Original Article

A novel nomogram for predicting post-operative recurrence for patients with intermediate and high-risk non-muscle invasive bladder cancer after thulium laser resection of bladder tumors or conventional transurethral resection of bladder tumors followed by intravesical bacille Calmette-Guérin immunotherapy

Meng-Yao Xu[1#], Jian-Xuan Sun[1#], Yu-Xi Xiang[2#], Zi-Jin Hua[3], Chen-Qian Liu[1], Ye An[1], Jin-Zhou Xu[1], Si-Han Zhang[1], Zheng Liu[1*], Shao-Gang Wang[1*], Qi-Dong Xia[1*]

[1]Department and Institute of Urology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [2]Division of Endocrinology, Department of Internal Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [3]Department of Urology, 920th Hospital of Joint Logistics Support Force of Chinese People's Liberation Army, Kunming, China

Contributions: (I) Conception and design: MY Xu, JX Sun, YX Xiang; (II) Administrative support: SG Wang, QD Xia; (III) Provision of study materials or patients: Z Liu; (IV) Collection and assembly of data: MY Xu, JX Sun, ZJ Hua; (V) Data analysis and interpretation: MY Xu, JX Sun; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work as co-first authors.

[*]These authors contributed equally to this work.

Correspondence to: Qi-Dong Xia, PhD; Shao-Gang Wang, PhD; Zheng Liu, PhD. Department and Institute of Urology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095 Jiefang Avenue, Wuhan 430030, China. Email: qidongxia_md@163.com; sgwangtjm@163.com; lz2013tj@163.com.

Background: Post-operative recurrence for patients with intermediate and high-risk non-muscular invasive bladder cancer (NMIBC) is common. This study aims to evaluate the potential factors of tumor recurrence, and construct a novel nomogram to predict the probability of tumor recurrence.

Methods: We retrospectively enrolled patients with intermediate and high-risk NMIBC who received thulium laser resection of bladder tumors (TmLRBT) or transurethral resection of the bladder tumor (TURBT) followed by intravesical bacille Calmette-Guérin (BCG) immunotherapy. The risk factors were screened by the least absolute shrinkage and selection operator (LASSO) regression method. And multivariate logistic regression was applied to recognize the independent risk factors of bladder cancer recurrence. A nomogram was established, and the recurrence probability was calculated based on the model scores.

Results: A total of 90 patients with intermediate and high-risk NMIBC were included in this study, of whom 53 underwent TURBT and 37 underwent TmLRBT. During the follow-up period, 22 patients (24.4%) experienced bladder cancer recurrence. Three variables were screened out in the LASSO regression. The multivariate logistic analysis suggested that surgery of TURBT [odds ratio (OR) =6.86760; 95% confidence interval (CI): 1.5048–31.34300] and previous bladder tumor (OR =14.73600; 95% CI: 2.81180–77.23000) were independent risk factors of recurrence, while more BCG treatment sessions (OR =0.26504; 95% CI: 0.12455–0.56398) was independent protective factor of recurrence.

Conclusions: Patients with TURBT and previous bladder tumor history were more likely to develop recurrent bladder cancer, while more BCG treatment sessions was independent protective factor of recurrence.

Keywords: Non-muscular invasive bladder cancer (NMIBC); recurrence; nomogram; thulium laser resection of bladder tumors (TmLRBT); transurethral resection of the bladder tumor (TURBT)

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Introduction

Bladder cancer is the tenth most common tumor around the world and the second most common malignancy in the urinary system (1-3). According to the pathological features, bladder cancer can be divided into muscular invasive bladder cancer (MIBC) and non-muscular invasive bladder cancer (NMIBC), and the latter accounts for approximately 75% of the newly diagnosed cases (4). NMIBC is further classified based on the depth of tumor invasion into Ta (limited to bladder mucosa), T1 (invading lamina propria) and Tis (tumor in situ) as per the different depth of tumor invasion (5). According to the World Health Organization (WHO) 2004/2016 or WHO 1973 grading classification system, NMIBC risk groups are categorized as low, intermediate, high and very high risk.

Transurethral resection of the bladder tumor (TURBT) is the standard and most commonly performed treatment for NMIBC, followed by intravesical immunotherapy with bacille Calmette-Guérin (BCG) or intravesical chemotherapy (6,7). Nevertheless, significant hematuria and urinary tract infections are common complications following intravesical BCG therapy after surgery, while bladder perforation and obturator nerve reflex (ONR) are serious complications of TURBT (8). With the increasing adoption of laser therapy, thulium laser resection of bladder tumors (TmLRBT) has emerged as an alternative to TURBT. This approach not only addresses the aforementioned complications but also prominently reduces catheterization time and recurrence rates in NMIBC patients (9).

