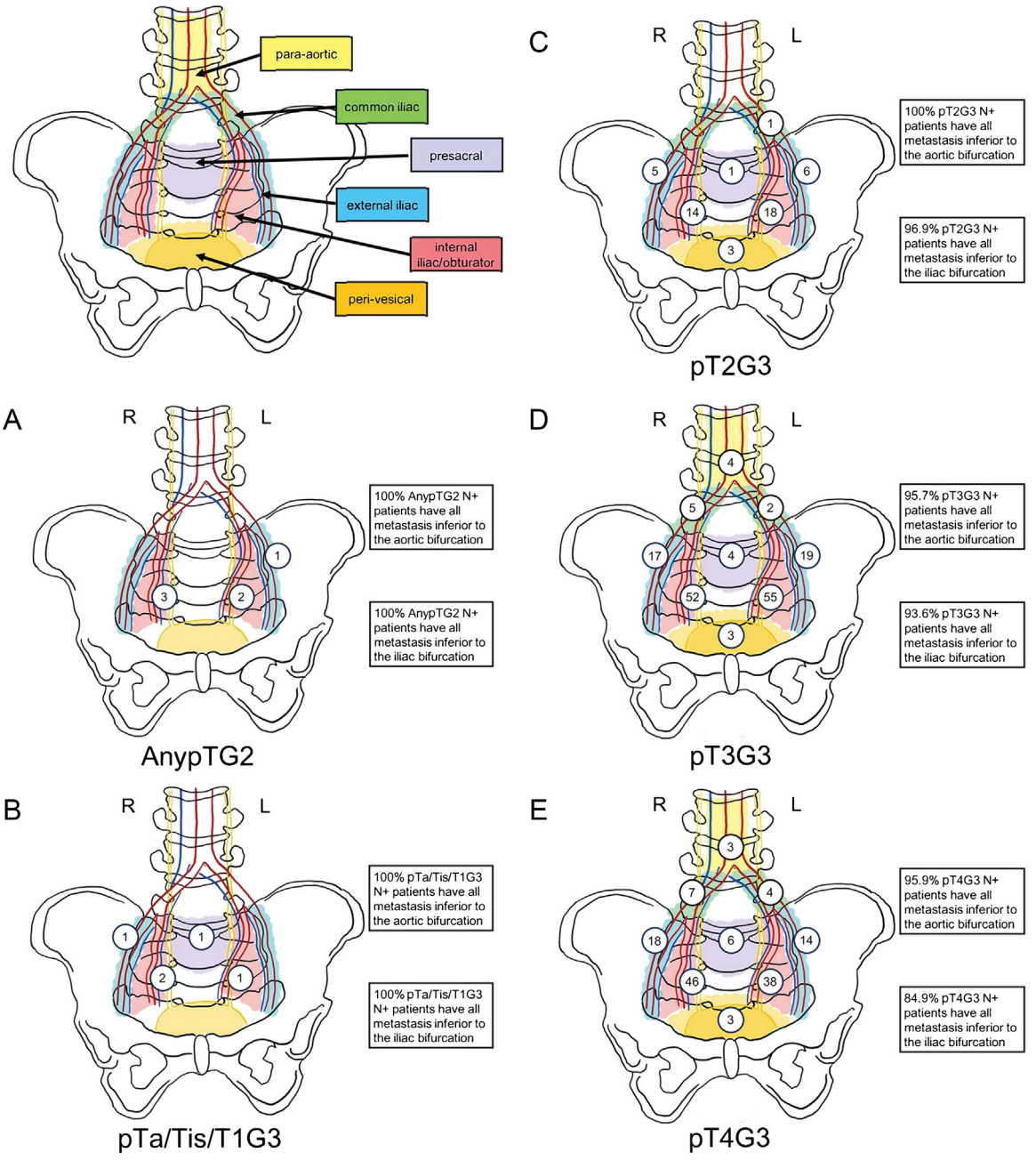

Figure 2 Stage- and grade-specific distribution of metastatic lymph nodes in the 210 mapped patients. (A) AnypTG2 (6 patients). (B) pTa/Tis/T1G3 (5). (C) pT2G3 (32). (D) pT3G3 (94). (E) pT4G3 (73). Numbers within circles indicate the count of patients with metastatic lymph nodes in each anatomic region. Because a single patient may have metastases in multiple regions, the sum of numbers may exceed the total number of lymph node-positive patients. Anatomic pelvic lymph node regions are color-coded: orange—peri-vesical, red—internal iliac/obturator, blue—external iliac, green—common iliac, purple—presacral, yellow—paraortic.

pT4G3 tumors. Similarly, paraortic nodes were uninvolved in pT2G3 tumors but accounted for 3.4% and 5.7% of metastases in pT3G3 and pT4G3 tumors, respectively (Fig. 3, Table E1).

