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# An Investigation of the Pathology Report of Bladder Cancer Patients with Radical Cystectomy in Southern Iran, 2013-2018: A Cross-Sectional Study

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## Abstract

**Background:** The oncological outcomes of bladder cancer are directly associated with disease pathology and surgical technique. Therefore, we investigated the pathologic factors of radical cystectomy (RC) specimens.

**Methods:** In this retrospective study, 365 patients who underwent RC between March 2013 to March 2018 in hospitals affiliated to Shiraz University were enrolled. The patients' clinicopathological parameters, such as tumor type, tumor grade, carcinoma in situ, lymph node (LN) involvement, lymphovascular invasion (LVI), perineural invasion (PNI), and age, were recorded from their pathology reports. For comparison of variables, an independent t test was used. $P < 0.05$ was regarded as significant. The statistical software SPSS version 22 was used to examine the data.

**Results:** The participants' mean age was 64.52 ± 11.54 years, and 320 (87.7%) patients were men and 45 (12.3%) were women. The mean dissected LN was 9.69 ± 8.70 nodes and 1.06 ±3.49 of the dissected LNs were involved by tumor. PNI and perivesical invasion were presented in 148 (40.5%) and 96 (26.3%) patients, respectively. Ureteral, urethral, and prostate involvements were seen in 23 (6.3%), 50 (13.7%), and 66 (18.1%) patients. Most patients had pathologic tumor stage 2 (36.4%). Factors such as LVI, PNI, perivesical invasion, and prostate involvement, were strongly correlated with positive LN ($P \leq 0.05$).

**Conclusion:** The examination of the RC specimen is critical for patient care, outcome, and justification of adjuvant therapy. Factors such as LVI, perineural invasion, perivesical invasion, and prostate involvement were strongly correlated with positive LN.

**Keywords:** Bladder Cancer, Radical Cystectomy, Pathology, Lymph Node

***Conflicts of Interest:*** *None declared*
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## Introduction

Bladder cancer (BC) is the most prevalent urinary tract cancer globally, and it is the 4th largest in men in the United States, resulting in significant morbidity and mortality (1). About 2.7 million people suffer from BC worldwide. In Iran, the incidence rate of RC is about 11.2 per 100,000 in men. It accounts for 8% and 3% of all ma-

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***↑What is "already known" in this topic:***
Pathologic evaluation of the soft tissue as well as the lymph node status has a significant influence on the outcome of patients with muscle-invasive bladder cancer (BC) after radical cystectomy (RC). Our study was conducted to investigate the pathologic factors of BC patients treated with RC in a cross-sectional study.

***→What this article adds:***
Findings of this study indicates that examination of the specimen obtained from RC is essential for patient management, outcome, and rationale of adjuvant therapy. Factors such as lymphovascular invasion, perineural invasion, perivesical invasion, and prostate involvement were strongly correlated with positive lymph node.



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lignancies in men and women; the age-standardized incidence rate of BC among Iranian women was lower than that of Iranian men (2.79 per 100,000) (2, 3). BC is usually treated with transurethral endoscopic surgical resection and the use of intravesical therapeutic agents. The recurrence rate ranged between 50% to 70%, while 10% to 15% of patients developed muscle invasion over 5 years (1). Nonmuscle-invasive BC, which represents a heterogeneous group of cancers that include those that are papillary and limited to the mucosa (Ta), high grade, flat and confined to the epithelium (Tis), and invasive into the submucosa, or lamina propria, accounts for 80% of patients who initially presented with BC (T1). However, between 35% to 48% of T1 BC patients will progress to muscle-invasive BC (MIBC) within 3 years if treated with transurethral resection alone (4).

The standard treatment for patients with clinically localized MIBC is RC with reciprocal pelvic lymph node dissection (PLND). The use of neoadjuvant chemotherapy might be a legitimate choice for MIBC. However, the benefit of neoadjuvant chemotherapy is still debated for all patients. In addition, it is appropriate to recommend urgent RC to patients with nonmuscle-invasive BC who are at high risk of disease progression and for all patients with nonmuscle invasive BC failing endovesical therapy (5).

