CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Effect of HALP Rate to Pathological Stage with Bladder Tumor Patients

HALP Oranının Mesane Tümörü Olan Hastalarda Patolojik Evreye Etkisi

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Abstract

Objective: In this study, to investigate the effect of preoperative hemoglobin, albumin, lymphocyte and platelet (HALP) ratio on the pathological stage in patients with bladder tumors larger than 3 cm.

Methods: In the study, 310 patients who met the inclusion criteria were evaluated who underwent transurethral resection of bladder tumors operation for the first time due to bladder tumor between 2010 and 2020 and whose data were fully collected were evaluated. The patients were divided into two groups as muscle invasive (MIBC) and non-muscle invasive bladder tumor (NMIBC) according to the pathology report. The difference between HALP values and ratios was evaluated for both groups.

Results: In the study, 310 patients included in the study with complete data, 227 (73.2%) had NMIBC and 83 (26.8%) had MIBC pathology results. Of the NMIBC patients, 157 (69%) had high-grade papillary urethelial carcinoma and 70 (31%) had low-grade papillary urethelial carcinoma. The mean HALP value for NMIBC is 28.36±2.83, the mean HALP value for MIBC is 21.45±3.14. According to the univariate analysis, it was concluded that high stage was associated with hypoalbuminemia, anemia and low HALP.

Conclusion: In this study, it was concluded that calculating the HALP rate, which is cheap, easy to apply and gives rapid results, may be a significant predictor of the pathological stages of the patients and indirectly in estimating the survival of the disease.

Keywords: HALP score, muscle invasive bladder tumor, non-muscle invasive bladder tumor

Öz

Amaç: Bu çalışmada, mesane tümörleri 3 cm'den büyük olan hastalarda ameliyat öncesi hemoglobin, albümin, lenfosit ve trombosit (HALP) oranının patolojik evreye etkisini araştırmak amaçlandı.

Yöntem: Çalışmada, 2010-2020 yılları arasında mesane tümörü nedeniyle ilk kez mesane tümörlerinin transüretral rezeksiyon operasyonu uygulanan, dahil edilme kriterlerine uyan ve verileri tam olan 310 hasta değerlendirildi. Hastalar patoloji raporuna göre kasa invaze (MIBC) ve kasa invaze olmayan mesane tümörü (NMIBC) olarak iki gruba ayrıldı. HALP değerleri ve oranları arasındaki fark her iki grup için değerlendirildi.

Bulgular: Çalışmaya verileri tam olarak dahil edilen 310 hasta, 227'si (%73,2) NMIBC ve 83'ü (%26,8) MIBC patoloji sonucuna sahipti. NMIBC hastalarının 157'sinde (%69) yüksek dereceli papiller üretel karsinom ve 70'inde (%31) düşük dereceli papiller üretel karsinom vardı. NMIBC için ortalama HALP değeri

Öz

28,36±2,83, MIBC için ortalama HALP değeri 21,45±3,14 idi. Tek değişkenli analize göre yüksek evre hipoalbüminemi, anemi ve düşük HALP ile ilişkili olduğu sonucuna varıldı.

Sonuç: Bu çalışmada ucuz, uygulaması kolay ve hızlı sonuç veren HALP oranının hesaplanmasının, hastaların patolojik evrelerinin önemli bir öngörücü olabileceği ve dolaylı olarak hastalık sağkalımını tahmin edebileceği sonucuna varıldı.

Anahtar Kelimeler: HALP skoru, kas invaziv mesane tümörü, kas invaziv olmayan mesane tümörü

Introduction

The degree of systemic inflammatory response measured before surgery is associated with survival in patients with cancer. Low albumin and lymphocyte levels and high C-reactive protein (CRP), leukocyte, neutrophil, and platelet levels are indicators of systemic inflammatory response. Combinations of these parameters revealed various prognostic factors based on inflammation[1]. Biochemical markers of the inflammatory response can be used to determine the prognosis of many malignant diseases[2]. Biochemical markers are used in autoimmune, inflammatory, and infectious diseases where the severity of inflammation is important[3]. It has been shown in different settings that hemoglobin, albumin, leukocytes, and thrombocyte (HALP) levels are associated with prognosis in oncological patients[4]. Albumin is an important prognostic factor in oncological patients, for example, hypoalbuminemia may indicate a poor prognosis[5]. Leukocytes and platelets both contribute to inflammation and play an important role in determining the prognosis by interacting with cancer cells in the bloodstream[6].

The aim of study is to investigate the effect of preoperative HALP ratio on the pathological stage in patients with bladder tumors larger than 3 cm.

Materials and Methods

The data of 411 patients who were operated for the first time due to bladder tumor in the Urology Clinic of University of Health Sciences Turkey, Education and Research Hospital between 2010 and 2020 were retrospectively analyzed. The data of the patients were taken from the hospital electronic database and analyzed retrospectively. Bladder tumor operations were performed by or under the supervision of experienced faculty members in the Urology Clinic. Ethical approval was obtained from Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital with approval number: 2021/12-01.