Notably, among pT2G3, pT3G3, and pT4G3 patients with lymph node metastasis, 96.9% (31/32), 93.6% (88/94), and 84.9% (62/73) of patients had metastases exclusively below the iliac bifurcation, whereas 100% (32/32), 95.7% (90/94), and 95.9% (70/73) of patients had metastases exclusively below the aortic bifurcation, respectively (Fig. 1). Analysis of 731 documented metastatic lymph nodes revealed consistent spatial patterns: In pTa/Tis/T1 and pT2 tumors, 100% and 98.8% of nodal metastases, respectively, were restricted to regions inferior to the iliac vessel bifurcation. In advanced-stage tumors (pT3-4), whereas most metastases (~90%) remained below the

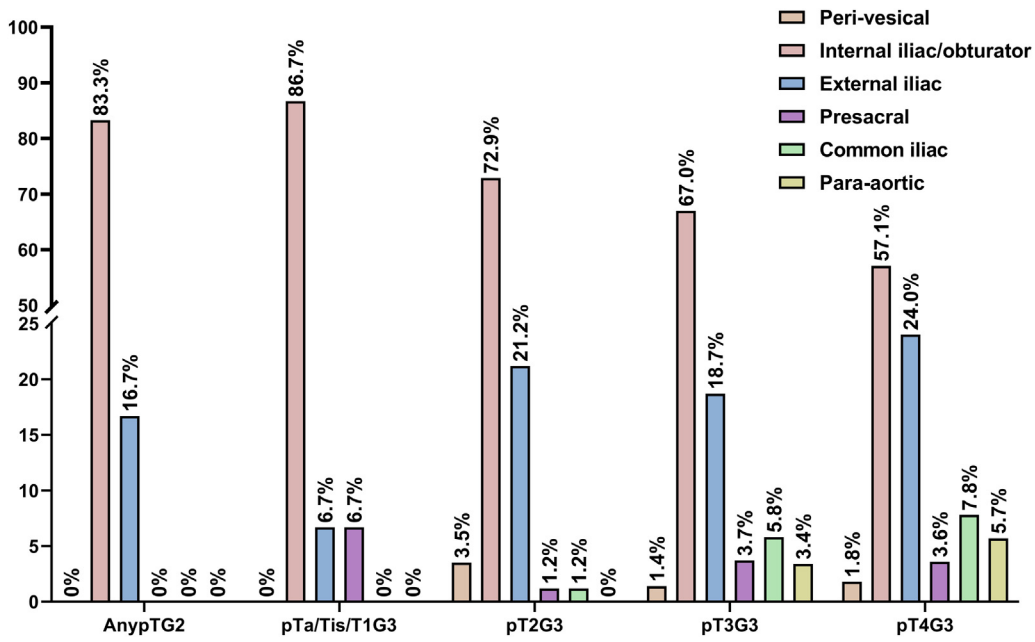

Figure 3 Proportion of metastatic lymph nodes in each anatomic zone in the 210 mapped patients, categorized by pathological T-stage and G-grade subgroups. Because individual patients may have disease in multiple regions, column totals may exceed 100%.

iliac vessel bifurcation, a proportion (~10%) extended superiorly to involve common iliac vessels and paraortic lymph nodes. Notably, 96.6% of metastatic lymph nodes in pT3G3 cases localized below the aortic bifurcation, contrasting with 5.7% supra-aortic bifurcation involvement in pT4G3 tumors (Fig. 2, Table E1).

We performed a subgroup analysis on the 112 patients receiving neoadjuvant chemotherapy (NAC), with full details in Supplementary Material. Among these, 18 (16.1%) had pathologically confirmed lymph node metastases (pN+), showing a T-stage-dependent increase in positivity: pT1 (2.5%), pT2 (9.7%), pT3 (28.6%), pT4 (46.2%), and a higher rate in G3 (20.5%) versus G2 (4.5%) tumors. Anatomic mapping in 11 node-positive patients revealed metastatic patterns correlated with T-stage: T1-T2 lesions were confined to the internal iliac/obturator and external iliac regions, while T3-T4 lesions extended to the common iliac and paraortic regions, aligning with progressive anatomic involvement. Although limited by sample size, this preliminary analysis suggests that the fundamental correlation between pathological T-stage and pelvic nodal spread may persist following NAC.