RC with PLND gives great local control and long-term survival for patients with MIBC and high-grade BC (6). Full surgical excision and pathological evaluation of soft-tissue margin and LN status have a significant influence on the outcome of MIBC patients following RC (6). Our study was conducted to investigate the pathologic factors of BC patients treated with RC in a cross-sectional study.

## Methods

This is a retrospective study, which was approved by the ethics committees of Shiraz University of Medical Sciences (ID code: 14828 and the ethics number: IR.SUMS.MED.REC.1397.258) and performed in accordance with Declaration of Helsinki.

### *Data Inclusion*

Consecutive patients with BC, treated with RC from March 2013 to March 2018 in Shiraz University hospitals, were enrolled in this study. Our BC database prospectively collects clinical and pathological data from patients who undergo RC. Patients who were inoperable at the time of exploration or had undergone cystectomy for other (nonbladder) pelvic malignancies were excluded.

### *Data Gathering*

Data on the tumour characteristic variables comprising the tumour type, grade, and stage, surgical margin status, LN involvement, lymphovascular invasion (LVI), age, and gender were gathered from the patients' medical records and pathology reports. The American Joint Committee on Cancer Tumor, nodes, and metastases classification was used for pathologic staging and the World Health Organization classification from 2004 for histological typing and grading (7).

### *Surgical Method*

RC incorporated a wide dissection of the perivesical tissue around the bladder and prostate in men and the urethra and vagina in women. The typical dissection of pelvic LN incorporated the distal common iliac, external iliac, and hypogastric and obturator nodes, which were submitted as isolated specimens for pathologic assessment (6). In a few elderly or sick patients, restricted LN dissection was submitted with the cystectomy specimen.

### *Statistical Analysis*

The mean and standard deviation was used to describe quantitative data, whereas the frequency was used to describe qualitative factors. For comparison of the equality of 2 mean values in qualitative variables and default equality of variances of independent variables, a t test or a nonparametric Mann-Whitney U test was applied. The Pearson correlation coefficient test was used to determine the correlation between different variables. $P < .05$ was considered significant. The data were analysed using statistical software SPSS Version 22 (SPSS Inc).

## Results

### *Patients' Characteristics*

Overall, 365 patients were identified who met our criteria during the study period. The mean age of the participants was 64.52 ± 11.54 years. All patients were deemed medically fit to undergo cystectomy, and all underwent a grossly complete resection of the regional and primary BC. The patients' pathology types were urothelial cell carcinoma (UCC) (94.5%), squamous cell carcinoma (SCC) (2.5%), adenocarcinoma (0.6%), prostatic carcinoma (0.5%), rhabdomyosarcoma (0.13%), and poorly differentiated carcinoma (0.3%).

About 320 (87.7%) patients were men and 45 (12.3%) were women. As for the histopathologic grade, the high grade 4, grade 3, grade 2, and well-differentiated ones were seen in 292 (80%), 47 (12.9%), 4 (1.1%), and 1 (0.3%) patients, respectively.

### *Clinicopathological Parameters*

From 301 patients under lymphadenectomy, about 219 (72,8%) had no LN involvement, and about 82 (27,8%) had LN involvement. The mean dissected LN was 9.69 ± 8.70 nodes, and 1.06 ± 3.49 of the dissected LNs were involved by tumour.

LVI was presented in 133 (36.4%) patients. Perineural invasion (PNI) and perivesical invasion were presented in 148 (40.5%) and 96 (26.3%) patients, respectively. Ureteral involvement was seen in 23 (6.3%) patients. Also, urethral involvement was seen in 50 (13.7%) patients. Prostate involvement in men was seen in 66 (18.1%) patients and uterus involvement in 5 (1.4%) women. Most patients had pathologic T2N0Mx (36.4%). A total of 74 (20.3%) patients had tumour necrosis in the pathologic specimen (Table 1).

