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# Evaluation of the prognostic value of LMR, PLR, NLR, and dNLR in urothelial bladder cancer patients treated with radical cystectomy

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**Abstract. – OBJECTIVE: Our aim was to evaluate the association between preoperative LMR, PLR, NLR, dNLR, and survival of urothelial bladder cancer (UBC) patients treated with radical cystectomy (RC). We also analyzed the relationship between preoperative blood-based inflammatory biomarkers' levels and postoperative in-hospital complications.**

**PATIENTS AND METHODS: This retrospective study included 144 UBC patients, who underwent RC between 2003 and 2015. The study endpoints were cancer-specific survival (CSS) and overall survival (OS).**

**RESULTS: Univariable analysis revealed that continuous LMR, PLR, NLR and dNLR were significantly associated with CSS and OS. On multivariable regression model analysis, continuous LMR, NLR, and dNLR independently predicted both endpoints. Furthermore, the group of patients with lower LMR values had a greater chance of developing postoperative in-hospital complications.**

**CONCLUSIONS: Our findings indicate that the cheap and simple blood-based biomarkers may be valuable in identifying UBC patients treated with RC, who are at higher risk of all-cause and cancer-related mortality.**

Key Words
Bladder cancer, Radical cystectomy, PLR, NLR, dNLR, LMR.

## Introduction

Bladder cancer (BC) is the ninth most common neoplasm worldwide with 4 times higher incidence in men than women[1]. The main risk factor of BC is tobacco use, which is responsible for approximately 50-65% of male and 20-30% of female cases of BC[2]. Despite a recently observed decline in the incidence of BC in western countries populations, we may expect constant or even rising problems worldwide, due to the growing prevalence of smoking in developing countries, ageing of the western countries populations and the fact that 9 out of 10 BC occur in patients over the age of 55[3]. Nowadays, there is a discussion on the optimal approach to patients with muscle-invasive bladder cancer (MIBC) and high-risk non-muscle-invasive bladder cancer (NMIBC)[4]. Radical cystectomy (RC) is a "gold-standard" management regardless of its association with high prevalence of perioperative complications and unsatisfactory long-term results[4,5]. Unfortunately, there are no easily obtainable biomarkers that could be helpful in the assessment of BC patients' prognosis. Improvement in that field may be found in novel inflammatory indicators, whose prognostic value was confirmed in various neoplastic and non-neoplastic diseases[6-10]. Regarding urothelial bladder cancer (UBC), which is the most common BC type and a well-known inflammation-related malignancy, continuing the search for potentially useful prognostic systemic inflammatory markers appears to be correct[11]. Lymphocyte-monocyte ratio (LMR), platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), and derived neutrophil-lymphocyte ratio (dNLR) are amongst those promising indicators. They can be effortlessly obtained from complete blood count (CBC) with differentials.

The primary goal of the study was to assess simultaneously the prognostic value of LMR, PLR, NLR, dNLR with reference to overall survival (OS) and cancer-specific survival (CSS) in patients suffering from UBC treated by RC. The secondary aim was to analyze the relationship between preoperative blood-based inflammatory biomarkers' levels and postoperative in-hospital complications.

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## Patients and Methods

### Patients

We examined the records of 228 BC patients who were treated with RC at the Department of Urology in Zabrze between 2003 and 2015. Patients were excluded from the investigation if they had a non-urothelial neoplasm, distant metastases, and severe inflammatory comorbidities. Also, subjects with a previous history of other solid tumors and hematological diseases, ones who died during the perioperative period, received neoadjuvant chemotherapy, as well as individuals with incomplete CBC data, were ruled out from the study. The final cohort included 144 patients.

Baseline patient characteristics and laboratory parameters were collected from medical records. Data concerning cancer clinicopathological features were obtained from histopathology reports. Preoperative blood cell count tests were performed median 3 (range 0-21) days before the RC, using the peripheral venous blood samples collected in the EDTA (ethylenediaminetetraacetic acid) tubes. CBC parameters were assessed by an automatic hematologic analyzer (ADVIA 120, Siemens Healthcare Diagnostics, Eschborn, Germany). The LMR, PLR, and NLR were calculated as the absolute count of monocytes, platelets or neutrophils divided by the absolute count of lymphocytes, respectively. Calculation of dNLR was performed by dividing the absolute neutrophil count by the absolute leukocyte count minus the absolute neutrophil count. The TNM classification was adjusted to the American Joint Committee on Cancer, 7$^{th}$ edition (2010)[12]. Tumor grading was obtained from the patients' medical records. To standardize the evaluation of postoperative in-hospital complications, the Clavien-Dindo grading system was implemented[4]. Taking into consideration some published studies regarding the matter, as well as our analysis of in-hospital postoperative complications' prevalence, we have decided to further divide the complications into 5 major categories: postoperative blood transfusions associated with badly tolerated anemia, infection, wound-related complications, gastrointestinal complications, and urinary extravasation[4,13]. OS and CSS were defined as the time from surgery to death (all causes) and bladder cancer-related death, respectively. Information regarding patients' overall survival was obtained on May 15 2016 from the Polish Ministry of Internal Affairs and Administration. Cause of death was acquired from the Polish National Cancer Registry and the National Health Fund. Complete 12-month follow-up was available for 94.4% (136/144) of patients. The Institutional Review Board at the Medical University of Silesia approved this study.

