e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(6); 1986-1990

Original Research Article

Predictive Factors for Early Recurrence after Transurethral Resection in Non-Muscle Invasive Bladder Cancer

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Received: 25-03-2024 / Revised: 23-04-2024 / Accepted: 26-05-2024
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Conflict of interest: Nil

Abstract:

Background: Non-muscle invasive bladder cancer (NMIBC) is well-known for its tendency to recur frequently following transurethral resection of the bladder tumour (TURBT). Understanding the factors that can predict early recurrence is essential for enhancing patient care and improving outcomes. The objective of this study is to analyse and assess various clinical and pathological factors, such as tumour size, number, grade, and inflammatory markers like the neutrophil-to-lymphocyte ratio (NLR), to determine their ability to predict early recurrence within 12 months after transurethral resection of bladder tumour (TURBT) in patients with non-muscle invasive bladder cancer (NMIBC).

Methodology: During the period from January 2020 to January 2022, a prospective cohort study took place at Osmania General Hospital in Hyderabad. The study involved patients with non-muscle invasive bladder cancer (NMIBC) who were undergoing transurethral resection of bladder tumour (TURBT). The researchers collected and recorded clinical, surgical, and pathological information from these patients. Patients who were diagnosed with muscle-invasive bladder cancer at staging or who did not consent to participate were excluded from the study. The statistical analysis was conducted using IBM SPSS. Chi-square tests were used to determine the significance of associations between tumour characteristics and recurrence rates.

Results: The research involved a sample of 100 individuals and revealed that within a year, 38% of them experienced a recurrence. Factors that were found to be significant in predicting the likelihood of recurrence were tumour size, with tumours larger than 3.5 cm having a recurrence rate of 34.7%, high tumour grade with a recurrence rate of 46.4%, and the presence of multiple tumours. A higher NLR (>2.8) also showed a significant correlation with increased recurrence rates, indicating its potential as a non-invasive biomarker for predicting outcomes.

Conclusion: The results highlight the significance of tumour size, grade, number, and NLR in predicting early recurrence in NMIBC. It is important to consider these factors when developing risk assessment tools in order to customise surveillance and treatment strategies. This could potentially lead to lower recurrence rates and better quality of life for patients.

Keywords: NMIBC, TURBT, Recurrence, Tumour, Neutrophil-To-Lymphocyte Ratio, Predictive Factors.

Introduction

Non-muscle invasive bladder cancer (NMIBC) accounts for a significant portion of bladder cancer (BC), which is one of the most prevalent cancers worldwide. NMIBC includes tumours that are confined to the bladder mucosa (Ta), those that invade the subepithelial connective tissue (T1), and carcinoma in situ (CIS), which are high-grade urothelial carcinomas that are non-invasive. NMIBC is characterised by high recurrence rates, which necessitate the implementation of targeted treatment strategies and rigorous postoperative surveillance in order to effectively manage the disease, despite the primary treatment being transurethral resection of bladder tumour (TURBT). One The high recurrence rate of NMIBC, which can reach as high as 80% within the first year of treatment, presents a substantial challenge in the management of the condition.[2] This highlights the significance of identifying predictive factors that can help stratify patients based on their risk of recurrence and adapt their follow-up accordingly. Numerous clinical and pathological variables have been identified as substantial predictors of recurrence. These include

the neutrophil-to-lymphocyte ratio (NLR), tumour size, grade, and number, which are indicative of the patient's underlying inflammatory state.[3,4]

The significance of tumour size and grade in predicting recurrence has been extensively documented. Higher recurrence rates and worse outcomes are linked to larger tumours and high-grade tumours.[5, 6] Additionally, the number of tumours at the time of the initial diagnosis is a critical factor; patients with multiple tumours have a higher probability of recurrence than those with a single tumour. [7] Intravesical therapies, particularly those that utilise agents such as Bacillus Calmette-Guérin (BCG) and mitomycin C, have been implemented to mitigate recurrence rates. Nevertheless, these treatments are accompanied by complications and limitations, such as systemic and localised side effects.[8, 9] The recurrence rates are also significantly influenced by the timing and completeness of TURBT, underscoring the importance of experienced surgeons and optimal surgical techniques.[10]

The accuracy of recurrence predictions has been demonstrated to be improved by recent developments in predictive models, which incorporate genetic and molecular markers. The objective of these models is to offer a more personalised risk assessment by combining them with traditional clinical and histopathological data. This has the potential to decrease the frequency of invasive surveillance procedures, such as cystoscopy.[11,12] For example, mutations in genes such as FGFR3, KDM6A, and STAG2 have been linked to recurrence and progression, making them potential biomarkers for risk stratification. [13,14]

The objective of this investigation is to assess the predictive factors for the early recurrence of NMIBC following TURBT, with a particular emphasis on clinical and pathological characteristics, including tumour size, number, grade, and NLR. Our objective is to enhance the management and surveillance protocols for NMIBC by identifying these factors, thereby reducing recurrence rates and enhancing patient outcomes.