Effective BCG immunotherapy highly relies on adequate intravesical administration, along with complete induction and maintenance therapy (10). The European Association of Urology (EAU) guidelines recommend that intermediate risk patients receive induction intravesical chemotherapy or BCG immunotherapy, followed by one year of maintenance therapy. For high-risk patients, it is recommended to extend the treatment for 3 years (4). However, a large proportion of patients do not respond satisfactorily to intravesical BCG therapy. After BCG treatment, the tumor may recur in a short time, and in some cases, it may even progress to MIBC and/or metastatic bladder cancer. For NMIBC patients initially classified as intermediate or high-risk who received conservative treatment, relapse after 10 years of disease-free survival is not uncommon (11).

To identify and manage NMIBC patients with tumor recurrence as early as possible, we assessed the potential risk factors in patients with intermediate and high-risk NMIBC who underwent TmLRBT or conventional TURBT followed by intravesical BCG immunotherapy. Based on our findings, we developed a novel nomogram to predict the probability of tumor recurrence. We present this article in accordance with the TRIPOD reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-535/rc).

Highlight box

Key findings

- A novel nomogram has been established, and the recurrence probability of non-muscular invasive bladder cancer (NMIBC) can be calculated based on the model scores.

What is known and what is new?

- Post-operative recurrence for patients with intermediate and high-risk NMIBC is common.
- Patients with transurethral resection of the bladder tumor (TURBT) and previous bladder tumor history are more likely to develop recurrent bladder cancer, while more bacille Calmette-Guérin (BCG) treatment sessions is independent protective factor of recurrence.

What is the implication, and what should change now?

- For patients with TURBT and previous bladder tumor history, further management should be strengthened. Moreover, NMIBC patients should receive regular BCG treatment.

Methods

This study was conducted in accordance with Declaration

of Helsinki (as revised in 2013). The Ethics Committee of Tongji Medical College approved this study (Grant number: TJ-IRB20210106). The informed consent was exempted by the ethics committee for this retrospective and observational study. The study data were searched from our institutional database. And we retrospectively included 90 patients with bladder cancer who underwent TmLRBT or TURBT between August 2018 and December 2019, including 68 non-recurrent cases and 22 recurrent cases.

Inclusion and exclusion criteria

The inclusion criteria of this study were as follows: (I) pathologically diagnosed as NMIBC; (II) stratified as intermediate or high-risk according to EAU guidelines (4); (III) undergoing conventional TmLRBT or TURBT; (IV) receiving standard BCG intravesical therapy postoperatively.

The follows were the exclusion criteria: (I) pathologically diagnosed as MIBC; (II) classification as low-risk NMIBC; (III) diagnosis of other tumor diseases; (IV) incomplete clinical information or insufficient follow-up time.

The main outcome of interest was the recurrence of bladder cancer. Cystoscopy is the foremost choice for postoperative reexamination in patients with NMIBC. According to current guidelines, patients with NMIBC should undergo their first cystoscopy 3 months after surgery (12). If suspicious lesions are observed on the bladder mucosa during this examination, a biopsy should be performed to confirm the pathological results and determine whether recurrence has occurred. Additionally, if necessary, urine exfoliative cytology, computed tomography (CT), CT urography (CTU), magnetic resonance imaging (MRI), or MR urography (MRU) may be utilized for further evaluation (4).

General information

We retrieved the medical records of all patients and collected their original characteristics from Tongji Hospital's database. The enumeration data included gender, type of surgery (TmLRBT, TURBT), history of previous bladder tumor, tumor multiplicity, tumor location (lateral, other), tumor stage (Tis, Ta, T1), tumor grade [papillary urothelial neoplasms of low malignant potential (PUNLMP), low grade, high grade], risk (intermediate, high), ONR, perforation, hematuria, irrigation, progression. The quantitative data information includes age, tumor number, tumor size, operative time, time of catheterization, hospital stay, the number of BCG therapy sessions.

All patients chose either TmLRBT or TURBT based on the merits and risks of the two procedures, after being fully informed. All surgeries were performed by experienced urologists following standard protocols. Patients with NMIBC received immediate intravesical instillation of 30 mg gemcitabine to prevent tumor cell implantation (13). The optimal perfusion time is within 6 hours after surgery. However, immediate perfusion is not recommended in cases of intraoperative bladder perforation or severe gross hematuria; in such cases, it should be completed within 24 hours. Intravesical BCG instillation is recommended for patients with intermediate or high-risk of NMIBC (4). For intermediate-risk patients, 2 g of BCG was added to 50 mL saline weekly for 6 weeks, then biweekly for 6 weeks, followed by biweekly instillation for 6 weeks, and then monthly for 10 months. For high-risk patients, BCG intravesical infusion should be extended monthly for 1–2 years.