The patients with a pathology other than transitional cell carcionam, with a secondary malignancy, with a tumor size less than 3 cm, that were previously operated for bladder tumor, having hematological disease, Patients with a history of infection in the last 1 month by "Have you had a fever in the last month have you taken any antibiotics or anti-inflammatory drugs" questions, diseases that may affect albumin values malnutrition patients, liver diseases having an autoimmune disease and using immunosuppressive drugs were excluded from the study because these conditions may affect the inflammatory response. Three hundred ten patients were included in the study.

In the study, the preoperative HALP and albumin ratios of the patients were evaluated and the HALP score was calculated. The pathology results of the patients were treated according to European Urology Association guideline (re transurethral resection, intravesical therapy, radical cystectomy etc.).

HALP score calculation: Hemoglobin (gr/dL) x Albumin (gr/dL) x Lymphocyte (count/μL)/Platelet (count/μL).

The relationship between the HALP score and the pathological stage of the patients was evaluated. Calculated a cutoff value with receiver operating characteristic (ROC) analysis determining predicting pathological stage.

All patients had given written informed consent before the surgery for permitting the use of the collected data at any time. Institutional review board has approved the study. The principles of the Helsinki Declaration were followed during the study, and the confidentiality of the patients' data was guaranteed.

Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS) 24 (SPSS Inc., Chicago, IL, USA) package program. The normal distribution of the data was evaluated with the Shapiro-Wilk test. Descriptive statistics were presented as numbers

(n) and percentages (%) for categorical variables, and mean and standard deviation for numerical variables. Chi-square test, Fisher exact test for categorical variables, Independet t-test and One-Way ANOVA test were used for quantitative variables in pairwise and multiple comparisons. Pearson correlation analysis was used in multiple correlation analysis. To determine the statistical significance level, p<0.05 was considered significant at the 95% confidence interval.

Results

Pre-operative biochemical parameters in the patients with muscle-invasive and non-muscle invasive bladder cancer and their significance are shown in Table 1. Non-muscle invasive (NMIBC) 227 patients were classified as group 1.198 (87%) of these patients were male; 29 (13%) of them were women. Eighty three patients with muscle-invasive bladder tumor (MIBC) were classified as group 2. Of these patients, 71 (86%) were male and 12 (14%) were female. The mean age of group 1 was 72.83±10.81 (minimum: 40-maximum: 96), group 2 was 74.98±10.2 (minimum: 45-maximum: 87) years. In group 1; 157 (69%) patients had high-grade tumors and 70 (31%) had low-grade tumors.

The median follow-up of patients was 41 months [interquartile range (IQR) 22-59].

The mean albumin was 4.3±08 g/dL in group 1 and 4.1±07 g/dL in group 2. Hypoalbuminemia was detected in 17 patients (7.48%) in group 1 and 10 patients (12.04%) in group 2. There was a statistical difference between the groups in terms of hypoalbuminemia (p=0.0049). Anemia was present in 52 patients (22.90%) in group 1 and 32 (38.45%) patients in group 2. There was a statistical difference between the groups in terms of anemia (p=0.0019).

Calculated a cutoff value with ROC analysis determining predicting pathological stage (Figure 1).

According to the ROC analysis, the cut-off value of the HALP score according to the pathology result was found 25.33, the sensitivity was 79% and the specificity was 72%.

The mean HALP value for group 1 was 28.36±2.83, the mean HALP value for group 2 was 21.45±3.14. There was a statistically significant difference between the two groups in terms of HALP value (p=0.014).

According to univariate analysis, high stage (T2 and above) was associated with hypoalbuminemia, anemia, and low HALP.

According to the results of Pearson correlation analysis; There was an inversely significant difference between tumor stage and HALP variable. The higher the HALP value, the smaller the tumor stage was found.

Table 1. Demographic and pre-operative biochemical parameters data of patients			
	NMIBC	MIBC	p value
Number of patients n=310	227	83	
Age	72.83±10.81	74.98±10.2	0.089
Gender			
Men	198	71	0.092
Woman	29	12	
Tumor grade			<0.001
Low grade	70	3	
High grade	157	80	
Hemoglobine	12.8±2.2	11.4±2.4	0.0019
Albumine	4.3±08	4.1±07	0.0049
Lymphocyte	2.12±08	1.98±07	0.0426
Platelets	278±88.5	274±86.5	0.872
Halp rate	28.36±2.83	21.45±3.14	0.014
NMIBC: Non-muscle invasive bladder tumor, MIBC: Muscle invasive bladder tumor			
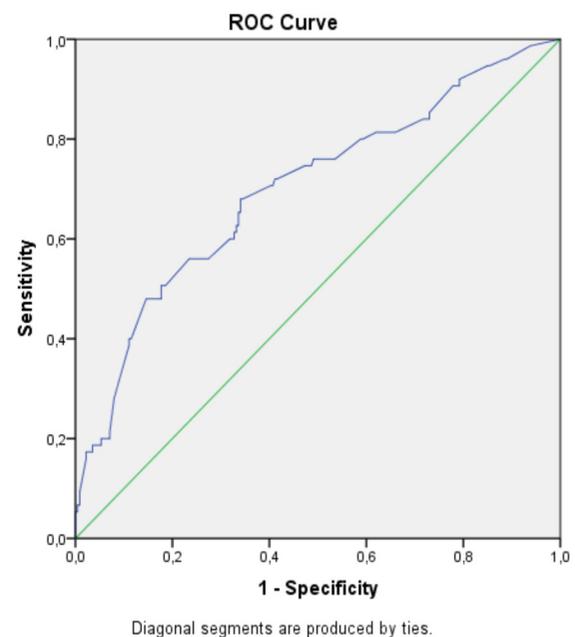
Figure 1. ROC curve

