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Association of Preoperative Hematological and Inflammatory Biomarkers with Pathological Tumor Stage in Bladder Cancer: A Retrospective Cohort Study

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Article

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Abstract

Background

Systemic inflammatory and hematological parameters derived from routine laboratory tests have been investigated as potential indicators of tumor-related biological characteristics in bladder cancer. However, their association with pathological tumor stage remains incompletely characterized. This study evaluated the association of routinely available preoperative hematological and inflammatory biomarkers with pathological tumor stage in patients undergoing transurethral resection of bladder tumor (TUR-BT).

Methods

This retrospective single-center cohort study included 182 patients with primary bladder cancer who underwent TUR-BT between January 2018 and January 2026. For the ordinal stage analysis, patients with pTa, pT1, and pT2 disease were included (n = 179); patients with pT4 (n = 2) or pTis (n = 1) were not included in the three-level ordinal analysis. Preoperative hemoglobin, red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and De Ritis ratio were evaluated. Tumor-related characteristics, including tumor size, number, multifocality, location, and pathological grade, were also recorded. Continuous variables were compared using the Kruskal–Wallis test with Dunn–Bonferroni post-hoc analysis. Spearman correlation analysis and age-adjusted ordinal logistic regression were performed. Multicollinearity was assessed using variance inflation factors.

Results

Among the 179 patients included in the ordinal stage analysis, 74 had pTa, 67 had pT1, and 38 had pT2 disease. Age, hemoglobin, RDW, NLR, SII, SIRI, and De Ritis ratio differed significantly across pathological stages. Median hemoglobin decreased from 14.9 g/dL in pTa to 14.2 g/dL in pT1 and 13.2 g/dL in pT2 disease ($p = 0.002$), whereas NLR, SII, SIRI, RDW, and De Ritis ratio increased with advancing stage. Higher pathological stage was also associated with larger tumor size, higher pathological grade, and greater multifocality. In the age-adjusted ordinal logistic regression model, age (OR = 1.041, 95% CI: 1.020–1.063, $p < 0.001$) and SII (OR = 1.001, 95% CI: 1.000–1.001, $p = 0.032$) were statistically significant, whereas hemoglobin, RDW, NLR, SIRI, and De Ritis ratio were not. The multivariable analysis included 178 patients with complete data for all model variables. Multicollinearity was most pronounced among NLR, SII, and SIRI.

Conclusions

Several routinely available hematological and inflammatory parameters were associated with pathological tumor stage in unadjusted analyses. After adjustment for age and the other evaluated biomarkers, age and SII remained statistically associated with higher pathological stage, whereas hemoglobin was no longer significant. These findings should be considered exploratory associations rather than evidence of validated predictive performance. Prospective studies incorporating established clinical, cystoscopic, cytological, and radiological variables are required to determine whether these biomarkers provide incremental information beyond conventional preoperative assessment.

BACKGROUND

Bladder cancer is one of the most common malignancies of the urinary tract and represents a substantial cause of cancer-related morbidity and healthcare burden worldwide (1, 2). The disease is characterized by marked biological and pathological heterogeneity, ranging from non–muscle-invasive tumors to muscle-invasive disease. Accurate assessment of tumor stage is therefore central to pathological classification and subsequent clinical management (1–3).

Inflammation has an important role in tumor biology and may influence carcinogenesis, angiogenesis, immune regulation, and tumor invasion (4). In this context, systemic inflammatory biomarkers derived from routine peripheral blood tests have attracted considerable research interest because they can be obtained without additional invasive procedures and are routinely available in clinical practice (5). Among these biomarkers, the neutrophil-to-lymphocyte ratio (NLR) has been extensively investigated in bladder cancer and has been associated with adverse oncological outcomes in several studies (6). Composite indices, including the systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), incorporate several circulating blood-cell populations and may provide a broader representation of systemic inflammatory and immune status (7, 8). Previous studies have reported associations between elevated systemic inflammatory indices and unfavorable oncological outcomes in patients with bladder cancer (9, 10). Other routinely available hematological and biochemical parameters may also reflect systemic processes associated with malignant disease. Red blood cell distribution width (RDW) has been investigated in relation to systemic inflammation and oncological outcomes (11). Similarly, the aspartate aminotransferase/alanine aminotransferase ratio, commonly referred to as the De Ritis ratio, has been associated with tumor progression and oncological outcomes in several solid malignancies (12). Although previous studies have primarily focused on recurrence, progression, and survival outcomes, the relationship between these routinely available laboratory parameters and pathological tumor stage remains incompletely characterized. Importantly, pathological tumor stage is determined after TUR-BT and should not be considered interchangeable with preoperative clinical staging. Conventional preoperative assessment relies on clinical, cystoscopic, cytological, and radiological information, whereas the present study focuses specifically on routinely available laboratory parameters.