Statistical analysis

Statistical analysis was conducted using Statistical Product and Service Solutions (SPSS) version 25.0 and R x64 4.1.2. Categorical variables were expressed as number (percentages), with differences between groups assessed using the Chi-squared test or Fisher's exact test. The Kruskal-Wallis *H* test was used to compare ordinal variables across multiple independent samples, with results shown as proportions. Continuous variables were presented as mean ± standard deviation. For normally distributed data, differences between groups were analyzed using the Student's *t*-test. The Mann-Whitney *U*-test was used for continuous variables with a skewed distribution, represented as median (interquartile range). The least absolute shrinkage and selection operator (LASSO) regression method was used to screen the risk factors. Multivariate logistic regression was applied to recognize the independent risk factors for bladder cancer recurrence. The regression coefficients were scaled to a 0–100 point scale (14), which was then used to develop a nomogram to predict the probability of recurrence. The model's predictive performance was evaluated using receiver operating characteristic (ROC) curves, calibration curves, decision curve analysis (DCA), and clinical impact curves (CICs) (15,16). All the statistical tests were bilateral tests, and the P value <0.05 indicated statistically significant.

Results

Patient characteristics

Twenty-two patients with recurrence and 68 patients without recurrence were finally enrolled in this study. The basic characteristics of the patients are presented in *Table 1*. Compared to the non-recurrence group, the recurrence group was characterized by previous bladder tumor (P=0.01), progression (P<0.001), and less BCG treatment sessions (P<0.001). Nevertheless, there were no significant statistical difference (P>0.05) between these two groups among gender, age, surgery type, tumor number, tumor multiplicity, tumor location, tumor grade, risk, tumor size, operative time, tumor stage, ONR, hematuria, perforation, irrigation, time of catheterization or hospital stay.

LASSO regression and multivariable logistic analysis

We identified three variables through LASSO regression: surgery type, history of previous bladder tumors, and the number of BCG therapy sessions (*Figure 1A*,*1B*). Subsequently, we conducted multivariate logistic analysis. Two independent risk factors for recurrence were identified (*Table 2*): surgery of TURBT [odds ratio (OR) =6.86760; 95% confidence interval (CI): 1.5048–31.34300] and a history of previous bladder tumors (OR =14.73600; 95% CI: 2.81180–77.23000). Conversely, a higher number of BCG treatment sessions (OR =0.26504; 95% CI: 0.12455–0.56398) was identified as an independent protective factor against recurrence.

To further support our findings, we performed univariate logistic regression for each parameter, with the results presented in Table S1. While some P values approached statistical significance, these results may have been influenced by the limited sample size in certain subgroups. Our multivariate analysis, which accounts for confounding variables and minimizes collinearity, remains the preferred method for identifying independent predictors of recurrence.

Predictive nomogram

The nomogram diagram integrated the above three prediction factors identified through multivariate regression analysis (17). Each predictive factor corresponds to a certain point, and the total scores is obtained by summing the points of each factor, which can be used predict the corresponding probability of bladder cancer recurrence.

For example, consider a patient with previous bladder tumor who underwent TURBT surgery and received 12 sessions of BCG therapy (*Figure 2*). The total score for this patient was 216, and the corresponding probability of bladder cancer recurrence was 0.949 (95% CI: 0.725–0.994).

The calibration curves proved that the predicted probabilities were in great agreement with the observed values, as confirmed by the Hosmer-Lemeshow (HL) test (P=0.95) (*Figure 3A*). To assess the model's performance of the model, we analyzed the ROC curve and area under the curve (AUC) value (*Figure 3B*). The AUC value of this model was 0.86, which was higher than those of other univariate models, such as the model based on the number of BCG therapy sessions (AUC =0.75), previous bladder tumor history (AUC =0.63), and surgery type (AUC =0.62). The DCA determined the clinical practicability of the prediction model by quantitatively verifying the net benefits under varying threshold probabilities in the data set (18). The DCA results revealed a wide threshold probability range, showing that using our nomogram model to predict postoperative bladder cancer recurrence was more beneficial than "treat-none" or "treat-all-patients" strategies (*Figure 4A*). Moreover, the CIC suggested the excellent clinical efficiency of the prediction model (*Figure 4B*), as the predicted number of positive cases closely aligned with the actual number of positive cases.