Discussion

This study provides a comprehensive mapping of PLNM patterns in bladder urothelial carcinoma that integrates both T-stage and histological grade (G-grade), offering a refined framework for risk assessment. Although T-stage has traditionally guided PLNM evaluation, we demonstrate that G-grade further stratifies metastatic risk and anatomic distribution. These findings enable personalized radiation therapy field design, optimizing risk-adapted coverage tailored to individual T/G characteristics.

Our data confirm a strong correlation between T-stage/G-grade and PLNM risk: lymph node metastasis rates escalate from 2.6% in pTa/Tis/T1 tumors to 50.0% in pT4 disease, with 97.0% of metastatic cases involving high-grade (G3) tumors. These findings align with the T-stage-dependent metastatic patterns historically reported by Stein et al.[15] in cystectomy series (5.0% for pT1, 18.0% for pT2, 28.0% for pT3a, 46.0% for pT3b, and 42.0% for pT4 disease), while extending prior observations through quantitative integration of histological grade—a key marker of biologic aggressiveness. The <5% PLNM rate in patients with G1-2 tumors or NMIBC aligns with prior studies,[16,17] supporting the classification of these patients as a low-risk population for pelvic nodal metastasis. In contrast, MIBC with G3 demonstrated a significantly higher PLNM rate of 25.9% (285/1,099), highlighting the necessity of comprehensive nodal coverage for effective PLNM treatment.

At the clinical practice level, our anatomic mapping reveals distinct spatial progression patterns of lymph node metastasis across T/G subgroups. Among patients with G3 MIBC, over 95% of pT2G3 cases had metastases confined below the iliac bifurcation plane, suggesting a lesser propensity for distal nodal dissemination. This spatially restricted distribution pattern may provide valuable insights for lymphadenectomy boundaries or radiation

therapy field design in pT2G3 patients. By contrast, nodal spread above the bifurcation was observed in 6.4% of pT3G3 and 16.1% of pT4G3 node-positive cases, indicating greater distal involvement with advanced pathological T-stage and suggesting a need for extended treatment fields. These observations align with the adjuvant radiation therapy recommendations of Verghote et al,[18] who recommended that the clinical target volume for patients with high-risk MIBC (pT3-4, pN+) should include the entire common iliac nodal region, regardless of surgical margin status, because of the high risk of recurrence in this area. Because the common iliac region is not typically covered in standard pelvic lymph node dissection, recurrences likely originate from undetected primary metastatic nodes that remain post surgery. Our data provide anatomic validation for this approach and reinforce the clinical rationale for extended-field irradiation in advanced-stage disease. This consistency also affirms the validity of our mapping approach. Notably, although irradiation below the aortic bifurcation covered 95.9% of pT4G3 patients with nodal metastases, it encompassed only 94.3% of metastatic nodes. This residual risk of distant nodal spread, combined with the higher metastatic burden in pT4G3 cases (median 4.08 nodes vs 2.34 in pT2G3), underscores the potential need to integrate multimodal therapeutic strategies—such as systemic therapies—to optimize nodal control.

Although the necessity of PLN-RT remains debated in consensus guideline,[10] our data may offer additional insights to refine its application. The apparent contradiction between BC2001 trial[8,9] (supporting bladder-only radiation therapy) and RTOG protocols[3-6] (advocating whole-pelvic irradiation) could potentially reflect variations in the prevalence of PLNMs among different T-stage, G-grade bladder cancers. First, the BC2001 trial primarily recruited patients with T2 disease—a subgroup with only 11.0% PLNM rate in our cohort. Second, even without intentional PLN-RT, the planning target volume expansion (2 cm) in the BC2001 trial might have inadvertently irradiated pelvic lymph node regions with the highest risk of metastasis (eg, the internal iliac/obturator lymph node regions),[9] possibly explaining the acceptable PLN control in the bladder-only group. Conversely, T3-4 tumors exhibit a broader distribution of metastatic lymph nodes (~10% metastases involving the common iliac/paraortic regions), and these patients may potentially derive benefit from the RTOG protocols that recommend extended pelvic field irradiation to mitigate the risk of recurrence. Thus, trial discrepancies arise not from flawed methodology but from divergent patient risk profiles, underscoring the need for T/G-based patient selection in future trials. It should be noted that this study included patients across the pathologic spectrum, including 29.3% with NMIBC, to comprehensively map nodal metastatic patterns in urothelial carcinoma. However, because these patients are not typically candidates for radiation therapy, all analyses pertaining to radiation therapy field delineation are derived exclusively from the MIBC subgroup (n = 1099), ensuring direct clinical relevance to this population.