Therefore, the aim of this study was to evaluate the association between preoperative hematological and inflammatory biomarkers and pathological tumor stage in patients undergoing TUR-BT. We additionally evaluated available tumor-related characteristics, including tumor size, tumor number, multifocality, tumor location, and pathological grade, to provide a more complete characterization of the study population. The study was designed to investigate associations rather than to develop or validate a comprehensive preoperative prediction model.

METHODS

Study design and patient population

This retrospective single-center observational cohort study included consecutive patients who underwent transurethral resection of bladder tumor (TUR-BT) for primary bladder cancer between January 2018 and January 2026 at the Department of Urology, University of Health Sciences, Elazığ Fethi Sekin Training and Research Hospital. The dataset contained 182 patients with available clinical, pathological, and laboratory information. For the primary ordinal analysis of pathological tumor stage, patients were categorized into three ordered groups according to the final pathological examination: pTa, pT1, and pT2. Two patients with pT4 disease and one patient with pTis disease were not included in this three-level ordinal analysis because these categories were not part of the predefined three-stage comparison. Accordingly, 179 patients were included in the primary stage-group analysis. Patients with incomplete laboratory information and those with active infection, hematological disorders, chronic inflammatory

disease, or significant hepatic dysfunction that could potentially influence systemic inflammatory parameters were excluded according to the predefined study criteria.

Clinical and pathological variables

Demographic, tumor-related, pathological, and laboratory variables were obtained from the electronic medical record system. Demographic variables included age and sex. Available tumor-related characteristics included tumor number, tumor size, multifocality, tumor location, and pathological grade. Pathological stage was determined from TUR-BT specimens according to the pathological examination. Several conventional preoperative variables relevant to clinical staging were not systematically available for all patients. In particular, a standardized clinical T stage, detailed cystoscopic findings, urinary cytology results, and comprehensive CT/MRI-based clinical staging information were not consistently recorded and therefore could not be incorporated into the multivariable analysis. The available muscle-invasion variable represented pathological rather than preoperative clinical information and was not used as a surrogate for clinical T stage.

Laboratory parameters

Preoperative laboratory values were obtained from routine blood tests performed as close as possible to TUR-BT. The evaluated laboratory parameters included hemoglobin, red blood cell distribution width (RDW), absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, platelet count, aspartate aminotransferase (AST), and alanine aminotransferase (ALT). The neutrophil-to-lymphocyte ratio (NLR) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. The systemic immune-inflammation index (SII) was calculated as platelet count × neutrophil count / lymphocyte count. The systemic inflammation response index (SIRI) was calculated as neutrophil count × monocyte count / lymphocyte count. The De Ritis ratio was defined as the AST/ALT ratio.

Statistical analysis

Statistical analyses were performed using R statistical software. Sample size estimation was initially performed using G*Power version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). For approximation across three pathological tumor-stage groups, a fixed-effects one-way analysis of variance model assuming a medium effect size (Cohen's f = 0.25), $\alpha = 0.05$, and 80% power yielded a minimum sample size of 159 patients. Continuous variables were summarized as median and interquartile range (IQR), and categorical variables as number and percentage. Differences among pTa, pT1, and pT2 groups were evaluated using the Kruskal–Wallis test for continuous variables and the chi-square or Fisher exact test for categorical variables, as appropriate. Dunn–Bonferroni post-hoc analysis was used for pairwise comparisons following a significant Kruskal–Wallis test (13). Associations between pathological tumor stage and continuous laboratory parameters were assessed using Spearman rank correlation analysis (14). Because age differed significantly across pathological tumor-stage groups and represented a potential confounding variable, age was included in the multivariable analysis together with hemoglobin, RDW, NLR, SII, SIRI, and De Ritis ratio. Ordinal logistic regression was used to examine associations between these variables and the ordered pathological tumor-stage outcome. Odds ratios (ORs), 95% confidence intervals (CIs), and p-values were reported (15). Because NLR, SII, and SIRI are mathematically related composite inflammatory indices, multicollinearity was assessed using the variance inflation factor (VIF). The proportional odds assumption underlying ordinal logistic regression was formally assessed. Because this assumption was not adequately supported, the multivariable ordinal regression findings were interpreted cautiously as exploratory associations. A two-sided p-value < 0.05 was

considered statistically significant (16). The patient selection process and the composition of the final study cohort are presented in **Fig. 1.**

RESULTS

Baseline and tumor characteristics

The final dataset contained 182 patients. The pathological stage distribution was pTa in 74 patients, pT1 in 67 patients, pT2 in 38 patients, pT4 in 2 patients, and pTis in 1 patient. Because the primary ordinal analysis was predefined for the three ordered categories pTa, pT1, and pT2, the three patients with pT4 or pTis disease were excluded from the ordinal stage-group analysis, resulting in 179 patients.The baseline demographic, tumor-related, and laboratory characteristics of the 179 patients are summarized in **Table 1.**