Discussion

Approximate 30–80% of NMIBC cases will recur (19,20) and 1–45% of NMIBC cases will develop into MIBC within 5 years (21), indicating that carcinoma control for NMIBC remains unsatisfactory. The causes of recurrence include failure to detect tumors during cystoscopy, metastasis from upper tract urothelial carcinoma, incomplete surgical resection, and postoperative tumor reimplantation (22). The recurrence rate of bladder cancer in our study was 24.4%, lower than that reported in previous researches. This difference can likely be attributed to the strict management and follow-up protocols for patients diagnosed with bladder cancer in Tongji Hospital. Early prediction and intervention are significant for the prevention and management of NMIBC. In this study, we developed a novel predictive nomogram model, incorporating surgery type, previous bladder tumor history and number of BCG therapy sessions, to estimate the probability of recurrence in intermediate and high-risk NMIBC patients treated with TmLRBT or TURBT followed by BCG immunotherapy.

Table 1 Basic characteristics of including patients

Characteristics	Overall (n=90)	Recurrence (n=22)	Not recurrence (n=68)	P value
Gender				0.95
Male	72 (80.0)	17 (77.3)	55 (80.9)	
Female	18 (20.0)	5 (22.7)	13 (19.1)	
Age (years)	60.94±10.63	61.55±14.13	60.75±9.35	0.76
Surgery type				0.08
TmLRBT	37 (41.1)	5 (22.7)	32 (47.1)	
TURBT	53 (58.9)	17 (77.3)	36 (52.9)	
Previous bladder tumor				0.01*
No	75 (83.3)	14 (63.6)	61 (89.7)	
Yes	15 (16.7)	8 (36.4)	7 (10.3)	
Tumor number	2.53±3.59	3.27±6.07	2.29±2.31	0.27
Tumor multiplicity				0.46
No	45 (50.0)	9 (40.9)	36 (52.9)	
Yes	45 (50.0)	13 (59.1)	32 (47.1)	
Tumor size (cm)	1.99±0.98	1.85±1.00	2.04±0.98	0.46
Location				0.96
Lateral	63 (70.0)	16 (72.7)	47 (69.1)	
Other	27 (30.0)	6 (27.3)	21 (30.9)	
Stage				0.052
Tis	5 (5.6)	2 (9.1)	3 (4.4)	
Ta	36 (40.0)	4 (18.2)	32 (47.1)	
T1	49 (54.4)	16 (72.7)	33 (48.5)	
Grade				0.41
PUNLMP	2 (2.2)	0 (0.0)	2 (2.9)	
Low grade	19 (21.1)	3 (13.6)	16 (23.5)	
High grade	69 (76.7)	19 (86.4)	50 (73.5)	
Risk				0.24
Intermediate	18 (20.0)	2 (9.1)	16 (23.5)	
High	72 (80.0)	20 (90.9)	52 (76.5)	
Operative time (min)	36.11±21.20	40.68±27.14	34.63±18.89	0.25
ONR				0.64
No	82 (91.1)	19 (86.4)	63 (92.6)	
Yes	8 (8.9)	3 (13.6)	5 (7.4)	
Perforation				>0.99
No	87 (96.7)	21 (95.5)	66 (97.1)	
Yes	3 (3.3)	1 (4.5)	2 (2.9)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Overall (n=90)	Recurrence (n=22)	Not recurrence (n=68)	P value
Hematuria				0.27
No	48 (53.3)	9 (40.9)	39 (57.4)	
Yes	42 (46.7)	13 (59.1)	29 (42.6)	
Irrigation				0.21
No	28 (31.1)	4 (18.2)	24 (35.3)	
Yes	62 (68.9)	18 (81.8)	44 (64.7)	
Catheterization (days)	2.71±1.46	3.14±1.88	2.57±1.27	0.12
Hospital stay (days)	3.76±2.50	4.09±2.71	3.65±2.44	0.47
Progression				<0.001*
No	80 (88.9)	12 (54.5)	68 (100.0)	
Yes	10 (11.1)	10 (45.5)	0 (0.0)	
Number of BCG therapy sessions	20.29±6.84	15.32±6.88	21.90±6.05	<0.001*

Data are presented as n (%) or mean ± standard deviation. *, P value <0.05 was considered statistically significant. TmLRBT, thulium laser resection of bladder tumors; TURBT, transurethral resection of bladder tumors; Tis, tumor in situ; PUNLMP, papillary urothelial neoplasms of low malignant potential; ONR, obturator nerve reflex; BCG, bacille Calmette-Guérin.

