STRESZCZENIE W JĘZYKU ANGIELSKIM

Introduction: Bladder cancer (BCa) is one of the most commonly diagnosed cancer in Poland and worldwide. Non-muscle invasive bladder cancer (NMIBC) accounts for about 75% of bladder cancer cases and is characterized by a high rate of recurrence and progression. NMIBC confine to the mucosa (Ta, CIS) or submucosa (T1). It is necessary to perform cystoscopy to diagnose BCa. During transurethral resection of bladder tumor (TURB) all pathological lesions should be removed. Then based on the histopathological results and risk factors patients should be stratified into one of the four risk groups, what implies follow-up and/or treatment methods. Although some molecular markers are available, they do not allow to replace cystoscopy or perform it less frequently during surveillance.

Objectives: The main objective of this study was to evaluate the prognostic value of the biomarkers associated with inflammation and plasminogen activation system in prediction of NMIBC recurrence or progression. The secondary aim of the study was to assess whether the investigated set of biomarkers can decrease the amount of performed follow-up cystoscopies.

Materials and methods: The study was designed as a pilot prospective observational study. It included 223 patients hospitalized in Urology Clinic of Wroclaw Medical University for NMIBC in 2020-2022. Before TURB blood and urine were drawn in all included subjects. Assessed biomarkers included blood: plasminogen activator inhibitor 1 (PAI-1), soluble urokinase plasminogen activator receptor (suPAR), interleukin 8 (IL-8) and urine: IL-8, vascular endothelial growth factor (VEGF) and apolipoprotein E (APOE). Additionally, complete-blood-count (CBC) biomarkers and nutritional risk scores were evaluated: NLR (*neutrophile-to-lymphocyte ratio*), dNLR (*derived neutrophile-to-lymphocyte ratio*), MLR (*monocyte-to-lymphocyte ratio*), PLR (*platalet-to-lymphocyte ratio*), (modified) Glasgow Prognostic Score ((m)GPS) and Prognostic Nutritional Index (PNI).

Results: After a 3-month follow-up period with cystoscopy or TURB 92 patients were tumor free (Group 1). In 131 subjects (Group 2) a recurrence of NMIBC or progression to muscle invasive bladder cancer (MIBC) was observed. No major clinical differences between these two groups were noted. The Group 2 has shown with significantly higher concentrations of blood IL-8 and suPAR as well as urine VEGF and APOE. The blood IL-8 and urine VEGF presented the highest prognostic abilities with AUROC of 0.611 (95% CI: 0.534 – 0.687, p=0.0044) and 0.632 (95% CI: 0.557 – 0.707, p=0.0006), respectively. Machine learning model (ML) which included studied biomarkers and European Organisation for Research and Treatment of Cancer

(EORTC) risk scores has allowed to discriminate the two patient entities with AUROC of 0.84 (95% CI: 0.73-0.95, $p<0.0001$). Among CBC biomarkers, NLR showed the highest AUROC of 0.618 (95% CI: 0.536-0.699), for discrimination of the study outcomes. None of the nutritional risk scores predicted disease progression or recurrence. NLR, MLR and dNLR enhanced the diagnostic performance for EORTC recurrence and progression points.

Discussion: In this study, urine VEGF and blood IL-8 showed low prognostic value for predicting recurrence or progression of NMIBC after TURB. The remaining biomarkers had lower predictive value. The amount of comparative literature data is scarce. Among CBC inflammatory markers and nutritional indexes no parameter with consistent prognostic value was identified. Based on these results, it is impossible to reduce the amount of performed surveillance cystoscopies with the use of the examined biomarkers.

Conclusions:

1. A panel of inflammatory and plasminogen activation system biomarkers, consisting of blood PAI-1, suPAR, IL-8 and urine VEGF, APOE, IL-8 combined with EORTC model has predicted the recurrence or progression of NMIBC after TURB.
2. Individual biomarkers associated with systemic inflammatory response and plasminogen activation system, including CBC biomarkers have shown insufficient predictive value for predicting the study outcome.
3. None of the nutritional risk scores was predictive of treatment results.
4. Investigated biomarkers cannot replace cystoscopy or reduce its frequency during patients' surveillance.