### *Relationship Between Positive LN and Other Pathological Parameters*

The association between the numbers of LN assessed





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*Table 1.* Characteristics of the enteric population

| | |
|---|---|
| Age (year) ±SD | 64.52 ± 11.54 |
| Gender, N (%) | |
| Male | 320 (87.7%) |
| Female | 45 (12.3%) |
| Pathologic tumor grade, N (%) | |
| Grade 4 | 292 (80%) |
| Grade 3 | 47 (12.9%) |
| Grade 2 | 3 (0.8%) |
| Grade 1 | 5 (1.4%) |
| Not reported | 18 (4.9%) |
| Concomitant carcinoma in situ, N (%) | 60 (16.4%) |
| LVI, N (%) | 133 (36.4%) |
| Perineural invasion, N (%) | 148 (21.1%) |
| Perivesical invasion, N (%) | 96 (26.3%) |
| Ureteral invasion, N (%) | 23 (6.3%) |
| Urethral invasion, N (%) | 50 (13.7%) |
| Prostate involvement, N (%) | 66 (18.1%) |
| Uterus involvement, N (%) | 5 (1.4%) |
| Pathologic tumor stage, N (%) | |
| T0/pTa/pTis | 5 (1.4%) |
| T1 | 42 (11.5%) |
| T2 | 131 (35.9%) |
| T3 | 96 (26.3%) |
| T4 | 91 (24.9%) |
| Tumor necrosis, N (%) | 74 (20.3%) |

LVI; Lymphovascular invasion, SD; Standard deviation

*Table 2.* Relationship between positive lymph node and other pathological parameters

| Factor | Presentation | positive lymph node (Mean Rank) | p-value |
|---|---|---|---|
| LVI | Absent | 126.78 | ≤ 0.001 |
| | Presented | 185.77 | |
| Perineural invasion | Absent | 134.27 | ≤ 0.001 |
| | Presented | 168.80 | |
| Perivesical invasion | Absent | 141.51 | ≤ 0.001 |
| | Presented | 129.52 | |
| Ureteral involvement | Absent | 146.71 | 0.098 |
| | Presented | 171.95 | |
| Urethral involvement | Absent | 133.95 | 0.105 |
| | Presented | 151.28 | |
| Prostate involvement | Absent | 127.65 | 0.020 |
| | Presented | 148.85 | |
| CIS | Absent | 146.97 | 0.414 |
| | Presented | 155.21 | |
| Tumor necrosis | Absent | 146.68 | 0.452 |
| | Presented | 153.79 | |
| Pathologic tumor stage | pT0/pTa /pTis | 0.00 | ≤0.001 |
| | PT1 | 106.00 | |
| | PT2 | 108.94 | |
| | PT3 | 116.08 | |
| | PT4 | 239.87 | |

Note: P-values of <0.05 were considered significant.
CSI; Carcinoma in situ, LVI; Lymphovascular invasion.

and the number of positive LNs was extremely significant among individuals who had positive LN (r = 0.139; P = 0.020).

Indeed, factors such as LVI, PNI, perivesical invasion, and prostate involvement, were strongly correlated with positive LN (P ≤ 0.05). However, there was no correlation with urethral, ureteral involvement, and carcinoma in situ (CIS) (Table 2).

## Discussion

Our results showed that examination of the specimen obtained from RC was critical for patient management, outcome and rationale of adjuvant therapy. Factors such as LVI, PNI, perivesical invasion, and prostate involvement were strongly correlated with positive LN.

The incidence of BC increased with age and peaked in the 6th and 7th decades. About 80% of cases occurred in patients aged 65 and over (8, 9). Previous metanalysis conducted in Iran showed that the male to female sex age-standardized incidence rate ratio was 3.9. and the highest incidence rate which was reported from Mazandaran province was 31 for men (18.5 per100,000) (3). Our results were in the same line with those of the mentioned study.

In the West, more than 90% of the primary BCs are transitional cell carcinoma (TCC). The remnants consist of SCC (5%), adenocarcinoma (2%), and rare tumours, such as sarcoma, melanoma, and lymphoma (8). Soave et al reported that 80.2% of the patients had pure UCC,




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squamous cell differentiation (12.6%), sarcomatoid (2.7%), and small cell differentiation (2.1%) (10). We showed similar rates of TCC and other bladder cancer subtypes.

The rate of patients with pathologic tumor stage 2 disease reported in our study is similar to those observed in previous studies (9, 11). However, if we only consider the patients classified as pT3-pT4 and compare them with the study of Renato et al (9), we observe a higher percentage of patients in this pathologic stage in our study. Our explanation was that some patients in our study refused cystectomy at an earlier stage because of religious and cultural reasons, and they underwent RC in an advanced stage.