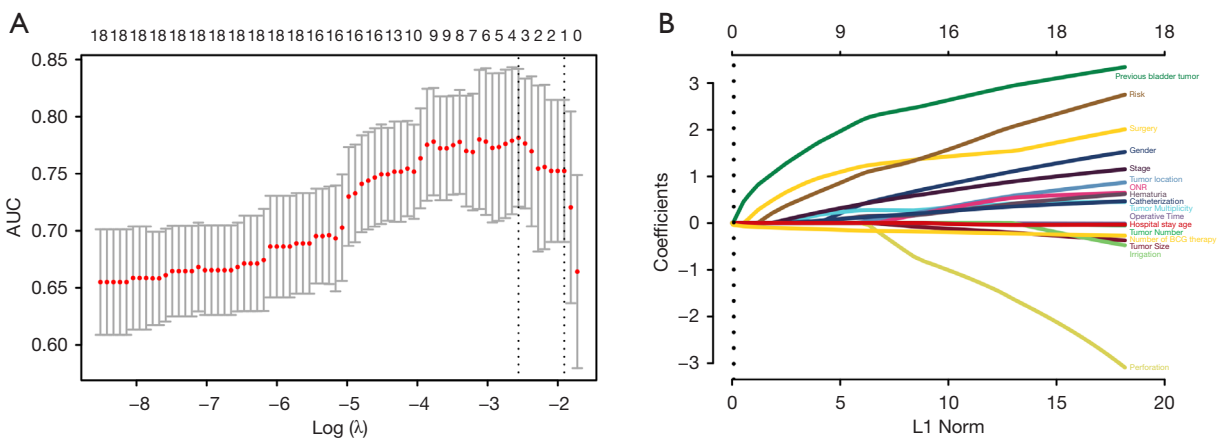

Figure 1 Selection of risk predictors through the LASSO logistic regression model. (A) The optimal predictor (λ) in the LASSO model was identified through fivefold cross-validation, guided by the minimum criteria. The relationship between the area under the receiver operating characteristic curve and log(λ) was visualized. Vertical dotted lines indicate the optimal values determined by the minimum criteria and the 1 SE of the minimum criteria. (B) Coefficient profiles of the 20 predictors in the LASSO model are displayed. The profile plot was generated based on the log(λ) sequence, with a vertical line marking the point identified through fivefold cross-validation, where three predictors were retained as optimal. AUC, area under the curve; ONR, obturator nerve reflex; BCG, bacille Calmette-Guérin; LASSO, least absolute shrinkage and selection operator; SE, standard error.

Based on this model, we provide a personalized prognosis prediction tool to guide further disease management for clinical patients.

At present, the "gold standard" for treating intermediate and high-risk NMIBC is TURBT followed by intravesical therapy (4,23). Nevertheless, one of the causes of tumor recurrence is the spread of fragmented tumor cells during TURBT (24,25), and TURBT is also associated with

Table 2 Multivariable logistic regression analysis of predictors of recurrence

Variables	B	SE	OR [95% CI]	P value
Surgery type	1.9268	0.7746	6.86760 [1.50480–31.34300]	0.01
Previous bladder tumor	2.6903	0.8452	14.73600 [2.81180–77.23000]	0.002
Number of BCG therapy	–0.1967	0.0571	0.26504 [0.12455–0.56398]	<0.001

B, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval; BCG, bacille Calmette-Guérin.