Median age differed significantly across pathological stage groups, with median ages of 63 years (IQR, 55–70) in pTa, 72 years (IQR, 66.5–77) in pT1, and 70.5 years (IQR, 63.5–78) in pT2 disease ($p < 0.001$). Tumor-related characteristics also differed according to pathological stage. Median tumor size increased from 2.0 cm (IQR, 1.5–3.0) in pTa to 3.0 cm (IQR, 2.0–5.0) in pT1 and 4.0 cm (IQR, 3.0–5.0) in pT2 disease ($p < 0.001$). Pathological grade showed a marked stage-related distribution: high-grade tumors accounted for 8.1% of pTa, 58.2% of pT1, and 100% of pT2 tumors ($p < 0.001$). Multifocal tumors were present in 14.9%, 29.9%, and 36.8% of the pTa, pT1, and pT2 groups, respectively ($p = 0.021$). Tumor number did not differ significantly among the three groups ($p = 0.053$). Sex distribution was also similar among the groups ($p = 0.785$). Among the laboratory parameters, hemoglobin decreased with advancing pathological stage, whereas RDW, NLR, SII, SIRI, and De Ritis ratio generally increased. Median hemoglobin values were 14.9 g/dL (IQR, 13.6–16.1), 14.2 g/dL (IQR, 12.7–15.2), and 13.2 g/dL (IQR, 11.7–14.7) in the pTa, pT1, and pT2 groups, respectively ($p = 0.002$). Median NLR increased from 2.23 to 2.60 and 3.28 ($p = 0.001$), while median SII increased from 540.2 to 598.9 and 884.2 ($p = 0.004$). Median SIRI increased from 1.26 to 1.67 and 2.22 ($p = 0.001$). RDW and De Ritis ratio also differed significantly across the groups ($p = 0.034$ and $p = 0.002$, respectively). The distributions of hemoglobin and the evaluated inflammatory biomarkers according to pathological stage are shown in **Fig. 2.**

Pairwise comparisons

Dunn–Bonferroni post-hoc analysis demonstrated that the most consistent differences occurred between pTa and pT2 disease. Hemoglobin was lower in pT2 compared with pTa disease (adjusted $p = 0.002$), while RDW ($p = 0.034$), NLR ($p < 0.001$), SII ($p = 0.003$), SIRI ($p < 0.001$), and De Ritis ratio ($p = 0.004$) were higher in pT2 than in pTa disease. Detailed pairwise comparisons are presented in **Table 2.**

The comparison between pTa and pT1 showed a significant difference for De Ritis ratio ($p = 0.021$), whereas the other evaluated laboratory parameters did not reach statistical significance after Bonferroni adjustment. None of the evaluated laboratory parameters showed a statistically significant difference between pT1 and pT2 after adjustment.

Correlation analysis

Spearman correlation analysis demonstrated a negative correlation between pathological tumor stage and hemoglobin ($\rho = -0.263$, $p < 0.001$). Positive correlations were observed for RDW ($\rho = 0.194$, $p = 0.009$), NLR ($\rho = 0.276$, $p < 0.001$), SII ($\rho = 0.232$, $p = 0.002$), SIRI ($\rho = 0.269$, $p < 0.001$), and De Ritis ratio ($\rho = 0.266$, $p < 0.001$). Detailed correlation results are presented in **Table 3**

Age-adjusted multivariable analysis

In the age-adjusted ordinal logistic regression analysis, age was significantly associated with higher pathological tumor stage (OR = 1.041, 95% CI: 1.020–1.063, p < 0.001). SII also showed a statistically significant association (OR = 1.001, 95% CI: 1.000–1.001, p = 0.032). Hemoglobin was no longer statistically significant after adjustment for age and the other evaluated biomarkers (OR = 0.978, 95% CI: 0.893–1.071, p = 0.634). RDW (OR = 1.001, 95% CI: 0.949–1.056, p = 0.967), NLR (OR = 0.896, 95% CI: 0.746–1.075, p = 0.236), SIRI (OR = 1.011, 95% CI: 0.862–1.185, p = 0.897), and De Ritis ratio (OR = 0.923, 95% CI: 0.669–1.273, p = 0.626) were also not statistically significant. The multivariable analysis included 178 patients with complete data for all model variables. VIF values were 1.340 for age, 1.477 for hemoglobin, 1.114 for RDW, 5.358 for NLR, 5.167 for SII, 3.984 for SIRI, and 1.245 for De Ritis ratio. The relatively higher VIF values for NLR and SII were consistent with the mathematical overlap among the composite inflammatory indices. Because the proportional odds assumption was not adequately supported, the ordinal regression estimates were interpreted as exploratory associations rather than definitive independent predictive effects. Detailed results are presented in **Table 4.**

The multivariable analysis included 178 patients with complete data for all model variables. Because the proportional odds assumption was not adequately supported, the ordinal regression estimates should be interpreted cautiously as exploratory associations rather than definitive independent predictive effects. The corresponding odds ratios and 95% confidence intervals are illustrated in **Fig. 3.**