In our study, LVI was shown in 133 (36.4%) patients. In a series of 243 RCs by Tilki et al, it was found that 22 (9.1%) patients had LVI in the RC specimen; they concluded that positive LVI increased the risk of the recurrence of BC (12).

Microscopic invasion of perivesical fat was accompanied by a lower survival rate. We showed a similar rate of perivesical invasion with previously published articles such as that conducted by Scosyrev et al (13).

PNI has been recognized by numerous authors as an independent predictive factor for the survival rate (14). In our study, PNI was presented in 148 (40.5%) patients. In the study of Rao et al, PNI was identified in 101(23%) patients. It was suggested that PNI with UCC might be accompanied by inferior prognosis, specifically for extravesical and LN-positive disease subsequent RC (15). On the other hand, Antunes et al identified PNI in 10 (8.8%) out of 113 patients and concluded that PNI did not constitute an independent factor of cancer-free and survival rate (16). This different finding across all articles might be due to variable cohort sizes and varied study populations.

Ureteral involvement was seen in 23 (6.3%) patients. In a series of 402 RCs by Kim et al, of 11% of the primary positive frozen sections (FS), 8% had the ultimate positive ureteral segment. The hazard factors for ureteral involvement were the presence of CIS and intramural ureteral invasion (17). Positive final and initial margin status were attributed to upper urinary tract recurrence. Although the marginal status of the distal ureters was not accompanied by overall or cancer-specific survival, they concluded that change to negative margins was probable and is accompanied by reduced hazard of recurrence during the follow-up (18).

Assessment of the prostate sample after RC is essential for satisfactory staging (19). In our study, urethral and prostate involvement was seen in 50 (13.7%) and 66 (18.1%) patients. Brant et al reported that about 63 (35.6%) patients had prostatic urethral invasion accompanied by inferior survival rate (20). Additionally, Solsona et al found that about 21 (15.2%) patients had prostate involvement, which is consistent with the results of the present research (21).

Despite regular resection of gynaecological structures during RC, there is no proof of gynaecological findings in female patients in the existing research. For example, in a series of 382 RCs by Chang et al, it was found that only 3 women (7.5 %) who had intact gynaecologic organs removed at RC developed cancer within the gynaecological component, counting 2 with TCC accompanied by primary BC and 1 with stromal sarcoma initiating from the uterus (22). In another study by Stein et al, 8 patients had invasion to the vagina, uterus, and/or ovary. However, the tumour was locally extensive in all (23). Similar to previous studies, we found uterus involvement in 5 (1.4%) patients.

The biomolecular mechanisms of TN that affect the oncologic behaviour are still not completely understood. Rapid tumour cell proliferation expanding to the vascular supply makes a hypoxic environment and then TN. Finally, the TN promotes the metastatic cascade (24). In our study, about 74 (20.3%) patients had TN in their pathologic specimens. Accordingly, Soave et al, in a series of 517 RCs, revealed that TN was present in 156 (30.2%) patients. They concluded that TN was firmly associated with destructive tumour features and lower oncologic consequences (25).

In our study, 219 patients (72,8%) had no LN involvement, whereas 82 (27,8%) had LN involvement, which was higher than that previously reported by Train et al (26). In this study, 114 patients (19%) had LN involvement. They concluded that the increased risk of cancer-specific death was significantly accompanied by the number of positive LN (1 or 2 or more) (26). Our explanation for the high rate of positive LN was religious and cultural beliefs. Some patients refused cystectomy during the early stages and underwent RC in advanced stages.

In our study, among the patients who had positive LN, the association between the number of LN examined and the number of positive LN was highly significant. Besides, factors such as LVI, PNI, perivesical invasion, and prostate involvement had a strong correlation with positive LN. However, there was no correlation with urethral, ureteral involvement, and CIS. In the same line, Tilki et al reported that LVI and positive LN led to inferior outcomes and metastasis, which is a powerful factor in predicting the clinical outcomes after RC (12). Marks et al reported that metastases to LN was seen in 26.7% of patients, with 8% of patients having extranodal extension (27). Soave et al reported that advanced age, high tumour stage, metastases to the LN as well as positive surgical edge were the independent predictors for recurrence and CSM in RC patients (10). However, the small sample size of our study compared with other reports might mask the association between the positive LN, urethral involvement, ureteral involvement, and CIS.