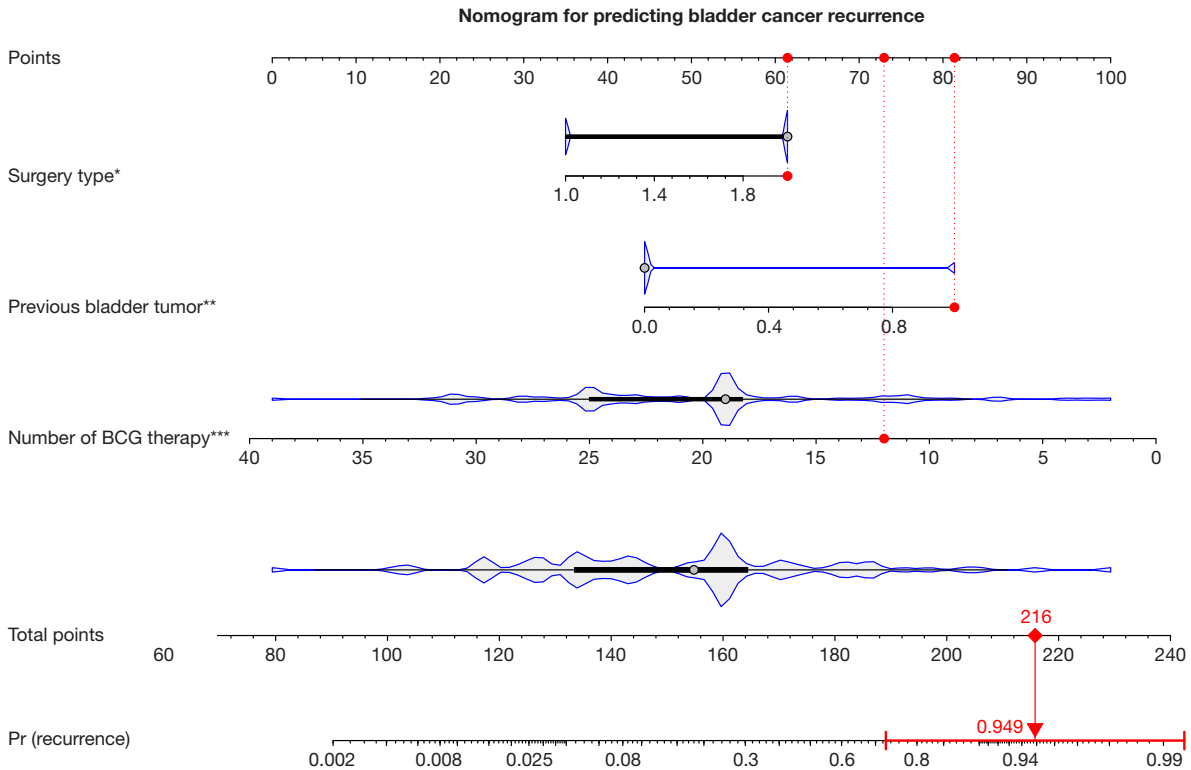

Figure 2 Nomogram for patients predicting postoperative tumor recurrence. The variables surgery, previous tumor history, and number of BCG treatments are assigned as "points." By summing these points, the total score can estimate the recurrence probability. A specific example involves a patient with bladder cancer who underwent TURBT surgery and received BCG therapy. The combined score of the relevant factors was 216, corresponding to a bladder cancer recurrence probability of 0.949 (95% CI: 0.725–0.994). Statistical significance is indicated by asterisks (*, P<0.05; **, P<0.01; ***, P<0.001). BCG, bacille Calmette-Guérin; TURBT, transurethral resection of bladder tumors.

complications such as urinary tract infection and severe hematuria (22). In contrast, TmLRBT offers advantages including simple operation, minimal thermal injury, and avoidance of complications like ONR and bladder perforation (26). Furthermore, complete enucleation of the lesion site and excellent hemostatic performance make TmLRBT more secure than TURBT (27,28). In our study, although more than half of the patients (58.9%) adopted TURBT, the proportion was higher in the recurrence group (77.3%), consistent with our LASSO regression results showing TURBT as an independent risk factor for recurrence. While univariate analysis did not reveal a significant difference in recurrence rates between TURBT and TmLRBT (*Table 1*), the multivariate logistic regression identified TURBT as an independent predictor of recurrence. This discrepancy is due to the ability of