### Statistical Analysis

Receiver operating characteristic (ROC) curves were plotted to evaluate the accuracy of PLR, NLR, dNLR, and LMR for CSS and OS prediction. Optimal cut-off values of CBC-based indices for CSS predicting were obtained when the Youden index was maximal. The normality of continuous variables distribution was examined using the Shapiro-Wilk test. Continuous variables which were distributed normally were presented as mean ± standard deviation and variables demonstrating non-normal distribution were presented as median (interquartile range). Dichotomous variables were expressed as percentages. Relationships between CBC-based inflammatory indices were evaluated using the Spearman correlation coefficient analysis. Patients were divided into groups according to LMR, PLR, NLR, and dNLR values. High and low PLR, NLR, and dNLR values were defined as higher than or equal to and lower than optimal cut-offs, respectively. Low and high LMR was regarded as lower than or equal to and higher than the optimal cut-off, respectively. To test the differences between groups, the Mann-Whitney U test and the Student's *t*-test were used for continuous variables. Categorical variables were compared using the chi-squared test. The associations between groups and CSS and OS were analyzed using the Kaplan-Meier method with log-rank testing. The Cox proportional hazards regression model was applied to perform univariable and multivariable analysis. Variables included in univariable analysis of predictors for CSS and OS were: PLR, NLR, dNLR, LMR, age, sex, presence of positive surgical margin, tumor grade, tumor necrosis, lymph node involvement, and age-adjusted Charlson Comorbidity Index (CCI). Variables that reached a *p*-value lower than 0.05 in the univariable analysis were entered into the multivariable analysis. As the correlations between CBC-based inflammatory indices were moderate/strong, separate multivariable models were determined for PLR, NLR, dNLR and LMR after adjustment for confounders. The Bonferroni

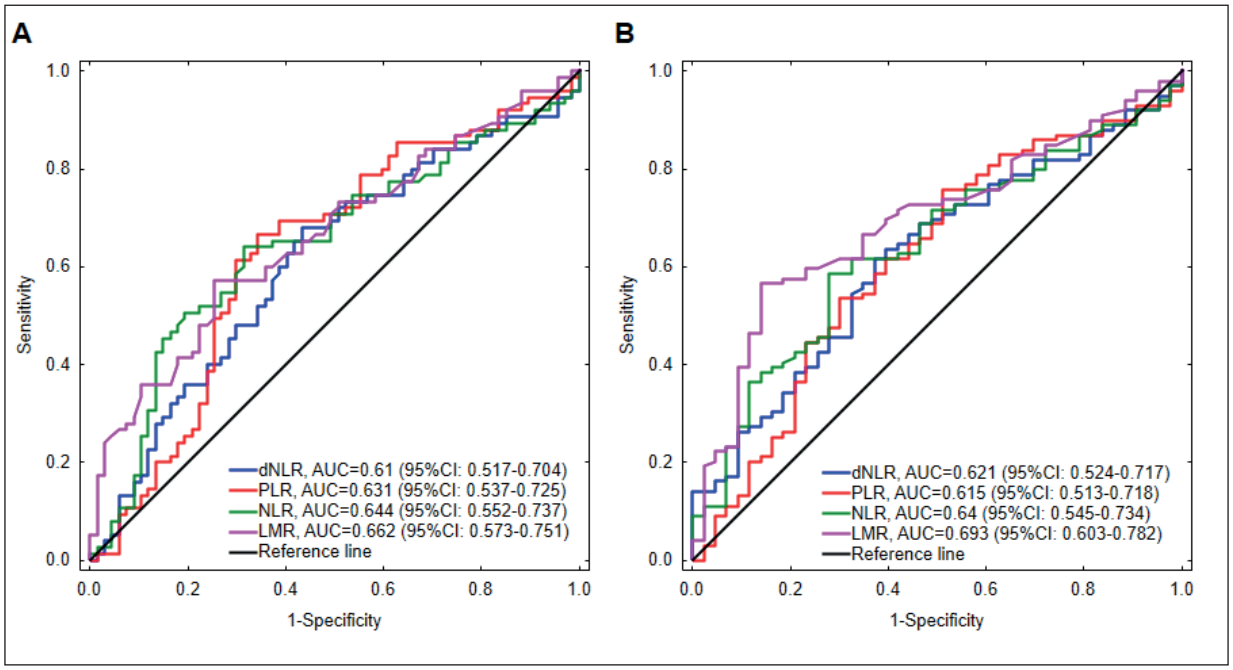


**Figure 1.** Receiver operating characteristic (ROC) curves for cancer-specific survival (**A**) and overall survival (**B**). Abbreviations: AUC = area under curve; CI = confidence interval.

corrected $p$-value < 0.0125 (0.05/4) was considered as the threshold of statistical significance. Statistical analyses were performed using the STATISTICA 12 software with Medical Bundle (StatSoft Inc., Tulsa, OK, USA) and MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium).

