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Preoperative Systemic Inflammatory Indices as Predictors of Malignant Pathology in Repeat Transurethral Resection for High-risk Non-muscle Invasive Bladder Cancer: Insights from a Cross-Sectional Study

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What's known on the subject? and What does the study add?

The clinical importance of repeat transuretral resection of bladder tumour (Re-TUR-BT) is to prevent understaging of non-muscle invasive bladder cancer (NMIBC), to remove any residual cancer that may have been overlooked during the first procedure, and to provide additional prognostic data. The pathological results from Re-TUR-BT operations are fundamental to the management of high-risk NMIBC patients. These results guide crucial decisions regarding bladder-sparing approaches versus radical cystectomy. The necessity for Re-TUR-BT procedures is well-documented in both the European Urological Association and American Urological Association guidelines. While the correlation between high-risk NMIBC and systemic inflammation indices has been extensively explored in the literature, our current study specifically investigates the impact of systemic inflammation indices derived from blood measurements taken immediately prior to Re-TUR-BT in predicting bladder cancer pathology. Our findings suggest that elevated levels of inflammation indices in patients with high-risk bladder cancer may significantly support the performance of Re-TUR-BT. This insight could enhance clinical decision-making and improve management strategies for patients facing high-risk NMIBC.

Abstract

Objective: This study investigates the predictive value of systemic inflammatory indices for repeat transuretral resection of bladder tumour (Re-TUR-BT) pathology in patients with high-risk non-muscle invasive bladder cancer (NMIBC).

Materials and Methods: We conducted a retrospective analysis of 83 patients diagnosed with primary bladder tumors who underwent Re-TUR-BT based on initial pathology results from January 2014 to December 2023. Patients were categorized into two groups based on Re-TUR-BT pathology: Group 1 (non-malignant at Re-TUR-BT) and group 2 (malignant at Re-TUR-BT). We compared systemic inflammatory markers between these groups.

Results: Of the 83 patients, 55 (82.5%) were in group 1 and 28 (17.5%) in group 2. Demographic characteristics showed no significant differences between the groups. However, upon comparison of operative and histopathological features, the incidence of T1 classification in first TUR-BT pathology, was significantly higher in group 2. Additionally, group 1 had a higher proportion of single tumors, whereas group 2 exhibited a greater incidence of two or more tumors, a difference that was statistically significant. Analysis of systemic inflammatory indices revealed no significant differences in the complete blood count results before the initial TUR-BT. However, both the systemic immune-inflammation index (SII) and neutrophil-to-lymphocyte ratio (NLR) showed significant differences before Re-TUR-BT.

Conclusion: Our study indicates that SII and NLR calculated prior to Re-TUR-BT can predict malignant pathology persistence in high-risk NMIBC patients. These findings underscore the potential of systemic inflammatory indices as valuable biomarkers in clinical practice.

Keywords: Bladder cancer, SII, NLR, TUR-BT

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Introduction

Bladder cancer (BC) is categorized into two main subtypes: Non-muscle-invasive BC (NMIBC) and muscle-invasive BC (MIBC), based on their clinical progression and prognosis. The standard treatment approach for NMIBC primarily consists of transurethral resection of the bladder tumour (TUR-BT), followed by intravesical instillation of either chemotherapy or immunotherapy, tailored to the patient's risk of disease recurrence and progression. To mitigate the risk of understaging that can occur during the initial TUR-BT, clinical guidelines recommend performing a second resection (Re-TUR-BT) within 4 to 6 weeks following the initial procedure (1). The rationale behind Re-TUR-BT is to prevent understaging of NMIBC, to remove any residual cancer that may have been overlooked during the first procedure, and to provide additional prognostic data. The incidence of understaging in NMIBC cases ranges from approximately 7% to 30%, and this figure can rise to as high as 45% when the initial TUR-BT specimen lacks detrusor muscle (2). The incidence of understaging in NMIBC cases is reported to range from approximately 7% to 30%. This percentage can increase to as much as 45% when the initial TUR-BT specimen does not contain detrusor muscle (2). Additionally, a recent study found that among 31 patients with T1 high-grade tumors, there was a high rate of Re-TUR-BT positivity, recorded at 58.5 % (3).

Despite patients achieving complete resection of NMIBC and undergoing adjuvant intravesical instillation therapy, it is noted that approximately 70% of them will experience disease recurrence. Furthermore, around 30% of these individuals may ultimately face disease progression (4). Recent studies have explored various prognostic models and biomarkers as potential predictors of BC recurrence to enhance clinical decision-making and patient counseling (5). Indeed, while the identification of biomarkers for BC has the potential to enhance prognostic accuracy and treatment personalization, several challenges have impeded their integration into routine clinical practice. High costs associated with these biomarkers, along with a lack of standardization across different laboratories and methods, have limited their widespread adoption.

The relationship between the body's inflammatory response and the development of cancer, including BC, has garnered significant attention in recent years. The connection between inflammation and tumors was first observed by Virchow in 1863 (6). Inflammation not only contributes to malignant transformation and metastasis but also forms an integral part of the tumor's local environment (7).