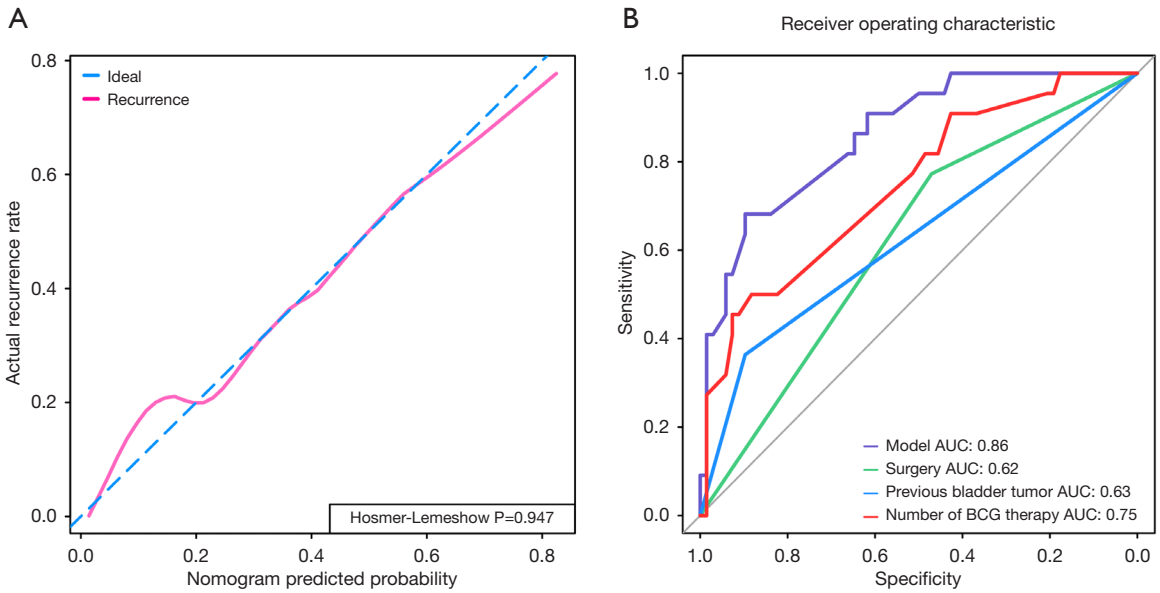

Figure 3 Predictive performance. (A) The calibration curve evaluates the model's fit, with an insignificant P value in the HL test confirming good calibration. (B) The ROC curve displays an AUC of 0.86, highlighting the model's strong discriminatory performance. AUC, area under the curve; BCG, bacille Calmette-Guérin; HL, Hosmer-Lemeshow; ROC, receiver operating characteristic.

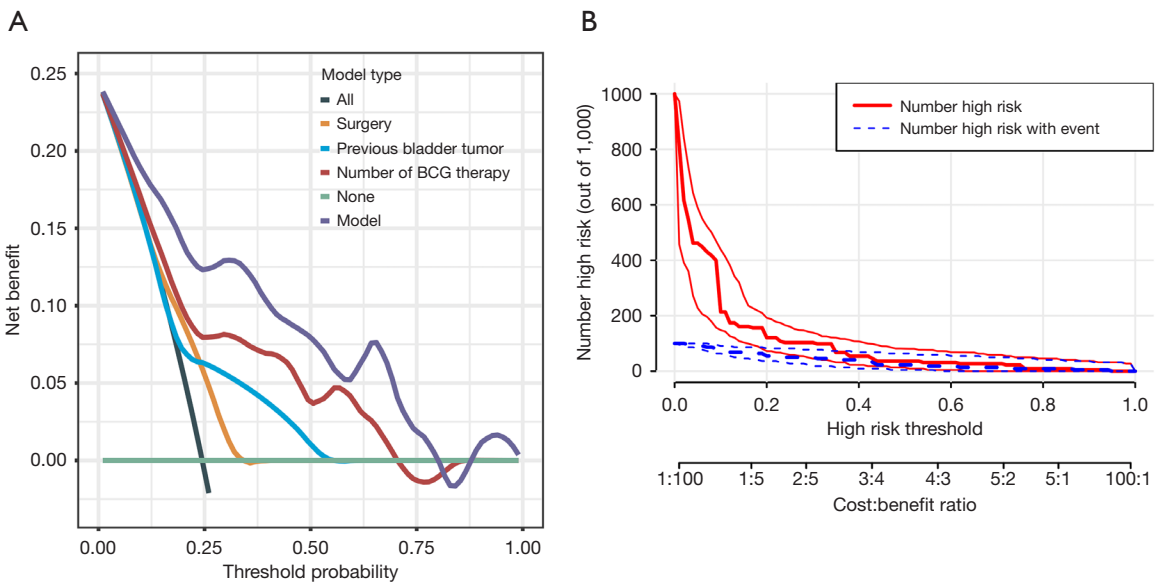

Figure 4 DCA and CIC. (A) DCA. When the risk threshold exceeds 2%, the net benefit of applying the model to guide interventions surpasses that of both the "treat-all-patient" and "treat-none" strategies. Moreover, the model outperforms individual factors such as surgery, prior bladder tumor history, or the number of BCG treatments. (B) CIC. The improved probability stratification of 1,000 samples is predicted on the CIC. The red curve shows the predicted improved number at different threshold probabilities and the blue curve represents actual improved patients. When the threshold probability was greater than 0.2, the predicted number was close to the actual number of positive cases, and the cost-benefit ratio was 0.2. BCG, bacille Calmette-Guérin; DCA, decision curve analysis; CIC, clinical impact curve.

multivariate analysis to adjust for confounding variables, which may have masked the effect of surgery type in the univariate analysis. By controlling for other clinical factors, multivariate analysis provides a more accurate estimate of the independent contribution of each variable to recurrence risk. Given the treatment principles of the guidelines, changing the surgical method in a short time may not be fully feasible. However, based on our study and other reports, we support the notion that TmLRBT may reduce the probability of recurrence of bladder cancer.