## Results

The median duration of follow-up for all patients was 14 (interquartile range: 7-40) months. One-year OS and CSS were 58.8% and 65.4%, respectively. During observation all-cause and cancer-related death occurred in 99 patients (68.8%) and 75 patients (52.1%), respectively. Based on the Clavien-Dindo classification, 93 (64.6%) patients experienced postoperative in-hospital complications. Ileal conduits, ureterocutaneostomy, and orthotopic neobladder were performed in 59 (41.0%), 48 (33.3%), and 37 (25.7%) patients, respectively.

Optimal cut-off values of LMR, PLR, NLR, and dNLR in predicting CSS were 2.44, 160.59, 3.00, and 1.95, respectively. The results of ROC analysis are presented in Figure 1. The correlations between PLR, NLR, dNLR, and LMR were moderate or strong (Table I). The association between low and high groups of LMR, PLR, NLR, dNLR, and clinicopathological features is reported in Table II. Higher gradings, advanced pathologic T-stage diseases and tumor necrosis were more frequent in groups with high PLR, NLR, dNLR, and low LMR values. Other clinicopathological features did not differ significantly across groups. In the Kaplan-Meier analysis, OS and CSS were decreased in patients with high PLR, NLR, dNLR, and low LMR values (Table II, Figures 2 and 3). The group of patients with LMR ≤ 2.44 had a greater chance of developing postoperative complications. In addition, a higher rate of gastrointestinal events in patients with low LMR values was observed (Table III).

**Table I.** Correlations between PLR, NLR, dNLR and LMR.

| | dNLR | PLR | NLR | LMR |
|---|---|---|---|---|
| dNLR | 1.000 | 0.592* | 0.905* | -0.654* |
| PLR | 0.592* | 1.000 | 0.719* | -0.663* |
| NLR | 0.905* | 0.719* | 1.000 | -0.813* |
| LMR | -0.654* | -0.663* | -0.813* | 1.000 |

*$p$<0.0001
Abbreviations: LMR = lymphocyte-monocyte ratio; PLR = platelet-lymphocyte ratio; NLR = neutrophil-lymphocyte ratio; dNLR = derived neutrophil-lymphocyte ratio.

**Table II.** Baseline characteristics, pathological findings and outcomes of patients with high and low values of PLR, NLR, dNLR, and LMR.