Emerging evidence indicates that inflammatory responses within the tumor microenvironment (TME) are crucial in BC tumorigenesis, proliferation, progression, and metastasis. The immune system, together with the inflammatory response and the TME, significantly influences the clinical and biological behavior and outcomes of BC (7).

Researchers have extensively investigated the prognostic value of inflammatory response markers in cancer through ratios such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio, and systemic immune-inflammation index (SII). These markers have been studied for their potential to predict cancer prognosis, offering insights into the complex interactions between inflammation and cancer dynamics (8).

To the best of our knowledge, no studies have specifically evaluated inflammatory indices for predicting Re-TUR-BT outcomes, despite their prognostic value in other BC contexts. In our study, we explored the relationship between inflammation indices and the likelihood of malignant pathology results in patients undergoing Re-TUR-BT for high-risk BC. Inflammatory indices may be important predictors of malignant pathology outcomes in patients undergoing Re-TUR-BT for high-risk BC, and their assessment may improve preoperative evaluation and treatment decision-making.

Materials and Methods

Ethics Statement

This research was carried out in accordance with the ethical guidelines established in the Declaration of Helsinki. All participants received comprehensive information regarding the study's objectives and provided their written informed consent. The Local Ethics Committee of Health Science University İstanbul Training and Research Hospital granted ethical approval for this study (approval number: 2024-97, date: 18.10.2024).

Study Design

In this study, we conducted a retrospective analysis of patients diagnosed with primary bladder tumors who underwent Re-TUR-BT operation based on their initial pathology results. The objective of the study was to investigate the predictive role of inflammatory indexes in assessing the likelihood of malignant pathology results within this high-risk patient cohort.

Selection of Participants

The study participants were high grade NMIBC patients who underwent Re-TUR-BT operation between January and December 2023. Patients with concomitant malignancies, a history of upper urinary tract transitional cell carcinoma, rheumatic diseases, prior cardiac surgery, and chronic renal failure were excluded from the analysis. A total of 83 patients who met the inclusion criteria were retrospectively analyzed (Figure 1).

Study Variables

Routine complete blood count measurements were obtained from all patients scheduled to undergo initial TUR-BT, diagnosed with primary bladder tumors, and from patients requiring Re-TUR-BT based on the findings of the initial pathology. These measurements were analyzed for the purpose of calculating systemic inflammatory indices. The time interval from the first operation to the second was recorded in days. The NLR, lymphocyte-to-monocyte ratio (LMR), PLR, monocyte-to-white blood cell ratio (MWR), SII, and systemic inflammatory response index (SIRI) were calculated using the following formulas: NLR = neutrophil/lymphocyte ratio; LMR = lymphocyte/monocyte ratio; PLR = platelet/lymphocyte ratio; MWR = monocyte/white blood cell ratio; SII = (neutrophil × platelet)/lymphocyte ratio; SIRI = (neutrophil × monocyte)/lymphocyte ratio.

At the commencement of the first operation, data regarding tumor size, number, and appearance type (papillary or solid) were retrospectively reviewed and utilized for analysis. Pathology specimens obtained from both the initial and Re-TUR-BT procedures were evaluated by the same pathologist at a single pathology clinic. Patients were categorized into two groups based on the pathology results of the Re-TUR-BT operation. The absence of any tumour detected on re-TURB was considered non-malignant, while the detection of Ta/T1 high-grade or carcinoma *in situ* (CIS) was considered malignant (group 1: Non-malignant at Re-TUR-BT, group 2: Malignant at Re-TUR-BT). Values were compared for both groups (Figure 1).

Statistical Analysis

Descriptive statistics were calculated for demographic and clinical characteristics. Continuous variables were expressed as median and interquartile range while categorical variables were expressed as frequencies and percentages. Mann-Whitney U test was used to compare non-normally distributed continuous variables, and chi-square tests were employed for categorical variables. The chi-square test was employed to analyze categorical data. A significance level of $p<0.05$ was established for all analyses.All statistical analyses were performed using SPSS version 28.0. Furthermore, a separate receiver operating characteristic (ROC) analysis was conducted to calculate the area under the curve (AUC) for distinguishing malignant pathology within each group.

Results

After applying the exclusion criteria, the study population was stratified into two groups based on the pathology results from the Re-TUR-BT operation. Group 1 consisted of 55 patients with non-malignant pathology findings, while group 2 included 28 patients with malignant pathology results.

The comparison of the demographic characteristics of the two groups is summarized in Table 1. There were no statistically significant differences in terms of age, gender, body mass index, smoking status, or comorbid conditions between the groups ($p>0.05$, for each).