This study has several limitations. As a single-center retrospective analysis, potential selection bias may persist despite the large sample size. Patients with common iliac and/or paraortic nodal involvement at diagnosis were likely excluded because of surgical ineligibility, potentially underestimating the true incidence of common iliac and paraortic nodal metastases. Second, despite the increasing guideline-recommended adoption of NAC as preoperative therapy,[19,20] only 7.2% (112/1550) of the cohort received documented NAC, primarily because of both incomplete documentation of early-case NAC administration in our database and the historical underutilization of preoperative chemotherapy during the initial study period. Although this maintains natural nodal metastatic patterns of untreated bladder urothelial carcinoma, it precludes definitive assessment of NAC's potential impact on lymphatic dissemination routes. An exploratory analysis of the small NAC-treated subset revealed a suggestive trend: T-stage-dependent anatomic patterns of lymphatic spread appeared maintained despite systemic therapy. However, the limited number of node-positive NAC patients leaves the question of whether neoadjuvant therapies alter nodal distribution patterns unanswered, necessitating future large-scale investigations. Additionally, although T-stage and histologic grade effectively stratified nodal risk, integrating molecular subtypes (eg, basal vs luminal) could further refine predictions, as The Cancer Genome Atlas data suggest basal tumors exhibit distinct nodal tropism.[21]

Future studies should evaluate the feasibility of individualized treatment strategies based on T/G-stage-specific nodal metastasis patterns. For instance, in patients with T2G3 tumors, could radiation therapy confined to fields below the iliac bifurcation achieve oncologic and survival outcomes comparable with current guideline-recommended protocols? A prospectively designed clinical trial is urgently warranted to validate these findings. Furthermore, although this study supports the clinical justification for pelvic irradiation in the treatment of G3 MIBC, the relatively low metastasis rate among T2G3 patients (12.3%) highlights the imperative to address overtreatment in node-negative T2G3 cases. Emerging modalities including radiomics,[22] artificial intelligence-driven analyses,[23] molecular biomarkers,[24] and novel radiotracers[25] are advancing early identification of lymph node-positive patients, thereby paving the way for precision diagnostics and patient management.

Conclusions

This study systematically elucidates the spatial distribution patterns of lymph node metastasis in bladder

urothelial carcinoma, showing that both T-stage and histological grade affect PLNM incidence and anatomic spread. Although therapeutic implications require validation in prospective trials, these data highlight the interplay of tumor stage and biologic aggressiveness in shaping PLNM patterns across risk strata. These insights may inform future personalized treatment strategies for bladder cancer based on tumor stage and grade.

Disclosures

None.

Ethics approval

Ethics approval was obtained from the Ethics Committee of the Peking University First Hospital (2025-111). All methods were carried out in accordance with relevant guidelines and regulations.

Acknowledgments

We acknowledge Qin Du and Tongtong Wang for their valuable assistance during the data collection phase of this research. Tian Cheng was responsible for statistical analysis.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.prro.2025.10.002.