DISCUSSION

In the present study, we evaluated the association between routinely available preoperative hematological and inflammatory biomarkers and pathological tumor stage in patients with bladder cancer undergoing TUR-BT. In the three-level pathological stage analysis, age, hemoglobin, RDW, NLR, SII, SIRI, and De Ritis ratio differed across pTa, pT1, and pT2 disease. In addition, tumor size, pathological grade, and multifocality were associated with pathological stage. Correlation analyses demonstrated negative associations between hemoglobin and pathological stage and positive associations between RDW, NLR, SII, SIRI, and De Ritis ratio and pathological stage. However, within the multivariable ordinal logistic regression model, only age and SII remained statistically associated with the ordered pathological stage outcome. Because the proportional odds assumption was not adequately supported, these multivariable estimates should be interpreted as exploratory associations rather than definitive independent effects. Bladder cancer is characterized by substantial biological and pathological heterogeneity, with pathological stage representing an important determinant of disease classification and subsequent management (1–3). Inflammation has been implicated in several aspects of tumor biology, including cytokine-mediated signaling, angiogenesis, immune dysregulation, and tumor invasion (4, 17, 18). In bladder cancer, the interaction between systemic inflammatory responses and tumor biology has therefore received increasing attention (19). The present findings are consistent with the concept that routinely measured peripheral blood parameters may be associated with differences in pathological tumor stage. However, an association with pathological stage does not establish that these parameters independently reflect tumor biology or that they provide clinically useful predictive information. NLR demonstrated a positive correlation with pathological stage and showed higher values in patients with pT2 compared with pTa disease. Previous studies have reported associations between elevated pretreatment NLR and adverse oncological outcomes or more advanced disease in bladder cancer (20, 21). The biological rationale for this relationship may involve the interaction between neutrophil-mediated inflammatory responses and lymphocyte-associated antitumor immunity. Nevertheless, in the present multivariable analysis, NLR was not independently associated with the ordered pathological stage outcome. Therefore, the current findings support an association between NLR and pathological stage but do not establish an independent association after multivariable adjustment. Similarly, SII and SIRI

demonstrated positive associations with pathological stage in the unadjusted analyses. SII integrates platelet, neutrophil, and lymphocyte counts, whereas SIRI incorporates neutrophil, monocyte, and lymphocyte counts, and both indices have been investigated as composite measures of systemic inflammatory status (7, 8). Previous studies and meta-analyses have reported associations between elevated SII and adverse oncological outcomes in bladder cancer (9, 10, 22). In the present study, SII remained statistically associated with pathological stage after adjustment for age and the other evaluated laboratory parameters, whereas SIRI did not. The relatively small effect estimate for SII should nevertheless be interpreted in the context of its continuous scale and should not be regarded as evidence of clinically meaningful predictive performance. RDW and De Ritis ratio also demonstrated positive correlations with pathological stage. RDW has been investigated as a marker associated with systemic inflammation and adverse outcomes in several malignancies (11). Similarly, the De Ritis ratio has been associated with tumor progression and oncological outcomes in several solid tumors (12). In the present study, both parameters differed across pathological stages in unadjusted analyses, but neither remained statistically significant in the multivariable model. These findings suggest that their observed relationships with pathological stage may partly reflect the influence of age or their relationships with other laboratory variables. The relationship between hemoglobin and pathological stage requires particular caution. Lower hemoglobin levels were observed in patients with more advanced pathological stage, and hemoglobin demonstrated a negative correlation with stage. However, the association disappeared after adjustment for age and the other evaluated laboratory parameters. This is important because hemoglobin concentration is influenced by multiple factors, including age, renal function, nutritional status, chronic disease, and blood loss. Cancer-related anemia may also arise through several mechanisms, including inflammation and impaired erythropoiesis (29). Because several potential determinants of hemoglobin were not systematically available in the retrospective dataset, residual confounding cannot be excluded. Therefore, the present data do not support interpreting hemoglobin as an independent marker of tumor aggressiveness. An important finding of the present analysis was the significant association between age and pathological tumor stage. Age differed substantially among the pathological stage groups and remained statistically significant after adjustment for the evaluated laboratory variables. This finding illustrates the importance of accounting for demographic confounding when investigating laboratory biomarkers and pathological stage. It also indicates that the unadjusted association observed for hemoglobin should not be interpreted independently of age. The present dataset also allowed evaluation of several conventional tumor characteristics. Tumor size increased across pathological stages, and higher pathological stage was associated with a higher proportion of high-grade and multifocal tumors. These findings are consistent with the established relationship between pathological stage and tumor characteristics in bladder cancer (1–3). Importantly, however, these variables should not be interpreted as substitutes for clinical T stage. Pathological grade and pathological muscle invasion are determined from the resection specimen and are therefore not equivalent to preoperative clinical staging. Conventional preoperative assessment of bladder cancer incorporates clinical and endoscopic findings together with urinary cytology and cross-sectional imaging, depending on the clinical context (1–3). Although tumor size, tumor number, multifocality, tumor location, and pathological grade were available in the present dataset, a systematically recorded clinical T stage, standardized cystoscopic assessment, urinary cytology, and comprehensive radiological staging information were not consistently available for all patients. Consequently, the present study cannot determine whether the evaluated hematological and inflammatory parameters provide incremental information beyond conventional preoperative assessment. The available retrospective data therefore did not permit reliable evaluation of these biomarkers within a comprehensive preoperative prediction model. Accordingly, the associations observed in the present study should be interpreted in the context of established clinical and pathological variables rather than as evidence that hematological or inflammatory biomarkers can replace conventional preoperative assessment. Prospective studies incorporating clinical T stage, standardized cystoscopic characteristics, urinary cytology, and CT/MRI-based staging are required to determine whether these routinely available laboratory parameters provide additional information regarding pathological tumor stage. The methodological characteristics of the