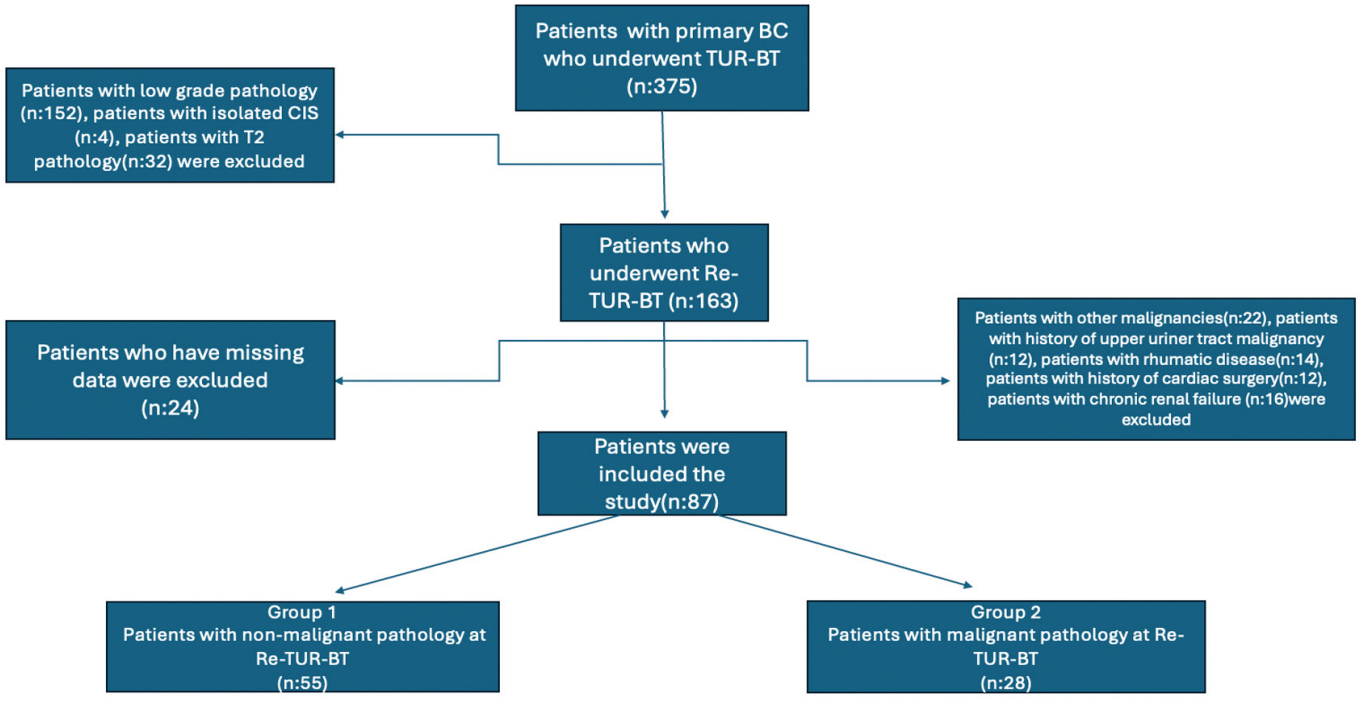

Figure 1. Flow chart of the patient's selection

CIS: Carcinoma in situ, TUR-BT: Transurethral resection of bladder tumor, BC: Bladder cancer

According to the results of initial TUR-BT pathology, forty (48.2%) of the patients had pTa high-grade pathology and 43 (51.8%) had pT1 high-grade pathology. In addition, 24 (28.9%) had concomitant CIS.

The comparison of the groups in terms of operative and histopathological features is summarised in Table 2. There were no statistically significant differences between the two groups regarding the presence of concomitant carcinoma in situ, tumor size, tumor characteristics (papillary or solid), and time to the second TUR-BT. However, the number of patients with initial TUR-BT pathology classified as T1 was significantly higher in group 2 ($p<0.05$). Additionally, group 1 exhibited a higher proportion of single tumors, whereas group 2 showed a greater proportion of two or more tumors ($p<0.05$).

The results of the comparison of the systemic inflammatory indices between the two groups are summarized in Table 3. There was no significant difference between the groups regarding the SII calculated from complete blood count results before the initial TURB. However, both the SII and the NLR showed statistically significant differences in the systemic inflammatory indices before Re-TUR-BT in group 2 ($p=0.017$ and $p=0.029$, respectively).

The SII values measured before the Re-TUR-BT operation demonstrated significant efficacy in differentiating between non-malignant and malignant pathology, with an AUC of 0.660 [95% confidence interval (CI): 0.538-0.783; $p=0.010$] as illustrated in Figure 1. Additionally, the NLR values obtained prior to the Re-TUR-BT were also significant, demonstrating