The current study had some limitations. First, the relationship among clinicopathologic markers and overall survival was not investigated. Therefore, we recommended a 5-year survival of the same population. Second, clinical outcomes, such as recurrence, requiring further treatment like radiotherapy, and adjuvant chemotherapy after surgical treatment, were not investigated. Third, the postoperative complication was not mentioned. The retrospective nature of our study was the next limitation. Finally, participants in this study underwent RC by different urologist surgeons and several pathologists assessed the specimens, leading to potential differences in diagnosis of





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histopathologic parameters and tumour.

## Conclusion

Assessment of the specimen obtained after radical cystectomy is critical for patient care, outcomes, and rationale of adjuvant therapy. Factors such as LVI, perineural invasion, perivesical invasion, and prostate involvement strongly correlated with a positive LN. Therefore, these variables should be used in managing this disease by improving the prevention and prognosis of the disease. Hence, we advocate that more research be performed to evaluate the correlation of clinicopathologic characteristics with survival rate to determine the relevance of these variables in comparison with the current research design.

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### *Ethical Approval*

The protocol of the study was approved by the local Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1397.258). The present article was extracted from the thesis written by Sara Saeedi, supported by Shiraz University of Medical Sciences.

### *Conflict of Interests*

The authors declare that they have no competing interests.

## References

1. Shariat SF, Sfakianos JP, Droller MJ, Karakiewicz PI, Meryn S, Bochner BH. The effect of age and gender on bladder cancer: a critical review of the literature. BJU Int. 2010;105(3):300-8.
2. Payandeh M, Sadeghi M, Sadeghi E. Characteristics of Patients With Transitional Cell Carcinoma of the Urinary Bladder in Kermanshah Province, Iran. Iran J Cancer Prev. 2015;8(6):e4038.
3. Hassanipour S, Delam H, Fathalipour M, Sharifi M, Abdzadeh E, Fouladseresht H, et al. The incidence of bladder cancer in Iran: a systematic review and meta-analysis. WCRJ. 2019;6(e1222):1-10.
4. Benidir T, Herrera-Caceres J, Wallis C, Lajkosz K, Fleshner N. Population-based analysis of perioperative chemotherapy use, interventions requiring hospitalization and atheroembolic events among patients with non-metastatic muscle-invasive bladder cancer. Cancer Med. 2021;10(8):2636-44.
5. Mari A, Campi R, Tellini R, Gandaglia G, Albisinni S, Abufaraj M, et al. Patterns and predictors of recurrence after open radical cystectomy for bladder cancer: a comprehensive review of the literature. World J Urol. 2018;36(2):157-70.
6. Stein JP, Lieskovsky G, Cote R, Groshen S, Feng AC, Boyd S, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. J Clin Oncol. 2001;19(3):666-75.
7. Karia PS, Morgan FC, Califano JA, Schmults CD. Comparison of Tumor Classifications for Cutaneous Squamous Cell Carcinoma of the Head and Neck in the 7th vs 8th Edition of the AJCC Cancer Staging Manual. JAMA Dermatol. 2018;154(2):175-81.
8. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, et al. Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology. 2005;66(6 Suppl 1):4-34.
9. Corradi RB, Galvao GJ, Oliveira GM, Carneiro VF, Miconi WG, Salles PG, et al. Radical cystectomy with pelvic lymphadenectomy: pathologic, operative and morbidity outcomes in a Brazilian cohort. Int Braz J Urol. 2016;42(3):431-7.
10. Soave A, Schmidt S, Dahlem R, Minner S, Engel O, Kluth LA, et al. Does the extent of variant histology affect oncological outcomes in patients with urothelial carcinoma of the bladder treated with radical cystectomy? Urol Oncol. 2015;33(1):21.e1-.e9.