multivariable analysis also warrant consideration. NLR, SII, and SIRI are mathematically related composite inflammatory indices, and the VIF analysis demonstrated relatively higher values for NLR and SII. Although these values do not indicate severe multicollinearity in isolation, they confirm the expected overlap among the composite inflammatory variables. More importantly, the proportional odds assumption underlying ordinal logistic regression was not adequately supported. Consequently, the multivariable ordinal regression findings should be regarded as exploratory associations rather than definitive evidence of independent effects. The present findings should therefore be considered hypothesis-generating. Although several routinely available hematological parameters demonstrated consistent associations with pathological tumor stage, the current analysis does not establish that these biomarkers provide incremental information for preoperative staging, risk classification, or clinical decision-making. Prospective studies incorporating established clinical, cystoscopic, cytological, and radiological variables are needed to determine whether these laboratory parameters provide incremental information beyond conventional preoperative assessment. Several limitations should be considered. First, the retrospective single-center design may have introduced selection bias and limits generalizability. Second, clinical T stage, standardized cystoscopic findings, urinary cytology, and comprehensive CT/MRI-based clinical staging were not systematically available and therefore could not be incorporated into the analysis. Third, although several tumor characteristics were available, the absence of standardized preoperative clinical staging prevented assessment of incremental value beyond conventional assessment. Fourth, hemoglobin may be influenced by renal function, nutritional status, chronic comorbidities, and blood loss, and these factors were not systematically available for adjustment. Residual confounding therefore cannot be excluded. Fifth, NLR, SII, and SIRI showed mathematical overlap, as reflected by their VIF values. Sixth, the proportional odds assumption for the ordinal regression model was not adequately supported, limiting interpretation of the multivariable estimates. Finally, the study lacked external validation. Despite these limitations, the study has several strengths. The analysis included multiple routinely available hematological and inflammatory parameters within the same cohort, allowing their associations with pathological stage to be evaluated simultaneously. The dataset also contained several tumor-related characteristics, including tumor size, tumor number, multifocality, location, and pathological grade, permitting a more complete description of the relationship between laboratory parameters and pathological disease characteristics. The use of routinely obtained laboratory measurements also facilitates reproducibility and provides a basis for future prospective investigations. Further prospective multicenter studies should integrate laboratory biomarkers with established clinical T stage, cystoscopic characteristics, urinary cytology, and CT/MRI-based assessment. Such studies would be required to determine whether systemic hematological and inflammatory parameters provide information beyond conventional preoperative assessment and whether their association with pathological stage has independent clinical relevance.

CONCLUSIONS

Several routinely available hematological and inflammatory parameters were associated with pathological tumor stage in this retrospective cohort of patients with bladder cancer. Higher pathological stages were characterized by lower hemoglobin levels and higher RDW, NLR, SII, SIRI, and De Ritis ratio in unadjusted analyses, while tumor size, pathological grade, and multifocality also differed across stage groups. After adjustment for age and the other evaluated laboratory parameters, age and SII remained statistically associated with the ordered pathological stage outcome, whereas hemoglobin was no longer significant.

These findings represent exploratory associations and should not be interpreted as evidence of validated predictive performance or established clinical utility. Because conventional preoperative clinical, cystoscopic, cytological, and radiological staging variables were not systematically available, the incremental value of these biomarkers beyond standard preoperative assessment could not be determined. Prospective multicenter studies incorporating these conventional variables together with routinely available hematological and inflammatory parameters are warranted.

Abbreviations

ALT
Alanine Aminotransferase
AST
Aspartate Aminotransferase
CI
Confidence Interval
NLR
Neutrophil–to–Lymphocyte Ratio
OR
Odds Ratio
RDW
Red Cell Distribution Width
SII
Systemic Immune–Inflammation Index
SIRI
Systemic Inflammation Response Index
TUR
BT–Transurethral Resection of Bladder Tumor

Declarations

Ethics approval and consent to participate

This study was approved by the Non-Interventional Clinical Research Ethics Committee of Elazığ Fethi Sekin City Hospital (Decision No: 2026/27-07). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent for the surgical procedure was obtained from all patients before surgery. The institutional surgical consent form explicitly stated that patients' clinical data and health information could be used for scientific research purposes. Accordingly, the use of routinely collected clinical and laboratory data for the present study was covered by the consent obtained during clinical care.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are publicly available in the Zenodo repository at https://doi.org/10.5281/zenodo.23034579.