| | PLR | | | NLR | | | dNLR | | | LMR | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | <160.59 | ≥160.59 | *p*-value | <3.00 | ≥3.00 | *p*-value | <1.95 | ≥1.95 | *p*-value | ≤2.44 | >2.44 | *p*-value |
| Sex | | | 0.26 | | | 0.23 | | | 0.58 | | | 0.09 |
| Male [%] | 76.1 | 83.6 | | 76.0 | 84.1 | | 77.8 | 81.5 | | 86.7 | 75.0 | |
| Female [%] | 23.9 | 16.4 | | 24.0 | 15.9 | | 22.2 | 18.5 | | 13.3 | 25.0 | |
| Age [years] | 61.9±7.7 | 62.2±7.4 | 0.86 | 61.5±7.4 | 62.7±7.6 | 0.33 | 62.0±7.6 | 62.0±7.4 | 0.98 | 63.2±7.6 | 61.2±7.3 | 0.10 |
| BMI [kg/m$^2$] | 26.8±4.0 | 26.0±4.6 | 0.31 | 26.5±4.3 | 26.2±4.4 | 0.67 | 26.7±4.2 | 26.2±4.5 | 0.52 | 26.1±4.2 | 26.5±4.3 | 0.54 |
| ASA score | | | 0.33 | | | 0.47 | | | 0.97 | | | 0.59 |
| ASA I, II [%] | 79.6 | 86.4 | | 85.5 | 80.4 | | 83.3 | 83.1 | | 85.4 | 81.5 | |
| ASA III, IV [%] | 20.4 | 13.6 | | 14.5 | 19.6 | | 16.7 | 16.9 | | 14.6 | 18.5 | |
| Age-adjusted CCI | | | 0.40 | | | 0.27 | | | 0.52 | | | 0.09 |
| ≤3 [%] | 82.3 | 76.2 | | 83.1 | 75.0 | | 81.8 | 77.1 | | 71.4 | 84.2 | |
| >3 [%] | 17.7 | 23.8 | | 16.9 | 25.0 | | 18.2 | 22.9 | | 28.6 | 15.8 | |
| pT stage | | | 0.05 | | | <0.0001 | | | <0.0001 | | | 0.0004 |
| Ta/Tis | 5.6 | 4.1 | | 6.7 | 2.9 | | 7.9 | 2.5 | | 3.3 | 6.0 | |
| T1 | 8.5 | 1.4 | | 9.3 | 0.0 | | 11.1 | 0.0 | | 0.0 | 8.3 | |
| T2 | 29.6 | 17.8 | | 33.3 | 13.0 | | 33.3 | 16.1 | | 11.7 | 32.1 | |
| T3 | 40.9 | 46.6 | | 41.3 | 46.4 | | 41.3 | 45.7 | | 48.3 | 40.5 | |
| T4 | 15.5 | 30.1 | | 9.3 | 37.7 | | 6.4 | 35.8 | | 36.7 | 13.1 | |
| pN stage | | | 0.46 | | | 0.95 | | | 0.70 | | | 0.24 |
| N0 [%] | 78.9 | 73.6 | | 76.0 | 76.5 | | 77.8 | 75.0 | | 71.2 | 79.8 | |
| N≥1 [%] | 21.1 | 26.4 | | 24.0 | 23.5 | | 22.2 | 25.0 | | 28.8 | 20.2 | |
| Surgical margin | | | 1.00 | | | 0.82 | | | 0.65 | | | 0.19 |
| Positive [%] | 9.9 | 9.9 | | 9.3 | 10.5 | | 11.1 | 8.9 | | 13.8 | 7.1 | |
| Negative [%] | 90.1 | 90.1 | | 90.7 | 89.5 | | 88.9 | 91.1 | | 86.2 | 92.9 | |
| Tumor grade | | | 0.004 | | | 0.0001 | | | 0.0002 | | | 0.0005 |
| G1, G2 [%] | 69.0 | 45.2 | | 72.0 | 40.6 | | 74.6 | 43.2 | | 60.0 | 31.0 | |
| G3, G4 [%] | 31.0 | 54.8 | | 28.0 | 59.4 | | 25.4 | 56.8 | | 40.0 | 69.0 | |
| Tumor necrosis | | | 0.04 | | | 0.0008 | | | 0.007 | | | 0.004 |
| Present [%] | 5.6 | 16.4 | | 2.7 | 20.2 | | 3.2 | 17.3 | | 20.0 | 4.8 | |
| Absent [%] | 94.4 | 83.6 | | 97.3 | 79.8 | | 96.8 | 82.7 | | 80.0 | 95.2 | |
| Cancer-specific mortality [%] | 36.2 | 68.5 | <0.0001* | 37.0 | 69.6 | <0.0001* | 38.7 | 63.8 | <0.0001* | 71.7 | 39.0 | <0.0001* |
| Overall mortality [%] | 60.9 | 78.1 | <0.0001* | 57.5 | 82.6 | <0.0001* | 58.1 | 78.8 | <0.0001* | 90.0 | 54.9 | <0.0001* |

*log-rank test

Abbreviations: LMR = lymphocyte-monocyte ratio; PLR = platelet-lymphocyte ratio; NLR = neutrophil-lymphocyte ratio; dNLR = derived neutrophil-lymphocyte ratio; BMI = Body Mass Index; ASA = American Society of Anesthesiologists, CCI = Charlson Comorbidity Index