ROC: Receiver operating characteristic

Discussion

Systemic inflammatory response plays an important role in the course of both benign and malignant diseases. Markers obtained from routine biochemical test results of patients such as HALP and CRP are used in the evaluation of inflammatory response in many diseases. Bacillus Calmette-Guérin in bladder tumors reduces recurrence and progression. Based on this, many biochemical parameters have been evaluated so far to evaluate the progression in bladder tumors. The HALP score, which consists of HALP, is a newly established scoring tool for representing the status of both host inflammation and nutrition. In this study, we examined whether the preoperative HALP rate could predict the effect on pathological stage in patients with bladder tumors larger than 3 cm, and showed that this marker has a strong relationship with pathological stage and indirectly with survival. and other clinical parameters indicative of an aggressive phenotype. Multivariate analysis identified HALP score as a significant predictor of overall survival and progression-free survival in patients.

The role of nutrition and immunity in predicting the prognosis of cancer patients has recently attracted attention[7]. In their systematic review, Caro et al.[8] emphasized that anemia is an independent prognostic factor for cancer patients and found that the risk of death due to anemia increased by 47% in patients with prostate cancer. In addition, the serum albumin level serves as an auxiliary parameter in the evaluation of protein levels. The literature supports the hypothesis that serum albumin level is significantly associated with cancer survival[9,10]. Sejima et al.[11] showed that preoperative hypoalbuminemia may lead to the spread of localized prostate cancer and may be associated with biochemical recurrence. In our study, low hemoglobin and albumin levels were found to be significantly higher in patients with high-stage tumors. The mean albumin was 4.3±08 g/dL in group 1 and 4.1±07 g/dL in group 2 (p=0.0049) Other studies have reported that the tumor microenvironment is mainly regulated by inflammatory cells, which indispensably contribute to tumor progression[12].

Systemic inflammation is the factor that determines the treatment results in many diseases. The HALP score, calculated from HALP values, is an inflammatory marker that can strongly reflect the inflammatory response of patients. The HALP score has been used as a marker associated with poor prognosis and survival in patients with various gastrointestinal cancers such as bladder, prostate, stomach, and colon[13]. Each component of the HALP score is an element that can individually reflect the prognosis of diseases. Indeed, it is associated with low hemoglobin levels in bladder tumors larger than 3 cm[14]. Similarly, hypoalbuminemia is a factor that increases complications in patients undergoing abdominal surgery[15]. Studies have found that lymphocyte counts are also associated with prognosis in patients with colorectal and gastric cancer who have undergone surgery[16,17]. It has been suggested that low lymphocyte levels may predict the development of an intra-abdominal abscess in pediatric patients who have undergone appendectomy[18]. It has been shown that platelets, which play an active role in the development of the inflammatory response, are a putative indicator of postoperative complications[19]. The relationship between a bladder tumor larger than 3 cm and the HALP score has not been investigated before. Here we show a strong correlation between the HALP score and pathological stage and survival. It was observed that the tumor stage increased as the HALP score decreased.

Study Limitations

Our study has some limitations. The two most important limitations were that the study was retrospective, single-centered, and the number of patients was small. However, our study is the first of its kind to investigate stage and survival and compare inflammatory markers in patients with bladder tumors larger than 3 cm. It is the first study to show that it predicts visuals of their work in patients with bladder tumors with a HALP score greater than 3 cm. Prospective studies with larger patient series are needed to validate and standardize the data.

Conclusion

In conclusion, HALP, which is inexpensive, fast, and easily accessible, preoperatively measured is valuable in predicting the pathological stage and survival in patients with bladder tumors larger than 3 cm. It may be beneficial to use these inflammatory markers in conjunction with other diagnostic tools.

Ethics

Ethics Committee Approval: Ethical approval was obtained from Ethics Committee University of Health Sciences Turkey İzmir Tepecik Education and Research Hospital with decision no: 2021/12-01, date: 15.12.2021.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Concept: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Design: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Data Collection or Processing: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Analysis or Interpretation: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Literature Search: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K., Writing: M.Y., B.K., C.Y., E.K., G.K., H.Ü., T.S., M.Z.K.

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