Materials and Methods

This study was conducted at the Department of Urology, Osmania General Hospital in Hyderabad, from January 2020 to January 2022, after receiving approval from the Institutional Research and Ethical Committee. The study involved patients who were diagnosed with non-muscle invasive bladder cancer (NMIBC) and underwent a procedure called transurethral resection of the bladder tumour (TURBT). The eligibility criteria included patients who had recently been diagnosed with bladder cancer, whether it was a new case or a recurrence. The types of bladder cancer that were considered were Carcinoma In Situ (CIS), papillary urothelial neoplasm of low malignant potential (PUNLMP), or Stage Ta/T1 bladder cancer.

Patients who were diagnosed with muscle-invasive bladder cancer (MIBC) during staging TURBT, those who had incomplete initial resection revealing stage T2/MIBC upon second-look TURBT, and patients with associated upper tract urothelial malignancy or those who did not consent to participate were excluded from the study.

For data collection, we gathered detailed patient histories, conducted clinical examinations, and performed routine blood tests to calculate the neutrophil to lymphocyte and platelet to lymphocyte ratios. Additionally, we conducted urine cultures prior to TURBT. During the TURBT procedure, we carefully documented the characteristics of the tumour, including its location, size, and number.

After the TURBT procedure, tissue samples were collected for histopathological examination in order to determine the grade and stage of the cancer. The administration of BCG induction intravesical therapy followed the guidelines for CIS and high-grade tumours.

The patients were monitored for short-term recurrence, which is defined as recurrence within 12 months after TURBT, through clinical and cystoscopic examinations that continued for over a year.

We performed statistical analysis using IBM SPSS version 24. We used chi-square tests for bivariate analysis, considering a p-value below 0.05 as statistically significant.

Results

Table 1: Demographic and Clinical Characteristics of Patients

Characteristic	Value
Total Patients	100
Mean Age (years)	63 ± 9.714
Gender Distribution	91 males, 9 females
Smoking History	50%
Diabetes Status	50%
Delay to Treatment (months)	Mean 4.225 ± 7.3551

The study included a total of 100 patients, with an average age of 63 years, and a standard deviation of 9.714. The majority of individuals in the study were male, with 91 males compared to 9 females. Approximately half of the individuals in the study had a smoking history, while the other half were found to have diabetes. The typical time between diagnosis and treatment was around 4.225 months, with a variation of 7.3551 months.

Table 2: Characteristics and Outcomes of Tumors

Characteristic	Value	p-Value
Number of Tumors	1, 2-3, >3	0.000031
Tumor Size	<1 cm, 1-3.5 cm, >3.5 cm	<0.001
Tumor Grade	Low (74%), High (26%)	0.009
Site of Lesions	Lateral walls (92%)	-
Neutrophil to Lymphocyte Ratio	>2.8	0.017

The recurrence rates were found to be significantly influenced by the characteristics of the tumour. There were different numbers of tumours, categorised as 1, 2-3, and more than 3. The last category had a strong statistical correlation with early recurrence (p-value = 0.000031). The sizes of the tumours were categorised into three groups: less than 1 cm, between 1 and 3.5 cm, and greater than 3.5 cm. It was found that larger tumour sizes were strongly linked to higher rates of recurrence (p-value < 0.001). The tumour grade played a crucial role in determining the outcome. Around 74% of the tumours were classified as low grade, while 26% were classified as high grade. It was found that the high-grade tumours had a significant correlation with recurrence (p-value = 0.009). Most of the tumours were found on the side walls (92%). The Neutrophil to Lymphocyte Ratio greater than 2.8 also demonstrated a noteworthy association with recurrence (p-value = 0.017).

Table 3: Statistical Analysis of Predictive Factors for Recurrence

Predictive Factor	Significant Correlation	p-Value
Tumor Size	Yes	<0.001
Number of Tumors	Yes	0.000031
Tumor Grade	Yes	0.009
Neutrophil to Lymphocyte Ratio	Yes	0.017
Platelet to Lymphocyte Ratio	No	0.192

Several factors were found to be predictive of recurrence, including tumour size, number of tumours, tumour grade, and the Neutrophil to Lymphocyte Ratio. These factors demonstrated significant correlations with recurrence rates. Notably, bigger tumour size, a greater number of tumours, and high-grade tumours were linked to a higher chance of recurrence (p-values less than 0.001, 0.000031, and 0.009, respectively). The Neutrophil to Lymphocyte Ratio also showed a significant correlation with recurrence (p-value = 0.017). Unfortunately, the Platelet to Lymphocyte Ratio did not demonstrate a noteworthy correlation with recurrence (p-value = 0.192).