Table 1. Comparison of demographic characteristics of groups

	Group 1 (non-malignant at Re-TUR-BT) (n=55)	Grup 2 (malignant at Re-TUR-BT) (n=28)	p
Age [year, median (IQR), (min-max)]	63.05 (18) (41-86)	63.8 (15) (36-86)	0.962[m]
Sex (M/F) [n (%)]	49 (89.1)/6 (10.9)	27 (96.4)/1 (3.6)	0.255[k]
BMI [median (IQR), (min-max)]	26.12 (5.2) (17-39)	25.86 (6.6) (20-33)	0.847[m]
Smoking [n (%)]	46 (83.6)	24 (85.7)	0.805[k]
Diabetes mellitus [n (%)]	10 (18.2)	2 (7.1)	0.176[k]
Hypertension [n (%)]	20 (36.4)	9 (32.1)	0.703[k]
COPD [n (%)]	9 (16.4)	4 (14.3)	0.805[k]

[m]: Mann-Whitney U test, [k]: Chi-square test, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, Re-TUR-BT: Repeat transuretral resection of bladder tumour, M/F: Male/female, min-max: Minimum-maximum, IQR: Interquartile range

Table 2. Comparison of operative and histopathological features between groups

	Group 1 (non-malignant at Re-TUR-BT) (n=55)	Grup 2 (malignant at Re-TUR-BT) (n=28)	p
Tumour T stage (pT) [n (%)]			
pTa	31 (56.4)	9 (32.1)	**0.037[k]**
pT1	24 (43.6)	19 (67.9)	
CIS [n (%)]	14 (25.5)	10 (35.7)	0.330[k]
Tumour size [n (%)]			
<3 cm	20 (36.4)	9 (32.1)	0.703[k]
≥3 cm	35 (63.6)	19 (67.9)	
Tumour number [n (%)]			
1	30 (54.5)	7 (25)	**0.037[k]**
2-7	21 (38.2)	18 (64.3)	
>7	4 (7.3)	3 (10.7)	
Tumour characteristics [n (%)]			
Papillary	42 (76.4)	22 (78.6)	0.821[k]
Solid	13 (23.6)	5 (21.4)	
Time to re-TUR-BT [day, median (IQR), (min-max)]	36 (20) (20-114)	38 (17) (19-99)	0.167[m]

CIS: Carcinoma *in situ*, [k]: Chi-square test, [m]: Mann-Whitney U test, Re-TUR-BT: Repeat transuretral resection of bladder tumour, IQR: Interquartile range, min-max: Minimum-maximum

diagnostic value in predicting malignant pathology. This was confirmed through ROC analysis, yielding an AUC of 0.647 (95% CI: 0.524-0.770; p=0.020), as shown in Figure 2.

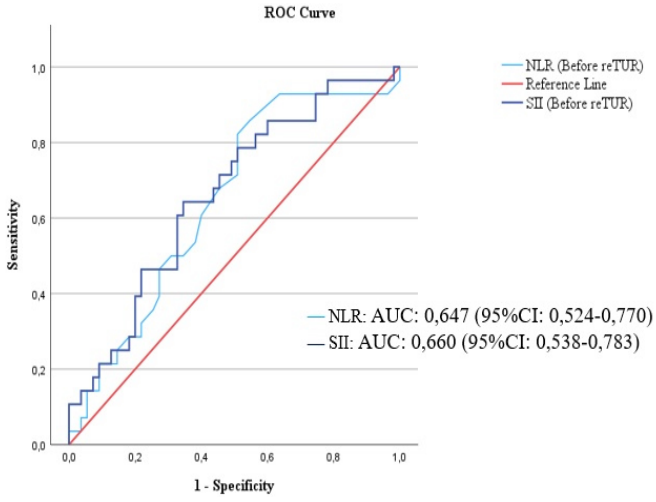

Figure 2. The effectiveness of the before Re-TUR-BT SII and NLR values in predicting malignant pathology

Re-TUR-BT: Repeat transurethral resection of bladder tumor, SII: Systemic immune-inflammation index, NLR: Neutrophil-to-lymphocyte ratio, AUC: Area under the curve

Discussion

The SII, a composite marker derived from peripheral blood counts, has garnered increasing attention in recent years due to its prognostic utility across various medical fields. Studies have demonstrated its relevance not only in oncology but also in cardiovascular diseases, autoimmune disorders, and infectious diseases, where systemic inflammation plays a critical role in disease pathophysiology and progression (3,9). The ability of SII to reflect the dynamic balance between immune activation and suppression positions it as a potentially valuable tool in clinical decision-making, especially in oncology. Its accessibility, cost-effectiveness, and reproducibility make it an attractive option for risk stratification and patient management across diverse clinical contexts (10,11). While the role of SII in oncology (particularly in predicting outcomes in malignancies such as bladder cancer) has been well documented, emerging evidence suggests that SII may also serve as a valuable biomarker in the diagnosis, monitoring, and prognostication of various cancers. This underscores its potential to enhance clinical practice by improving patient outcomes through more tailored management strategies.