Although the effect of previous tumor history on the prognosis of bladder cancer has not been clearly determined (29), as a risk factor for recurrence and progression, previous bladder cancer can result in chronic irritation and infection to the bladder (30). A multivariate analysis of 1,062 patients with primary and recurrent intermediate and high-risk NMIBC revealed a significant association between a history of previous tumors and an increased risk of recurrence (31). Another retrospective study involving 191 patients showed that non-primary T1 NMIBC treated with BCG had a significantly higher risk of progression to MIBC compared to those with primary tumors (32). Our study also proved that a history of bladder tumor was an independent risk factor for bladder cancer recurrence. We hypothesize that this may be due to the diffusion and colonization of residual tumor cells in patients who have previous bladder cancer treatments, creating an environment conducive to recurrence. Schrier *et al.* explained that the faster recurrence and progression observed in patients with a history of bladder tumors may be attributed to the presence of both BCG-sensitive and BCG-insensitive cells in intermediate and high-risk NMIBC. The intravesical BCG therapy can effectively destroy the sensitive cells but may also promote the growth of more invasive, resistant cells (33). In addition, if the primary tumor is inadequately treated, the probability of recurrence will increase (34).

The standard BCG regimen consists of induction therapy for 6 weeks, followed by maintenance therapy for three weeks at 3, 6, and 12 months respectively (a total of 15 times) (4). BCG immunotherapy is not only the adjuvant therapy recommended by the EAU, but also demonstrates superior efficacy in preventing recurrence compared to intravesical chemotherapy (35). A retrospective study of 475 patients with intermediate and high-risk NMIBC who received incomplete BCG intravesical infusion or chemotherapy infusion showed that both BCG and chemotherapy reduced the risk of recurrence and were associated with better relapse-free survival (RFS) when the total number of instillation exceeded 12 (36). A randomized phase III clinical trial, "NIMBUS", revealed that in 170 high-grade NMIBC patients, reducing the number of infusions of BCG infusions shortened the time to bladder cancer recurrence, leading to the cessation of patient recruitment (37). The main side effects of intravesical instillation are BCG-related toxicity and chemical cystitis (36), which are influenced by the dose and frequency of instillation. Additionally, the shortage of BCG limits the ability to provide sufficient BCG infusion therapy for patients with bladder cancer (38). In our study, a higher number of BCG treatments was identified as an independent protective factor against bladder cancer recurrence, consistent with the findings of the studies mentioned above. Therefore, considering multiple factors, the standard BCG infusion sessions remains the guideline for treating intermediate and high-risk NMIBC treatment.

There are several limitations in this study. The primary drawbacks are its retrospective and observational design, which are associated with inherent biases (39). First, some patients lacked sufficient documentation of their information and follow-up records, which resulted in a limited sample size and potentially introduced selection bias. Although the type of surgery (TmLRBT *vs.* TURBT) was included in the nomogram due to its statistical significance in our cohort, its interpretation should be cautious given the absence of prospective randomized trials confirming its oncological superiority. Future studies are needed to validate this factor in a prospective setting. Additionally, our data were derived from a single institution, limiting its external applicability and generalizability. Treatment adherence to the EAU guidelines was also suboptimal, as treatment strategies were influenced by the preferences of the surgeons and the patients' willingness. Furthermore, certain factors, such as male sex, older age, and a higher number of tumors, which have been shown to be associated with an increased risk of bladder cancer recurrence (30), were not included in this model. Therefore, to obtain more rigorous conclusions, it is necessary to include a larger, more diverse patient cohort with complete clinical information through further prospective, multicenter studies.

Conclusions

We established a novel nomogram to predict the recurrence of bladder cancer in patients with intermediate and high-risk NMIBC after TmLRBT or TURBT followed by

intravesical BCG immunotherapy. Our findings indicated that patients who underwent TURBT and had a history of previous bladder tumors were more likely to experience recurrence. In contrast, a greater number of BCG treatment sessions emerged as an independent protective factor against recurrence.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-535/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with Declaration of Helsinki (as revised in 2013). The Ethics Committee of Tongji Medical College approved this study (Grant number: TJ-IRB20210106). The informed consent was exempted by the ethics committee for this retrospective and observational study.

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