**Table III.** Postoperative in-hospital complications of patients with high and low values of PLR, NLR, dNLR and LMR.

| | PLR | | | NLR | | | dNLR | | | LMR | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | <160.59 | ≥160.59 | *p*-value | <3.00 | ≥3.00 | *p*-value | <1.95 | ≥1.95 | *p*-value | ≤2.44 | >2.44 | *p*-value |
| Clavien–Dindo classification system | | | 0.42 | | | 0.07 | | | 0.49 | | | 0.002 |
| No complications [%] | 36.6 | 32.9 | | 42.7 | 26.1 | | 39.7 | 30.9 | | 18.3 | 46.4 | |
| Low grade complications (1-2) [%] | 52.1 | 48.0 | | 46.7 | 53.6 | | 47.6 | 51.9 | | 60.0 | 42.9 | |
| High grade complications (3-5) [%] | 11.3 | 19.2 | | 10.7 | 20.3 | | 12.7 | 17.3 | | 21.7 | 10.7 | |
| Postoperative blood transfusions | | | 0.9 | | | 0.72 | | | 0.69 | | | 0.44 |
| Yes [%] | 35.2 | 34.3 | | 33.3 | 36.2 | | 36.5 | 33.3 | | 38.3 | 32.1 | |
| No [%] | 64.8 | 65.7 | | 66.7 | 63.8 | | 63.5 | 66.7 | | 61.7 | 67.9 | |
| Postoperative infection | | | 0.75 | | | 0.34 | | | 0.2 | | | 0.32 |
| Yes [%] | 12.7 | 11.0 | | 9.3 | 14.5 | | 7.9 | 14.8 | | 15.0 | 9.5 | |
| No [%] | 87.3 | 89.0 | | 90.7 | 85.5 | | 92.1 | 85.2 | | 85.0 | 90.5 | |
| Wound-related complications | | | 0.83 | | | 0.12 | | | 0.16 | | | 0.68 |
| Yes [%] | 9.9 | 11.0 | | 6.7 | 14.5 | | 6.3 | 13.6 | | 11.7 | 9.5 | |
| No [%] | 90.1 | 89.0 | | 93.3 | 85.5 | | 93.7 | 86.4 | | 88.3 | 90.5 | |
| Gastrointestinal events | | | 0.43 | | | 0.27 | | | 0.87 | | | 0.02 |
| Yes [%] | 15.5 | 20.5 | | 14.7 | 21.7 | | 17.5 | 18.5 | | 26.7 | 11.9 | |
| No [%] | 84.5 | 79.5 | | 85.3 | 78.3 | | 82.5 | 81.5 | | 73.3 | 88.1 | |
| Urinary extravasation | | | 0.63 | | | 0.71 | | | 0.46 | | | 0.94 |
| Yes [%] | 4.2 | 2.7 | | 4.0 | 2.9 | | 4.8 | 2.5 | | 3.3 | 3.6 | |
| No [%] | 95.8 | 97.3 | | 96.0 | 97.1 | | 95.2 | 97.5 | | 96.7 | 96.4 | |

Abbreviations: LMR = lymphocyte-monocyte ratio; PLR = platelet-lymphocyte ratio; NLR = neutrophil-lymphocyte ratio; dNLR = derived neutrophil-lymphocyte ratio.