Table 3. Comparison of systemic inflammatory indices between groups

	Group 1 (non-malignant at Re-TUR-BT) (n=55)	Grup 2 (malignant at Re-TUR-BT) (n=28)	p
SII before initial TUR-BT [median (IQR), (min-max)]	475.4 (332.9) (175.4-1621.2)	525.1 (562.5) (219.4-2642.2)	0.272[m]
SIRI before initial TUR-BT [median (IQR), (min-max)]	1.17 (1.1) (0.4-4.2)	1.08 (1.3) (0.4-8.7)	0.441[m]
NLR before initial TUR-BT [median (IQR), (min-max)]	2.17 (1.3) (0.7-7)	2.15 (2) (0.9-13.8)	0.303[m]
LMR before initial TUR-BT [median (IQR), (min-max)]	4 (1.9) (1.4-9.2)	3.55 (3) (0.9-6.9)	0.765[m]
PLR before initial TUR-BT [median (IQR), (min-max)]	104.9 (42.7) (48.1-278.3)	120.7 (76.7) (64.2-379.3)	0.141[m]
MWR before initial TUR-BT [median(IQR), (min-max)]	0.07 (0) (0-0.1)	0.07 (0) (0-0.1)	0.729[m]
SII before Re-TUR-BT [median (IQR), (min-max)]	443.4 (355.6) (179.8-1809.9)	576.4 (532) (219.4-2857.6)	**0.017[m]**
SIRI before Re-TUR-BT [median (IQR), (min-max)]	1 (0.9) (0.4-5)	1.3 (1.3) (0.4-4.7)	0.088[m]
NLR before Re-TUR-BT [median (IQR), (min-max)]	1.9 (1.7) (1-8.2)	2.35 (2) (0.9-8.3)	**0.029[m]**
LMR before Re-TUR-BT [median (IQR), (min-max)]	4,3 (1.7) (1.4-9.2)	3.7 (2.4) (1.4-7.3)	0.285[m]
PLR before Re-TUR-BT [median (IQR), (min-max)]	110.3 (31.5) (60.9-258.4)	119.1 (96.6) (73.1-416.6)	0.134[m]
MWR before Re-TUR-BT [median (IQR), (min-max)]	0.07 (0) (0-0.1)	0.07 (0) (0.1-0.1)	0.531[m]

SII: Systemic inflammatory index, SIRI: Systemic inflammatory response index, NLR: Neutrophil/lymphocyte ratio, LMR: Lymphocyte/monocyte ratio, PLR: Platelet/lymphocyte ratio, MWR: Monocyte/white blood cell ratio, [m]: Mann-Whitney U test, IQR: Interquartile, Re-TUR-BT: Repeat transuretral resection of bladder tumour, min-max: Minimum-maximum

In this single-center retrospective study, we examined the clinical significance of preoperative blood-based systemic inflammatory indices in patients with high-risk NMIBC who required Re-TUR-BT. Our findings demonstrated that elevated levels of the SII and NLR were independent predictive factors for malignant pathology in Re-TUR-BT specimens. This suggests that these inflammatory markers may serve as valuable tools in the preoperative assessment and risk stratification of patients undergoing Re-TUR-BT for high-risk NMIBC.

Numerous recent studies have highlighted the benefits of Re-TUR-BT in patients with high-risk NMIBC (3,12). This procedure improves diagnostic precision and aids in the removal of any remaining cancerous tissue. A recent meta-analysis that included 29 studies found a combined prevalence of 56% for residual tumors and 10% for upstaging to T2 among 3,566 and 2,556 patients, respectively (13). The pathology results from Re-TUR-BT hold significant prognostic value and are deemed the most important predictor of early recurrence and progression. Herr and Donat (14) reported that the presence of T1 tumors at second-look TUR-BT is associated with a progression rate of 76% within five years. Palou and colleagues conducted an analysis involving a cohort of 2,451 patients to investigate the prognostic significance of pathology findings from second-look TUR-BT. Their study established that T1 tumors identified during the second-look TUR-BT were associated with a higher likelihood of recurrence, progression, and mortality due to the disease. In a multivariate model that included factors such as tumor multiplicity, concomitant CIS, and BCG maintenance, second-look TUR-BT pathology emerged as the most critical prognostic factor for these outcomes (15).

Additionally, the therapeutic benefits of Re-TUR-BT have been noted. Comparisons between second-look TUR-BT and observation have shown significantly lower recurrence rates at 3 to 6 months post-cystoscopy for both T1 and high-grade Ta tumors (16). A recent study indicated that patients who underwent second-look TUR-BT had statistically significant improvements in cancer-specific survival (CSS) ($p=0.009$) and overall survival ($p<0.001$) compared to those who did not (17).

In this study, we aimed to identify the factors that may serve as predictors of tumor persistence following the initial TUR-BT. Specifically, we focused on patients' cohort whose tumors were found to be persistent based on the pathological findings from the subsequent Re-TUR-BT procedure. Our investigation involved a comprehensive analysis of various biochemical, pathological, and demographic variables that could potentially influence the likelihood of tumor persistence.