Competing interests

The authors declare that they have no competing interests

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Author Contributions

Mehmet Sezai Oğraş contributed to the study conception and design, statistical analysis, data interpretation, manuscript drafting, critical revision of the manuscript, and supervision of the study.

Eyüp Andaç Karataş contributed to the study design, data collection, manuscript drafting, and administrative and technical support.

Erdoğan Ağlamış contributed to data collection, data interpretation, critical revision of the manuscript, and administrative support.

Fatih Yıldırım contributed to data collection, statistical analysis, and critical revision of the manuscript.

All authors reviewed and approved the final version of the manuscript.

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Tables

Tables are available in the Supplementary Files section.

Figures

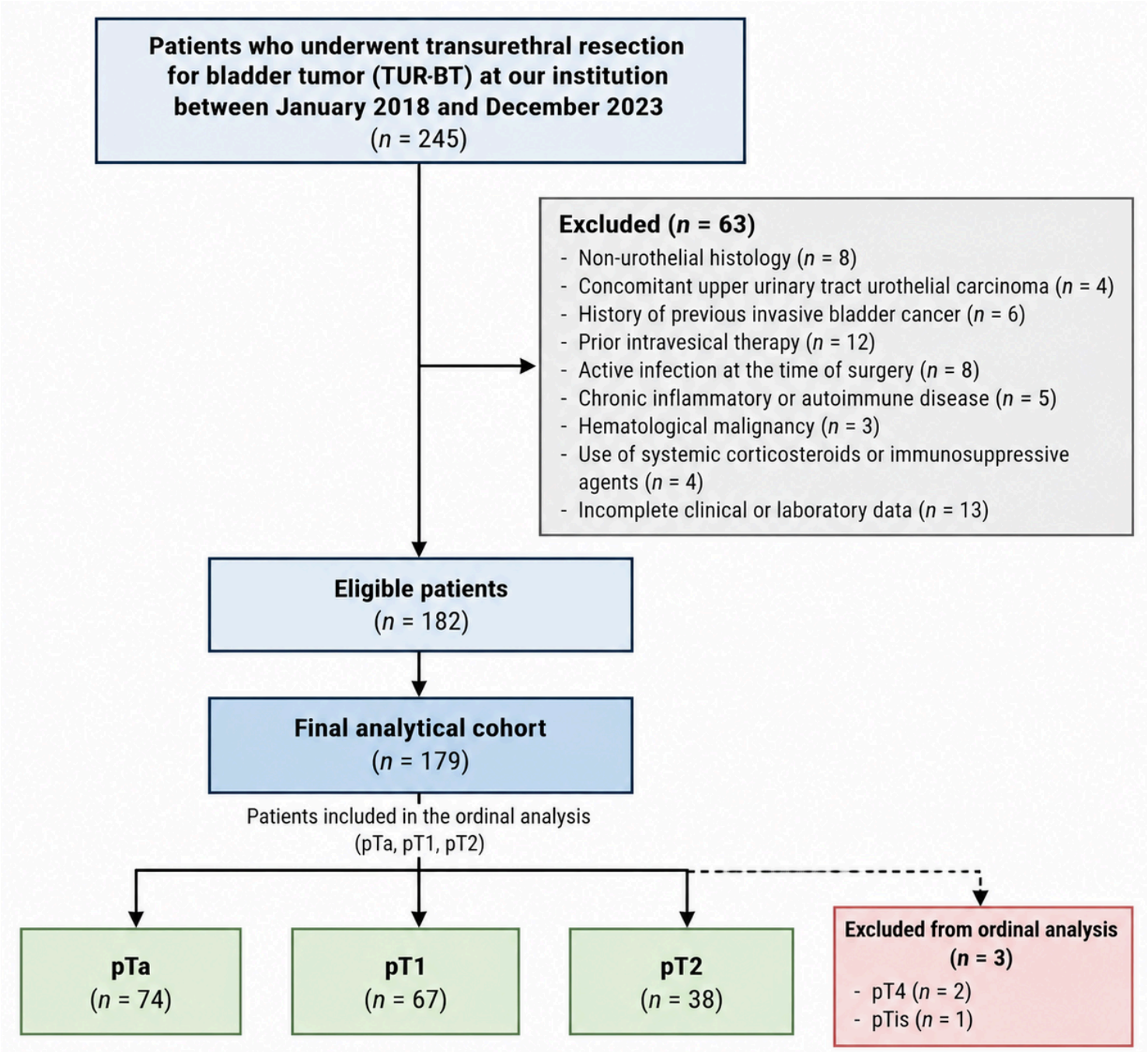


Fig. 1 Flow diagram of patient selection and analytical cohort. A total of 245 patients who underwent transurerthral resection for bladder tumor (TUR-BT) between January 2018 and December 2023 were screened. After applying the predefined exclusion criteria, 182 patients were eligible. Two patients with pT4 disease and one patient with pTis disease were not included in the three-level ordinal analysis, resulting in 179 patients (pTa, pT1, and pT2) in the final analytical cohort.