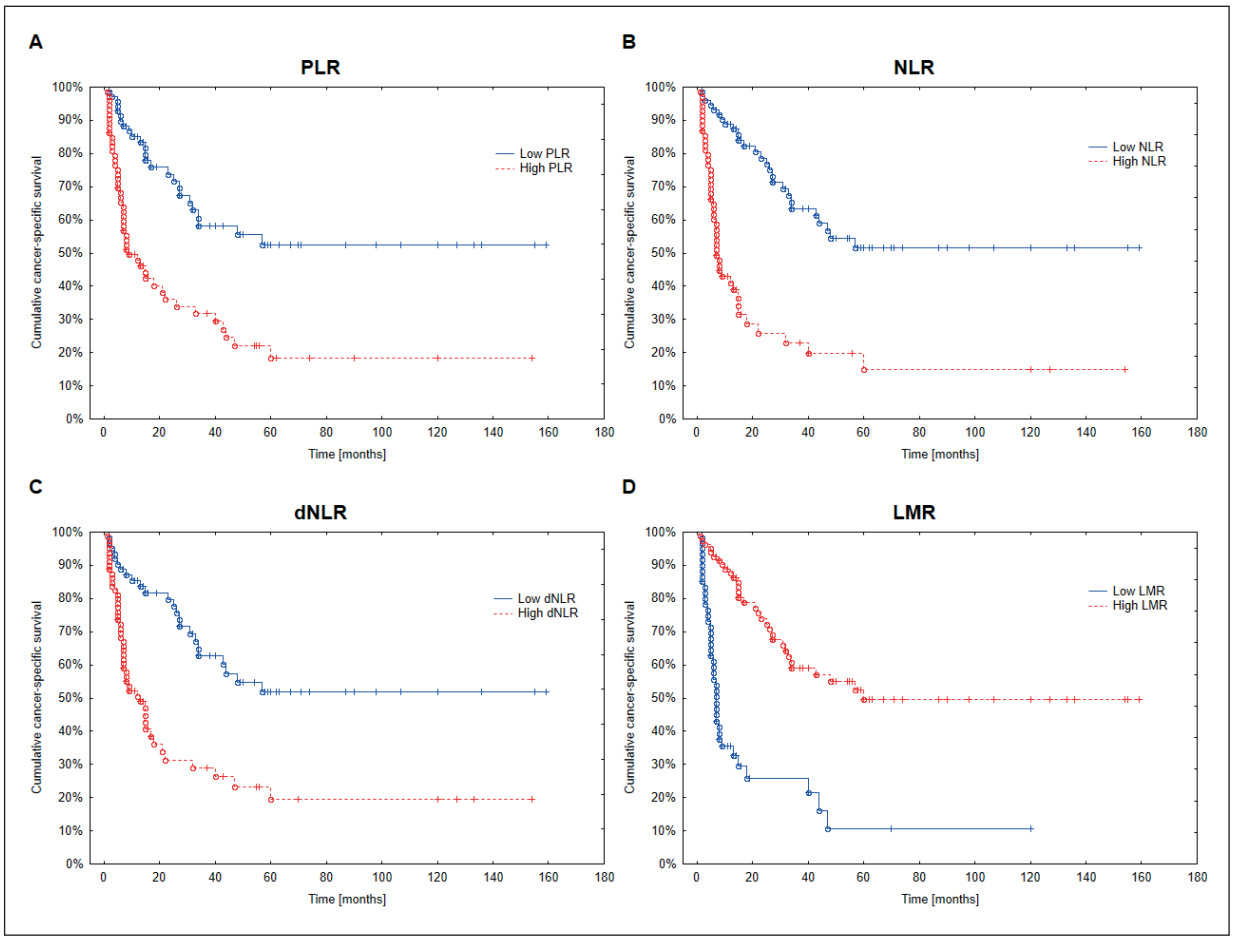


**Figure 2.** Kaplan-Meier curves for cancer-specific survival according to PLR (**A**), NLR (**B**), dNLR (**C**) and LMR (**D**).

Univariable analysis has revealed that continuous PLR, NLR, dNLR, and LMR were significantly associated with CSS and OS (Tables IV and V). In multivariable Cox proportional hazard regression analysis for CSS and OS, LMR, NLR, and dNLR, adjusted for confounding variables, met the Bonferroni-corrected threshold of significance for both analyzed endpoints. PLR was the only evaluated blood-based indicator that did not significantly influence survival of UBC patients (Tables IV and V).

## Discussion

In the present study, we have analyzed the association between pretreatment LMR, PLR, NLR, dNLR, and survival of patients with the diagnosis of UBC treated by RC. To the best of our knowledge, data regarding the prognostic value of these CBC-based indicators in bladder cancer patients is limited and inconclusive. Several researches assessed the prognostic value of LMR, PLR, NLR, dNLR in UBC subjects, although it should be highlighted that none of them evaluated simultaneously all four markers in terms of predicting CSS and OS. The results of our research have revealed that, in multivariable models, continuous LMR, NLR, and dNLR acted as significant prognostic factors for CSS and OS, whereas continuous PLR did not achieve independent predictor status for both endpoints.

Numerous reports[14-16] have highlighted the correlation between novel CBC-based indices and well-known inflammatory proteins like procalcitonin, CRP, and interleukins. In addition, the simple CBC-based biomarkers have been identified as prognostic factors in patients suffering from diseases with inflammatory etiology such as acute coronary syndrome, heart failure, and Behcet's disease[17-19]. The present state of the art confirms the association between inflammation and pathophysiology of cancer[20]. Well-known an-