Table 4: Recurrence Rates by Tumor Characteristics

Tumor Characteristic	Recurrence within 12 months (%)
Overall	38%
Tumor Size >3.5 cm	34.7%
High Grade Tumor	46.4%

Within a year, the recurrence rate stood at 38%. Certain factors also played a role in the likelihood of recurrence. Tumours that were larger than 3.5 cm had a recurrence rate of 34.7%, while high-grade tumours had an even higher recurrence rate of 46.4%. The findings highlight how tumour characteristics play a crucial role in predicting the likelihood of short-term recurrence in individuals with non-muscle invasive bladder cancer after undergoing transurethral resection.

Discussion

The results of this investigation shed important light on the predictive variables linked to the early recurrence of non-muscle invasive bladder cancer (NMIBC) after bladder tumour transurethral resection (TURBT). In the first 12 months following TURBT, this cohort's overall recurrence rate was 38%. This rate is in line with earlier research that found that, depending on a variety of clinical and pathological factors, recurrence rates could range from 31% to 80%. [1,15]

Tumour Size and Recurrence: Our analysis showed that tumours larger than 3.5 cm had a 34.7% recurrence rate, supporting previous research findings that larger tumours have a higher chance of recurrence.[3]

This is in line with the guidelines of the European Association of Urology (EAU), which state that tumour size is a major risk factor for recurrence.[16] Bosschieter et al. discovered that in patients with larger tumours, immediate intravesical mitomycin C instillation following TURBT significantly decreased recurrence.[17] Tumour Grade: A higher recurrence rate of 46.4% was observed in high-grade tumours. The literature consistently demonstrates that high-grade tumours are more aggressive and prone to recurrence in comparison to low-grade tumours, which supports this finding.[18]This is crucial because, in order to manage the elevated risk, high-grade tumours require more stringent surveillance and possibly adjunctive treatments.[19] Sylvester et al. also demonstrated the significance of tumour grade in risk stratification by reporting that recurrence rates were significantly higher for high-grade tumours.[20]

Number of Tumours: Another important predictor was the quantity of tumours. The recurrence rate was significantly higher in patients with more than three tumours, which is in line with the results of multivariate analyses that highlight tumour multiplicity as a crucial component in recurrence prediction.[15] The number of tumours is regarded by the EAU and NCCN guidelines as a crucial factor in risk stratification models.[21, 22] Early intravesical chemotherapy post-TURBT in patients with multiple tumours significantly reduced recurrence rates, as shown by Gudjónsson et al. (2009), underscoring the significance of prompt postoperative management.[22]

Neutrophil to Lymphocyte Ratio (NLR): A study found a significant correlation between an elevated NLR (>2.8) and recurrence. This finding is consistent with other research that has highlighted the role of systemic inflammation in cancer prognosis. An underlying inflammatory state, which has been associated with worse outcomes in a number of cancers, including NMIBC, is reflected in high NLR.[24] According to Lenis et al., NLR was found to be a significant predictor of recurrence, indicating that it can be used as a readily accessible, non-invasive biomarker for recurrence risk assessment.[25]

Comparison with Other Studies: Sylvester et al.'s 12-month recurrence rate of roughly 47% in a larger cohort is similar to the recurrence rate we observed in our study.[20] Recurrence rates, however, can be impacted by modifications to treatment regimens, such as the application of intravesical therapies. The slightly lower recurrence rate in our study compared to studies where a higher percentage of patients received adjunctive intravesical treatment may be explained by the fact that only 25% of patients received BCG therapy.[26]

Limitations: This study's single-center design and comparatively small sample size in comparison to multicenter trials are its main drawbacks. Further research involving larger cohorts and longer follow-up periods is required to confirm these results and improve risk stratification models.

Conclusion

The study's conclusion emphasises the significance of tumour size, grade, number, and NLR as early recurrence predictors in NMIBC patients following TURBT. It is recommended that risk assessment tools incorporate these factors in order to enhance surveillance strategies and elevate patient outcomes.

By customising follow-up protocols according to these predictive factors, recurrence rates may be decreased and patients with NMIBC may have a higher quality of life.

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