11. Bochner BH, Dalbagni G, Sjoberg DD, Silberstein J, Keren Paz GE, Donat SM, et al. Comparing Open Radical Cystectomy and Robot-assisted Laparoscopic Radical Cystectomy: A Randomized Clinical Trial. Eur Urol. 2015;67(6):1042-50.
12. Tilki D, Reich O, Svatek RS, Karakiewicz PI, Kassouf W, Novara G, et al. Characteristics and outcomes of patients with clinical carcinoma in situ only treated with radical cystectomy: an international study of 243 patients. J Urol. 2010;183(5):1757-63.
13. Scosyrev E, Yao J, Messing E. Microscopic invasion of perivesical fat by urothelial carcinoma: implications for prognosis and pathology practice. Urology. 2010;76(4):908-13; discussion 14.
14. Leissner J, Koeppen C, Wolf HK. Prognostic significance of vascular and perineural invasion in urothelial bladder cancer treated with radical cystectomy. J Urol. 2003;169(3):955-60.
15. Rao M, Vellos T, Barkan G, Gupta GN, Flanigan RC, Quek ML. Prognostic implications of perineural invasion following radical cystectomy for urothelial carcinoma. 2012;30(15_suppl):e15014-e.
16. Antunes AA, Nesrallah LJ, Dall'Oglio MF, Crippa A, Nesrallah AJ, Paranhos M, et al. Perineural invasion by transitional cell carcinoma of the bladder in patients submitted to radical cystectomy: what is the prognostic value? Int Braz J Urol. 2007;33(2):161-6.
17. Kim HS, Moon KC, Jeong CW, Kwak C, Kim HH, Ku JH. The clinical significance of intra-operative ureteral frozen section analysis at radical cystectomy for urothelial carcinoma of the bladder. World J Urol. 2015;33(3):359-65.
18. Tollefson MK, Blute ML, Farmer SA, Frank I. Significance of distal ureteral margin at radical cystectomy for urothelial carcinoma. J Urol. 2010;183(1):81-6.
19. Ariafar A, Zeighami S, Salehipour M, Ahmed F, Shahabi Z, Nikbakht H-A. An Investigation of the Pathology Report of Prostate Cancer Patients with Radical Prostatectomy in Southern Iran: A Cross-sectional Study Middle East J Cancer. 2021;12(1):69-78.
20. Brant A, Daniels M, Chappidi MR, Joice GA, Sopko NA, Matoso A, et al. Prognostic implications of prostatic urethral involvement in non-muscle-invasive bladder cancer. World J Urol. 2019;37(12):2683-9.
21. Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Almenar S. Extravesical involvement in patients with bladder carcinoma in situ: biological and therapy implications. J Urol. 1996;155(3):895-9; discussion 9-900.
22. Chang SS, Cole E, Smith JA, Jr., Cookson MS. Pathological findings of gynecologic organs obtained at female radical cystectomy. J Urol. 2002;168(1):147-9.
23. Stein JP, Cote RJ, Freeman JA, Esrig D, Elmajian DA, Groshen S, et al. Indications for lower urinary tract reconstruction in women after cystectomy for bladder cancer: a pathological review of female cystectomy specimens. J Urol. 1995;154(4):1329-33.
24. Park SY, Lee HS, Jang HJ, Lee GK, Chung KY, Zo JI. Tumor necrosis as a prognostic factor for stage IA non-small cell lung cancer. Ann Thorac Surg. 2011;91(6):1668-73.
25. Soave A, John LM, Dahlem R, Minner S, Engel O, Schmidt S, et al. The Impact of Tumor Diameter and Tumor Necrosis on Oncologic Outcomes in Patients With Urothelial Carcinoma of the Bladder Treated With Radical Cystectomy. Urology. 2015;86(1):92-8.].
26. Tarin TV, Power NE, Ehdaie B, Sfakianos JP, Silberstein JL, Savage CJ, et al. Lymph node-positive bladder cancer treated with radical cystectomy and lymphadenectomy: effect of the level of node positivity. Eur Urol. 2012;61(5):1025-30.
27. Marks P, Gild P, Soave A, Janisch F, Minner S, Engel O, et al. The impact of variant histological differentiation on extranodal extension and survival in node positive bladder cancer treated with radical cystectomy. Surg Oncol. 2019;28:208-13.



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