Tumor-related factors, including pathological tissue type, grade, and stage, are critical for predicting the progression and prognosis of cancer patients. These factors provide essential insights into the biological behavior of tumors, enabling clinicians to stratify patients according to their risk of recurrence and progression. In our study, we observed that the number of patients whose initial TUR-BT pathology was classified as T1 was significantly higher in group 2. These findings align with those of Divrik et al. (2), who conducted a prospective randomized trial involving T1 patients undergoing either a single TUR-BT or a second TUR-BT. They reported 5-year recurrence-free survival rates of 32% and 59%, respectively, and noted that 33% of patients had residual tumor at the time of the second TUR-BT. Additionally, our study revealed a higher incidence of single tumors in group 1, while group 2 exhibited a greater prevalence of multifocal tumors. Previous research has supported these results, for example, Ferro et al. (18) identified a statistically significant association between the presence of T1 high-grade BC at Re-TUR-BT and factors such as multifocality, tumor size greater than 3 cm, and the presence of CIS at the first TURB. Furthermore, Kamiya et al. (19) demonstrated that multifocality at the first TUR-BT is an independent predictor of high-grade T1, at Re-TUR-BT. In our study, although we noted a higher rate of tumor diameter exceeding 3 cm and the presence of concomitant CIS in group 2, these differences did not reach statistical significance. According to a recent study, the primary distinctions between patients with and without T1 high grade tumors at Re-TUR-BT were related to the size of the main lesion and multifocality. Notably, 13.9% of patients lacked a muscle layer, and 15.1% presented with CIS; however, the differences between those with and without T1 high grade at Re-TUR-BT were not significant (20).

In addition to these tumor-related factors, patient-related elements also play a crucial role in predicting cancer outcomes. One such area of interest is the assessment of systemic inflammatory indices (21). Inflammatory mechanisms, initiated by substances such as chemokines and cytokines, are essential for supporting the proliferation and persistence of cancer cells through several pathways, including the stimulation of blood vessel formation and the enhancement of metastatic spread. At the same time, the activation of oncogenes initiates inflammatory pathways from within the cancer cells themselves. This relationship underscores the significant connection between inflammation and cancer, as inflammatory responses can foster an environment that supports the development and advancement of tumors (22).

Our results identified the SII and NLR as two significant systemic inflammatory indices that can predict malignant pathology following Re-TUR-BT operations. The SII has been established as an independent prognostic indicator for patients with BC undergoing radical cystectomy (RC) or TUR-BT. A comprehensive meta-analysis conducted by Li et al. (23), which included ten studies, found that elevated SII levels are associated with markedly decreased overall survival rates, CSS rates, and

recurrence-free survival rates in BC patients. These findings also highlighted a considerable degree of heterogeneity across the studies. Furthermore, prior studies have demonstrated a correlation between adverse prognosis in BC and the NLR. The report by Mari et al. (24) highlighted that elevated preoperative NLR levels were independently linked to increased overall mortality in BC patients following RC. Additionally, a previous study has also found that high NLR is associated with high grade disease (25). An increased NLR indicates a relative increase in neutrophils, which release inflammatory factors and specific proteases that induce extracellular matrix remodeling. This creates a favorable microenvironment for tumor cell migration and progression (26). The results imply that SII and NLR appear to be valuable biomarkers in assessing the prognosis and potential outcomes of patients with BC, especially in relation to surgical interventions.

We further analyzed the diagnostic value of inflammatory indices in Re-TUR-BT pathology and calculated the AUC from ROC curves. Our findings indicate that SII and NLR possess diagnostic utility for predicting malignant pathology. According to established literature, an AUC value between 0.7 and 0.8 is considered acceptable, while values between 0.6 and 0.7 are regarded as poor, and values below 0.6 indicate no diagnostic ability (27). Although both SII and NLR, assessed prior to re-TURBT, demonstrate some diagnostic value for identifying malignant pathology, their AUC values fall within the range of 0.6 to 0.7. This suggests that while these indices can provide insights, their diagnostic capability for predicting malignant pathology is limited.

Study Limitations

To highlight some important strengths of our study, to our knowledge, this is the first investigation in the literature exploring the value of systemic inflammatory indices for predicting pathology outcomes following Re-TUR-BT. Furthermore, all surgical procedures were conducted at a single center by a uro-oncological surgeon who specializes in bladder cancer, and the pathology results were interpreted by a single pathologist with expertise in urooncology. This consistency in both surgical technique and pathological evaluation enhances the quality and reliability of our findings, suggesting that single-center research can provide valuable insights. Despite the strengths of the study, several limitations warrant acknowledgment. First, the small sample size associated with a single-institute study may restrict the generalizability of the findings. Secondly, the retrospective cohort design could introduce selection bias, and the reliance on existing medical records for data collection may result in underreporting of comorbidities. This underreporting could significantly impact the validity of the results, as unrecognized comorbid conditions may confound the relationship between the variable of interest and the observed outcomes. The other potential limitation of this study is the lack of multivariate analysis, which may have overlooked the influence of confounding variables on the observed outcomes. Additionally, the modest AUC values observed in our analysis suggest that the diagnostic power of the tested model is limited. This indicates that while the model may have some utility in distinguishing between conditions, its overall accuracy and reliability in a clinical setting may not be sufficient to warrant widespread application. Finally, the study did not assess several important inflammation-and nutrition-based indicators, such as the Glasgow prognostic score, the albumin/globulin ratio, and the C-reactive protein/albumin ratio. Including these metrics could have provided deeper insights into the relationship between systemic inflammation and patient outcomes. Given these limitations, we recommend larger, multicenter prospective cohort studies to confirm the preliminary results of this investigation and further evaluate the prognostic value of systemic inflammatory indices in high-risk NMIBC patients.