Figure 1

See image above for figure legend.

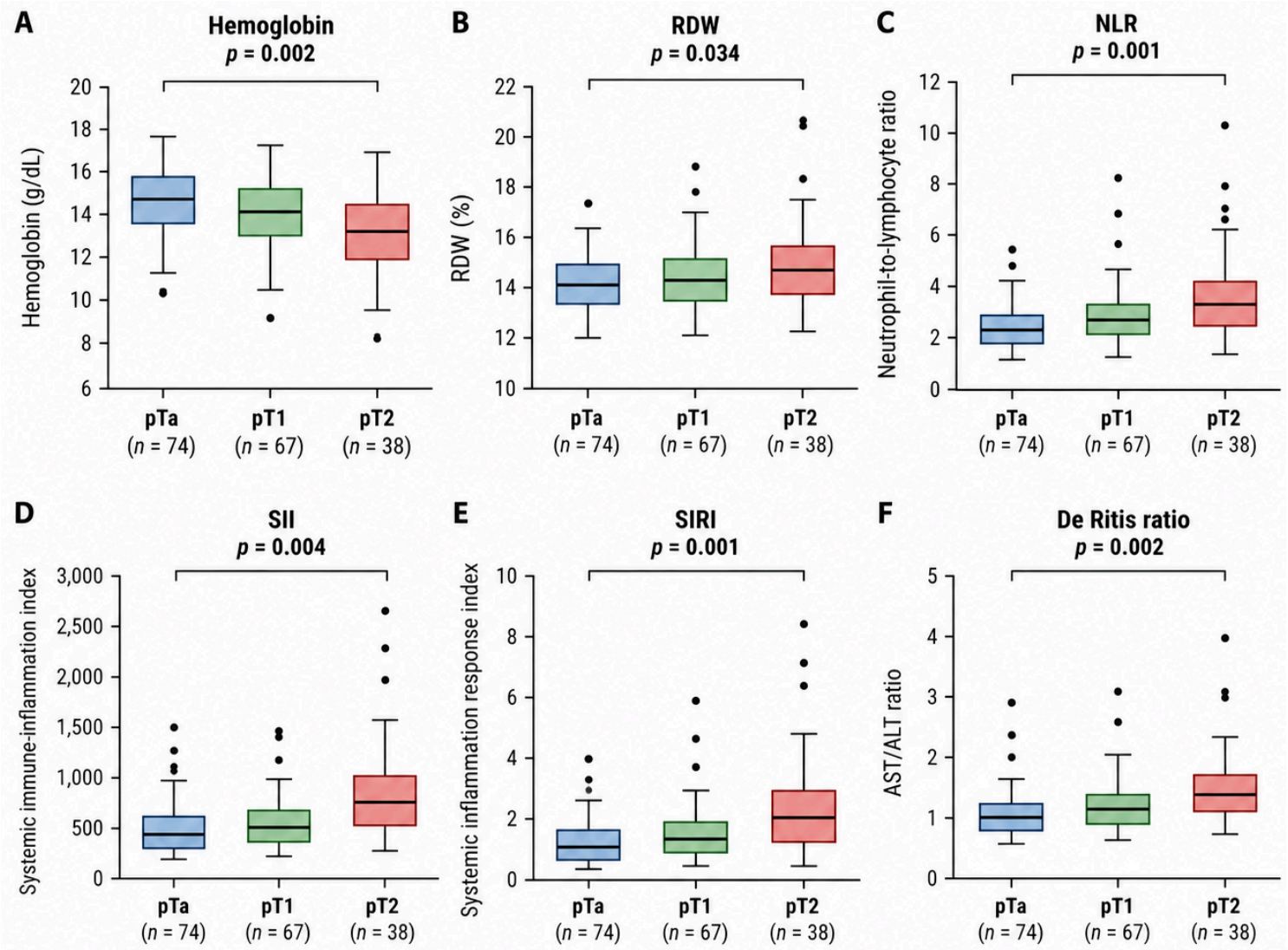


Fig. 2 Distributions of hematological and inflammatory biomarkers according to pathological tumor stage. Box plots show the median and interquartile range (IQR) of (**A**) hemoglobin, (**B**) red blood cell distribution width (RDW), (**C**) neutrophil-to-lymphocyte ratio (NLR), (**D**) systemic immune-inflammation index (SII), (**E**) systemic inflammation response index (SIRI), and (**F**) De Ritis ratio (AST/ALT ratio) in patients with pTa, pT1, and pT2 disease. *P*-values were obtained using the Kruskal–Wallis test.