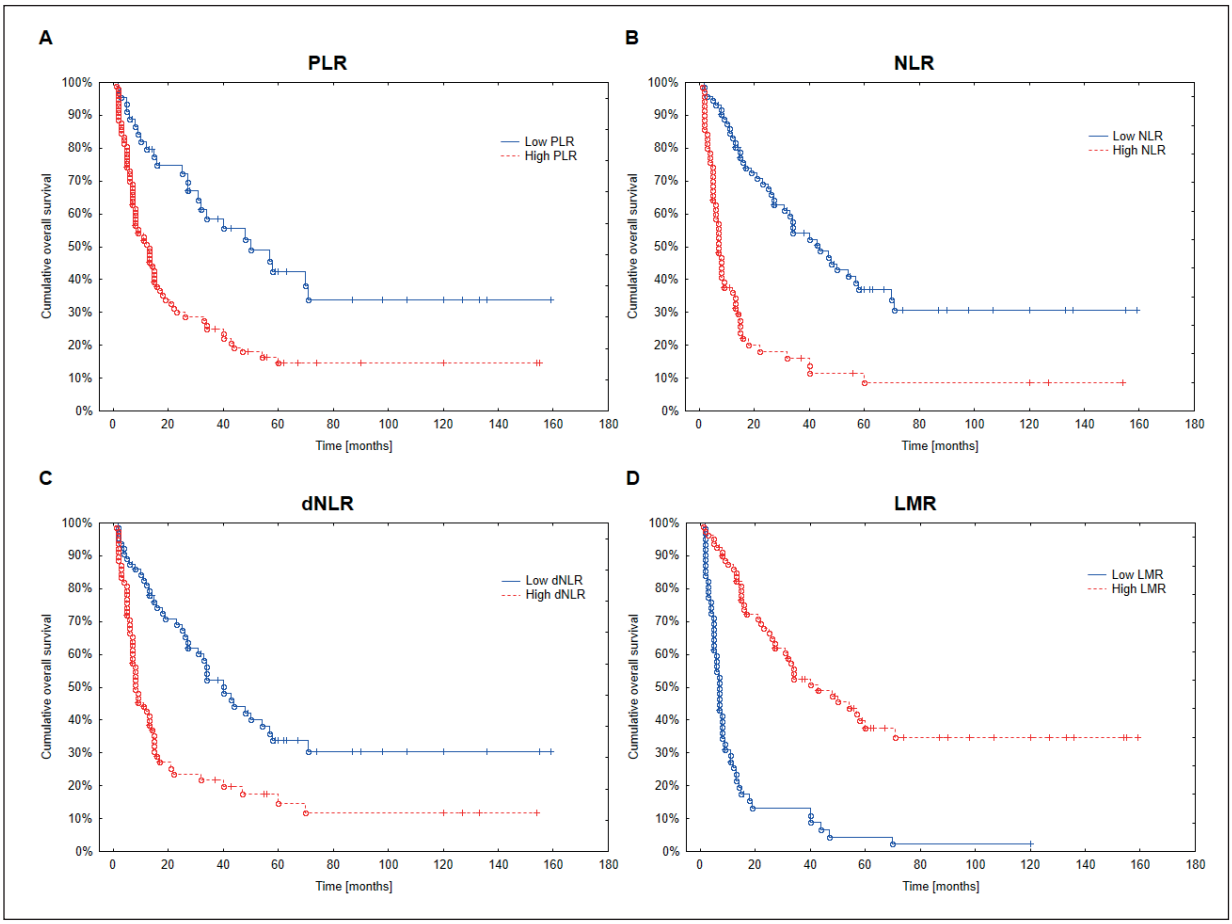


**Figure 3.** Kaplan-Meier curves for overall survival according to preoperative PLR (**A**), NLR (**B**), dNLR (**C**) and LMR (**D**).

ti-inflammatory drugs, such as Cox-2 inhibitors, have proven ability to induce cell apoptosis and reduce tumor mass in bladder cancer[21]. Impaired total cancer immunosurveillance seems to be an extremely complex and dynamic process. It has been proven that malignancy induces a network of interactions between the immune cells and the tumor[22]. The fact that immune cells may reflect systemic inflammatory burden is clinically useful.

Lymphocytes are a basal anti-tumor defense line[23]. Furthermore, a reduced number of lymphocytes is associated with unstable host defense to the advanced BC[24]. Sharma et al[25] revealed that a greater number of CD8 + infiltrating lymphocytes improves the prognosis of patients with MIBC. Cancer microenvironment cells stimulate monocytes and neutrophils to secrete, inter alia, interleukin 6 (IL-6), vascular endothelial growth factor (VEGF), and transforming growth factor β (TGF-β), causing general immunosuppression by inducing apoptosis of lymphocytes and a decrease in lymphopoiesis[22,26-28]. The same mediators stimulate myelopoiesis with an accompanying polarization of monocytes and neutrophils into pro-tumor functioning cells[22,28]. Moreover, neoplasms induce recruitment of neutrophils and monocytes capable of residing in the tumor microenvironment[22,26,27]. These cells, known as tumor-associated macrophages (TAMs) and tumor-associated neutrophils (TANs), facilitate – through numerous factors – cancer progression[22,26]. Also, platelets are involved in recruiting monocytes and neutrophils to tumor microenvironment[22]. In addition, thrombocytes are the major source of TGF-β in the circulation, which is the leading cytokine that favors protumorigenic activation of TANs[22,29-31]. Besides, thrombocytes, through cancer-induced release of VEGF, stimulate tumor angiogenesis[29]. As briefly described, interactions between the immune system and cancer are extremely interesting and complex with quoted examples being a drop in the ocean of cancer-related inflammation researches.

**Table IV.** Prognostic value of PLR, NLR, dNLR and LMR in predicting cancer-specific survival – univariable and multivariable analysis.

| | Univariable analysis | | | Multivariable analysis* | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *p*-value | HR | 95% CI | *p*-value |
| PLR | 1.003 | 1.001-1.005 | 0.0084 | 1.0001 | 0.999-1.003 | 0.38 |
| NLR | 1.047 | 1.022-1.073 | 0.0002 | 1.049 | 1.020-1.080 | 0.001 |
| dNLR | 1.164 | 1.075-1.259 | 0.0002 | 1.135 | 1.035-1.242 | 0.007 |
| LMR | 0.689 | 0.586-0.810 | <0.0001 | 0.752 | 0.640-0.885 | 0.0006 |

*Adjusted for: higher pT category (T≥2 vs. pT≤1), lymph node involvement (presence vs. absence), higher grade (G3-4 vs. G1-2), tumor necrosis (presence vs. absence)
Abbreviations: LMR = lymphocyte–monocyte ratio; PLR = platelet–lymphocyte ratio; NLR = neutrophil–lymphocyte ratio; dNLR = derived neutrophil–lymphocyte ratio; HR = hazard ratio; CI = confidence interval.