Conclusion

Our study shows that SII and NLR calculated before Re-TUR-BT have potential predictive values in detecting the persistence of malignant pathology in Re-TUR-BT among high-risk NMIBC patients. These findings highlight the potential utility of these systemic inflammatory indices as biomarkers in clinical practice. Given the significance of our results, we advocate for larger, multicenter studies to further validate these findings. Such research would enhance our understanding of the role of SII and NLR, helping to establish their potential as reliable tools for clinical decision-making in the management of high-risk NMIBC patients.

Ethics

Ethics Committee Approval: The Local Ethics Committee of Health Science University İstanbul Training and Research Hospital granted ethical approval for this study (approval number: 2024-97, date: 18.10.2024).

Informed Consent: All participants received comprehensive information regarding the study's objectives and provided their written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.Y., T.M., M.H.E.A., Concept: H.A.A., E.O., Y.Ş., E.S., E.E., Design: H.A.A., M.Ç., E.E., Data Collection or Processing: T.M., M.Ç., M.H.E.A., Analysis or Interpretation: U.Y., E.S., Literature Search: H.A.A., E.O., Writing: H.A.A., Y.Ş., E.E.

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References

1. Babjuk M, Burger M, Capoun O, Cohen D, Compérat EM, Dominguez Escrig JL, Gontero P, Liedberg F, Masson-Lecomte A, Mostafid AH, Palou J, van Rhijn BWG, Rouprêt M, Shariat SF, Seisen T, Soukup V, Sylvester RJ. European Association of Urology Guidelines on non-muscle-invasive bladder cancer (Ta, T1, and carcinoma in situ). Eur Urol. 2022;81:75-94. [Crossref]
2. Divrik RT, Sahin AF, Yildirim U, Altok M, Zorlu F. Impact of routine second transurethral resection on the long-term outcome of patients with newly diagnosed pT1 urothelial carcinoma with respect to recurrence, progression rate, and disease-specific survival: a prospective randomised clinical trial. Eur Urol. 2010;58:185-190. [Crossref]
3. Murat Akgül, Çağrı Doğan, Cenk Murat Yazıcı, Mehmet Fatih Şahin, Ayşegül İsal Arslan, Meltem Öznur. Which non-muscle invasive bladder cancer is more valuable for re-transurethral resection? Ann Clin Anal Med 2021;12:1258-1262. [Crossref]
4. Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffioux C, Denis L, Newling DW, Kurth K. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol. 2006;49:466-465; discussion 475-477. [Crossref]
5. Sahin Y, Yucetas U, Ates HA, Erkan E, Yucetas E, Temiz MZ, Toktas MG, Kadihasanoglu M, Topkaya BC. Improving the diagnosis of high grade and stage bladder cancer by detecting increased urinary calprotectin expression in tumor tissue and tumor-associated inflammatory response. Investig Clin Urol. 2019;60:343-350. [Crossref]
6. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? Lancet. 2001;357:539-545. [Crossref]
7. Thompson DB, Siref LE, Feloney MP, Hauke RJ, Agrawal DK. Immunological basis in the pathogenesis and treatment of bladder cancer. Expert Rev Clin Immunol. 2015;11:265-279. [Crossref]
8. Cantiello F, Russo GI, Vartolomei MD, Farhan ARA, Terracciano D, Musi G, Lucarelli G, Di Stasi SM, Hurle R, Serretta V, Busetto GM, Scafuro C, Perdonà S, Borghesi M, Schiavina R, Cioffi A, De Berardinis E, Almeida GL, Bove P, Lima E, Ucciero G, Matei DV, Crisan N, Verze P, Battaglia M, Guazzoni G, Autorino R, Morgia G, Damiano R, de Cobelli O, Mirone V, Shariat SF, Ferro M. Systemic inflammatory markers and oncologic outcomes in patients with high-risk non-muscle-invasive urothelial bladder cancer. Eur Urol Oncol. 2018;1:403-410. [Crossref]
9. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, Lin SJ, Chou CY, Chen JW, Pan JP, Charng MJ, Chen YH, Wu TC, Lu TM, Huang PH, Cheng HM, Huang CC, Sung SH, Lin YJ, Leu HB. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. Eur J Clin Invest. 2020;50:e13230. [Crossref]
10. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of Systemic immune-inflammation index in cancer: A meta-analysis. J Cancer. 2018;9:3295-3302. [Crossref]