References

1. National Comprehensive Cancer Network. Bladder Cancer (Version 1.2025). Accessed March 25, 2025. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf.
2. van der Heijden AG, Bruins HM, Carrion A, et al. European Association of Urology guidelines on muscle-invasive and metastatic bladder cancer: Summary of the 2025 guidelines. *Eur Urol*. 2025;87:582-600.
3. Kaufman DS, Winter KA, Shipley WU, et al. The initial results in muscle-invading bladder cancer of RTOG 95-06: Phase I/II trial of transurethral surgery plus radiation therapy with concurrent cisplatin and 5-fluorouracil followed by selective bladder preservation or cystectomy depending on the initial response. *Oncologist*. 2000;5:471-476.
4. Hagan MP, Winter KA, Kaufman DS, et al. RTOG 97-06: Initial report of a phase I–II trial of selective bladder conservation using TURBT, twice-daily accelerated irradiation sensitized with cisplatin, and adjuvant MCV combination chemotherapy. *Int J Radiat Oncol Biol Phys*. 2003;57:665-672.
5. Kaufman DS, Winter KA, Shipley WU, et al. Phase I-II RTOG Study (99-06) of patients with muscle-invasive bladder cancer undergoing transurethral surgery, paclitaxel, cisplatin, and twice-daily radiotherapy followed by selective bladder preservation or radical cystectomy and adjuvant chemotherapy. *Urology*. 2009;73:833-837.
6. Mitin T, Hunt D, Shipley WU, et al. Transurethral surgery and twice-daily radiation plus paclitaxel-cisplatin or fluorouracil-cisplatin with selective bladder preservation and adjuvant chemotherapy for patients with muscle invasive bladder cancer (RTOG 0233): A randomised multicentre phase 2 trial. *Lancet Oncol*. 2013;14:863-872.
7. Marcq G, Kool R, Dragomir A, et al. Benefit of whole-pelvis radiation for patients with muscle-invasive bladder cancer: An inverse probability treatment weighted analysis. *J Clin Oncol*. 2025;43:308-317.
8. Hall E, Hussain SA, Porta N, et al. Chemoradiotherapy in muscle-invasive bladder cancer: 10-yr follow-up of the phase 3 randomised controlled BC2001 trial. *Eur Urol*. 2022;82:273-279.
9. James ND, Hussain SA, Hall E, et al. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer. *N Engl J Med*. 2012;366:1477-1488.
10. Khalifa J, Supiot S, Pignot G, et al. Recommendations for planning and delivery of radical radiotherapy for localized urothelial carcinoma of the bladder. *Radiother Oncol*. 2021;161:95-114.
11. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: Long-term results in 1,054 patients. *J Clin Oncol*. 2023;41:3772-3781.
12. Amin MB, Edge SB, Greene FL, et al. *AJCC Cancer Staging Manual*. 1024. Springer; 2017.
13. Compérat EM, Burger M, Gontero P, et al. Grading of urothelial carcinoma and the new "World Health Organisation classification of tumours of the urinary system and male genital organs 2016". *Eur Urol Focus*. 2019;5:457-466.
14. Herr HW, Bochner BH, Dalbagni G, Donat SM, Reuter VE, Bajorin DF. Impact of the number of lymph nodes retrieved on outcome in patients with muscle invasive bladder cancer. *J Urol*. 2002;167:1295-1298.
15. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: Long-term results in 1,054 patients. *J Clin Oncol*. 2001;19:666-675.
16. Babjuk M, Burger M, Capoun O, et al. European association of urology guidelines on non-muscle-invasive bladder cancer (Ta, T1, and Carcinoma in Situ). *Eur Urol*. 2022;81:75-94.
17. Amling CL, Thrasher JB, Frazier HA, Dodge RK, Robertson JE, Paulson DF. Radical cystectomy for stages Ta, Tis and T1 transitional cell carcino ma of the bladder. *J Urol*. 1994;151:31-35. [discussion" 35-36].
18. Verghote F, Sargos P, Christodouleas JP, et al. International consensus guidelines for adjuvant radiation therapy for bladder cancer after radical cystectomy: Update from an IBIS workgroup. *Pract Radiat Oncol*. 2022;12:524-532.
19. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med*. 2003;349:859-866.
20. Advanced Bladder Cancer (ABC) Meta-analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: Update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. *Eur Urol*. 2005;48:202-205. [discussion: 205-206].

21. Robertson AG, Kim J, Al-Ahmadie H, et al. Comprehensive molecular characterization of muscle-invasive bladder cancer. *Cell*. 2017;171:540-556.e25.
22. Gresser E, Woźnicki P, Messmer K, et al. Radiomics signature using manual versus automated segmentation for lymph node staging of bladder cancer. *Eur Urol Focus*. 2023;9:145-153.
23. Harmon SA, Sanford TH, Brown GT, et al. Multiresolution application of artificial intelligence in digital pathology for prediction of positive lymph nodes from primary tumors in bladder cancer. *JCO Clin Cancer Inform*. 2020;4:367-382.
24. Seiler R, Lam LL, Erho N, et al. Prediction of lymph node metastasis in patients with bladder cancer using whole transcriptome gene expression signatures. *J Urol*. 2016;196:1036-1041.
25. Novruzov E, Dendl K, Ndlovu H, et al. Head-to-head intra-individual comparison of [(68)Ga]-FAPI and [(18)F]-FDG PET/CT in patients with bladder cancer. *Mol Imaging Biol*. 2022;24:651-658.