Up to now, only a few studies have analyzed simultaneously the prognostic value of LMR, PLR, NLR, and dNLR in patients with the diagnosis of cancer. In studies conducted by Gu et al[32] and Neal et al[33], high preoperative NLR was the sole independent prognostic factor for all-cause death in patients with sarcomatoid renal cell carcinoma and resectable colorectal liver metastases, respectively. On the contrary, in a study encompassing 389 patients with gastric cancer, all indices were statistically significant for OS prediction[34]. Regarding UBC, there are studies that evaluate the prognostic value of two or three of the biomarkers included in our research. Our findings are roughly similar to the results of D'Andrea et al[35], who conducted the largest multicenter study to date and determined LMR and NLR, but not PLR, as independent prognostic factors of CSS and OS. Conversely, Zhang et al[8] reported that low LMR was superior to high PLR and NLR as being the only independent predictor for OS. Also, Bhindi et al[36] discriminated PLR as an independent factor associated with OS and CSS, which is in line with our results. Concerning the recently implemented dNLR, only two researches evaluated its prognostic value in UBC patients[37-39]. Our findings concord with those of Ku et al[38], who evaluated 419 UBC patients and determined categorized dNLR ≥ 2 as an independent predictor for OS and CSS. van Kessel et al[39] analyzed a group of 123 MIBC patients treated with platinum-based pre-operative chemotherapy. They found that dNLR did not reach an independent predictor status for OS and progression-free survival[39]. Differences in our results as compared to those of van Kessel et al[39] may be due to the fact that their whole population was treated by preoperative chemotherapy and dNLR was obtained before chemotherapy and not before the RC, as we have done in our study.

Cancer grade and tumor necrosis have differed significantly across groups of analyzed indices, which may indicate that the biomarkers have relevantly reflected the undifferentiation and aggressiveness of the tumor cells. In the studies of Kaynar et al[40] and high Tazeh et al[41], higher NLR obtained before primary transurethral resection of bladder tumor (TURBT) was associ-

**Table V.** Prognostic value of PLR, NLR, dNLR and LMR in predicting overall survival – univariable and multivariable analysis.

| | Univariable analysis | | | Multivariable analysis* | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *p*-value | HR | 95% CI | *p*-value |
| PLR | 1.002 | 1.001-1.004 | 0.0006 | 1.002 | 1.000-1.004 | 0.03 |
| NLR | 1.051 | 1.028-1.074 | <0.0001 | 1.070 | 1.043-1.098 | <0.0001 |
| dNLR | 1.201 | 1.123-1.283 | <0.0001 | 1.227 | 1.131-1.330 | <0.0001 |
| LMR | 0.714 | 0.622-0.820 | <0.0001 | 0.785 | 0.677-0.911 | 0.001 |

*Adjusted for: age (continuous), positive margin (presence vs. absence), lymph node involvement (presence vs. absence), higher grade (G3-4 vs. G1-2), tumor necrosis (presence vs. absence); age adjusted CCI (≥3 vs. <3).
Abbreviations: LMR = lymphocyte–monocyte ratio; PLR = platelet-lymphocyte ratio; NLR = neutrophil-lymphocyte ratio; dNLR = derived neutrophil-lymphocyte ratio; CCI = Charlson Comorbidity Index; HR = hazard ratio; CI = confidence interval.

ated with higher prevalence of MIBC. Notably, our analysis has revealed that in the group of patients with baseline pretreatment high PLR, NLR, dNLR, and low LMR advanced pathologic T-stage diseases have been observed.

We attempted to find an association between pretreatment inflammation biomarkers and postoperative in-hospital complications. We have found that only patients in the group with preoperative LMR $\leq$ 2.44 were more likely to develop postoperative complications (standardized using the Clavien-Dindo classification). This may indicate that a key role in the development of complications is played by factors not directly related to the patient's inflammatory burden. However, it must be pointed out that, due to very rigorous inclusion criteria, analyzed subjects were not affected by other severe inflammatory disorders, which may influence the prevalence of postoperative complications[13].

We acknowledge that the retrospective nature of our research and the fact that we were not able to obtain data regarding neither lymphovascular invasion (LVI) nor postoperative therapy are limitations of our findings. Also, the small number of patients who were operated on by multiple urologists must be considered as a disadvantage. Due to the lack of complete information concerning preoperative CRP, procalcitonin and interleukins levels we were not able to compare CBC-based biomarkers with those well-known inflammatory indices. Nevertheless, despite these limitations, this paper is the first to analyze the predictive value of LMR, PLR, NLR, and dNLR in one cohort of UBC patients who underwent RC. Multicenter and prospective studies are warranted to further clarify the prognostic value of LMR, PLR, NLR, and dNLR in UBC patients undergoing RC.

## Conclusions

We determined LMR, NLR, and dNLR as independent prognostic factors for CSS and OS in UBC patients treated by RC. The findings of our study are clinically important as our results indicate that the use of cheap and simple CBC-based parameters may be valuable in identifying patients at a higher risk of all-cause and cancer-related mortality.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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