11. Arikan MG, Akgul M, Akdeniz E, Iskan G, Arda E. The value of hematological inflammatory parameters in the differential diagnosis of testicular torsion and epididymorchitis. Am J Clin Exp Urol. 2021;9:96-100. [Crossref]
12. Dobruch J, Borówka A, Herr HW. Clinical value of transurethral second resection of bladder tumor: systematic review. Urology. 2014;84:881-885. [Crossref]
13. Naselli A, Hurle R, Paparella S, Buffi NM, Lughezzani G, Lista G, Casale P, Saita A, Lazzeri M, Guazzoni G. Role of restaging transurethral resection for T1 non-muscle invasive bladder cancer: a systematic review and meta-analysis. Eur Urol Focus. 2018;4:558-567. [Crossref]
14. Herr HW, Donat SM. A re-staging transurethral resection predicts early progression of superficial bladder cancer. BJU Int. 2006;97:1194-1198. [Crossref]
15. Palou J, Pisano F, Sylvester R, Joniau S, Serretta V, Larré S, Di Stasi S, van Rhijn B, Witjes AJ, Grotenhuis A, Colombo R, Briganti A, Babjuk M, Soukup V, Malmstrom PU, Irani J, Malats N, Baniel J, Mano R, Cai T, Cha EK, Ardelt P, Varkarakis J, Bartoletti R, Dalbagni G, Shariat SF, Xylinas E, Karnes RJ, Gontero P. Recurrence, progression and cancer-specific mortality according to stage at re-TUR in T1G3 bladder cancer patients treated with BCG: not as bad as previously thought. World J Urol. 2018;36:1621-1627. [Crossref]
16. Gendy R, Delprado W, Brenner P, Brooks A, Coombes G, Cozzi P, Nash P, Patel MI. Repeat transurethral resection for non-muscle-invasive bladder cancer: a contemporary series. BJU Int. 2016;117(Suppl 4):54-59. [Crossref]
17. Gordon PC, Thomas F, Noon AP, Rosario DJ, Catto JWF. Long-term outcomes from re-resection for high-risk non-muscle-invasive bladder cancer: a potential to rationalize use. Eur Urol Focus. 2019;5:650-657. [Crossref]
18. Ferro M, Vartolomei MD, Cantiello F, Lucarelli G, Di Stasi SM, Hurle R, Guazzoni G, Busetto GM, De Berardinis E, Damiano R, Perdonà S, Borghesi M, Schiavina R, Almeida GL, Bove P, Lima E, Grimaldi G, Autorino R, Crisan N, Abu Farhan AR, Verze P, Battaglia M, Serretta V, Russo GI, Morgia G, Musi G, de Cobelli O, Mirone V, Shariat SF. High-grade T1 on re-transurethral resection after initial high-grade T1 confers worse oncological outcomes: results of a multi-institutional study. Urol Int. 2018;101:7-15. [Crossref]
19. Kamiya N, Suzuki H, Suyama T, Kobayashi M, Fukasawa S, Sekita N, Mikami K, Nihei N, Naya Y, Ichikawa T. Clinical outcomes of second transurethral resection in non-muscle invasive high-grade bladder cancer: a retrospective, multi-institutional, collaborative study. Int J Clin Oncol. 2017;22:353-358. [Crossref]
20. Gobbo A, Fasulo V, Contieri R, Uleri A, Avolio PP, Frego N, Lughezzani G, Saitta C, Taverna G, Zanoni M, Mancon S, Colombo P, Valeri M, Saita A, Lazzeri M, Buffi NM, Hurle R, Casale P. Clinical and pathological predictors of persistent T1 HG at second resection. Urologia. 2023;90:482-490. [Crossref]
21. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. Lancet Oncol. 2014;15:e493-e503. [Crossref]
22. Candido J, Hagemann T. Cancer-related inflammation. J Clin Immunol. 2013;33(Suppl 1):S79-S84. [Crossref]
23. Li J, Cao D, Huang Y, Xiong Q, Tan D, Liu L, Lin T, Wei Q. The prognostic and clinicopathological significance of systemic immune-inflammation index in bladder cancer. Front Immunol. 2022;13:865643. [Crossref]
24. Mari A, Muto G, Di Maida F, Tellini R, Bossa R, Bisegna C, Campi R, Cocci A, Viola L, Grosso A, Scelzi S, Lapini A, Carini M, Minervini A. Oncological impact of inflammatory biomarkers in elderly patients treated with radical cystectomy for urothelial bladder cancer. Arab J Urol. 2020;19:2-8. [Crossref]
25. Tang X, Wang S, An C, Du P, Yang Y. Preoperative high neutrophil-to-lymphocyte ratio is associated with high-grade bladder cancer. Anticancer Res. 2017;37:4659-4663. [Crossref]
26. De Larco JE, Wuertz BR, Furcht LT. The potential role of neutrophils in promoting the metastatic phenotype of tumors releasing interleukin-8. Clin Cancer Res. 2004;10:4895-4900. [Crossref]
27. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol. 2010;5:1315-1316. [Crossref]