Figure 2

See image above for figure legend.

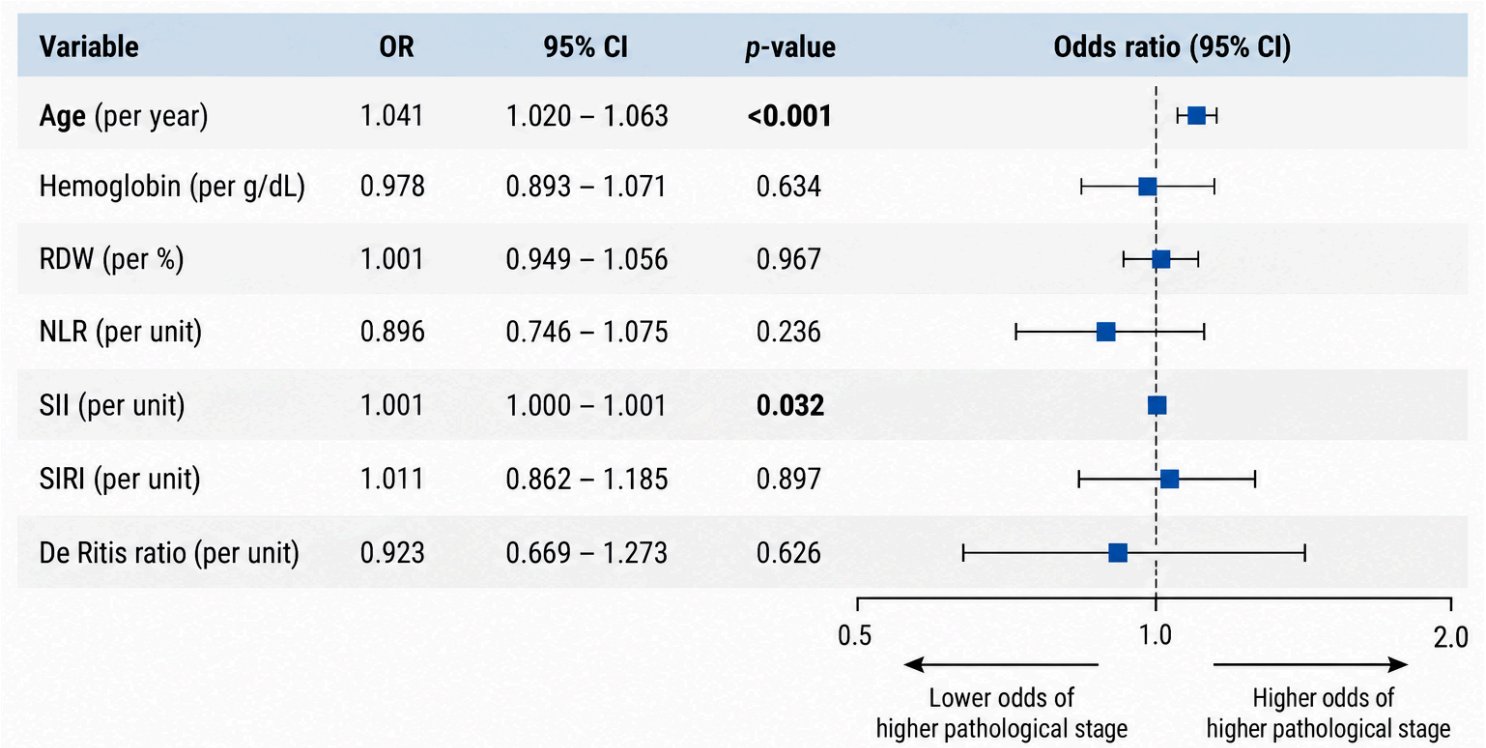


Fig. 3 Forest plot of age-adjusted ordinal logistic regression analysis for factors associated with pathological tumor stage. Squares represent odds ratios (ORs) and horizontal lines indicate 95% confidence intervals (CIs). The model included age, hemoglobin, red blood cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and De Ritis ratio. The multivariable analysis included 178 patients with complete data for all model variables. Because the proportional odds assumption was not adequately supported, the ordinal regression estimates should be interpreted cautiously as exploratory associations rather than definitive independent predictive effects.

Figure 3

See image above for figure legend.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.Baselinedemographictumorrelatedandlaboratorycharacteristicsaccordingtopathologicaltumorstage.odt
- Table2.Pairwisecomparisonsofhematologicalandinflammatoryparametersaccordingtopathologicaltumorstage.odt
- Table3.Spearmancorrelationsbetweenpathologicaltumorstageandhematologicalandinflammatoryparameters.odt
- Table4.Ageadjustedordinallogisticregressionanalysisoffactorsassociatedwithpathologicaltumorstage.odt