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Examination of the Hemoglobin, Albumin, Lymphocyte, and Platelet Score of Testicular Tumor: Comparison of Pre- and Postoperative and Non-Cancerous Patients

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

The purpose of this study was to determine whether the hemoglobin, albumin, lymphocyte, and platelet (HALP) score, which includes hemoglobin, albumin, lymphocyte, and platelet levels, is a significant parameter in the diagnosis of testicular tumors. The study included patients who underwent orchiectomy at our clinic with a preliminary diagnosis of testicular tumor and whose diagnosis was confirmed after the pathological examination. Preoperative and postoperative HALP scores were calculated and analyzed. The cases were compared based on their pathological diagnosis and tumor node metastasis staging. Additionally, the scores of all patients with testicular tumors were compared to those of the non-cancerous control group. Consequently, a significant cut-off value for the HALP score in testicular tumors was obtained, and this value suggests that the HALP score can be a useful diagnostic tool for testicular tumors.

Abstract

Objective: To determine and compare the pre-and post-operative hemoglobin, albumin, lymphocyte, and platelet (HALP) scores of patients who underwent radical orchiectomy for testicular tumor based on pathology and stage with those of patients without a testicular tumor.

Materials and Methods: One hundred nineteen patients diagnosed with testicular tumor between 2017 and 2022 were retrospectively analyzed. Patients' pre- and post-op HALP, neutrophil-lymphocyte ratio, and platelet-lymphocyte ratio values were saved. In the control group, 100 varicocelectomy patients aged 19 to 56 between 2018 and 2022 were questioned. The data were analyzed based on pathology and stage; tumor patients were compared with the control group.

Results: The tumor and control groups had mean ages of 31 and 30 years; the seminoma group had a pre-op HALP score of 59, while the mixed germ cell tumor (MGCT) group had a score of 55 (p=0.283). There was no statistical difference in HALP scores between pathological groups before and after surgery (p=0.327, 0.510). The testicular tumor group's mean pre-op HALP value was 57.75, whereas the control group's was 70.85 (p=0.000). There were 28 embryonal carcinomas among the 54 MGCT group patients. The pre-op and post-op HALP scores of both pathological groups were not significant (p=0.162, 0.104).

Conclusion: The HALP score is an important parameter that is higher in testicular cancer patients than in non-cancerous patients. There was no statistically significant difference in HALP scores based on pathological subtype, tumor stage, or lymph node metastasis status.

Keywords: Biomarker, hemoglobin, albumin, lymphocyte, platelet (HALP) score, nomogram, testicular cancer

Introduction

Testicular tumors comprise 1% of all adult neoplasms and 5% of all urological tumors (1). Its prevalence has risen in recent years, particularly in developed countries (2,3). Because it is diagnosed relatively early in life and develops silently, it can metastasize quickly. Only 1-2% of cases are diagnosed bilaterally, and germ cell tumors are the most common histological type (1).

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Recent research has focused on the nutritional status of patients and the hemoglobin, albumin, lymphocyte, and platelet (HALP) score, a new inflammation index that measures the immune system by proportionally combining hemoglobin, albumin, lymphocytes, and platelets. The HALP score has been identified as a prognostic predictor in patients with malignant tumors such as renal cell carcinoma, genitourinary cancer, and lung cancer (4-6).

There has been no study on whether the HALP score is significant in testicular tumor cases. We designed this study to obtain a new parameter that will help in the differential diagnosis of testicular tumors other than known tumor markers. We retrospectively analyzed patients who underwent orchiectomy for testicular tumors and patients who underwent varicocelectomy for primary infertility as controls.

Materials and Methods

Study Design

One hundred fifty two patients aged 20-65 years diagnosed with testicular tumors and who underwent orchiectomy at Kartal City Hospital between 2017 and 2022 were retrospectively analyzed.

Exclusion Criteria

Patients who were not pathologically diagnosed with testicular tumor (n=14), who had advanced comorbidities (n=9), and chronic disease anemia (n=10). Thus, 119 testicular tumor patients were included in the study, among whom there were no bilateral testicular tumors or solitary testicle.

Age, pre-operative and postoperative HALP, neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) levels were all measured. The hemograms obtained in the first three months after orchiectomy were used to calculate postoperative data. The control group included 100 patients aged 18 to 37 who had varicocelectomy for primary infertility and had no comorbidities. These patients' pre-op HALP score, NLR, and PLR values were calculated. The postoperative HALP score could not be calculated in the control group because the hemogram was not checked during the patients' routine follow-up.

Calculation

The HALP score was calculated as hemoglobin level (g/L) albumin level (g/L) lymphocyte (/L)/platelet count (/L). PLR and NLR were accounted for by dividing the platelet count by the lymphocyte count and the neutrophil count by the lymphocyte count (7).

Statistical Analysis

All data were analyzed using the SPSS IBM 25 program. According to their pathology, the patients were divided into seminoma and mixed germ cell tumor (MGCT) groups. In addition, two different groups formed testicular tumors and control patients. MGCT patients were analyzed according to the predominant type of pathology (based on tumor percentage). In addition, all testicular tumor patients were compared by calculating pre-operative and postoperative HALP, NLR, and PLR values according to tumor node metastasis staging. Paired samples t-test, Wilcoxon signed-rank test, Student's t-test, Mann-Whitney U test, receiver operating characteristic (ROC) curve analysis, and One-Way ANOVA tests were used for statistical analysis.

Results

There were 119 testicular tumors and 100 control group patients. The median age of the tumor patients was 31 (seminoma; 34, MGCT; 28), and the control group was 30 (p=0.352). Also, these patients, 65 were seminoma, and 54 had MGCT.

The median pre-operative and postoperative HALP scores in the seminoma group were 59 and 57, respectively (p=0.327), as opposed to 55 and 57.2 in the MGCT group (p=0.510). In terms of HALP scores, there was no discernible difference between the two groups before and after surgery (Table 1).

Seminoma patients' pre-operative and postoperative mean NLR values did not substantially differ; however, there was a significant difference between the pre-operative and postoperative NLR values for the MGCT group (p=0.008). In either diseased group, however, there was no statistically significant difference between pre- and postoperative PLR values (Table 1).

Table 1. Age, pre-op and post-op HALP, NLR and PLR values of the Seminoma and MGCT Group

	Seminoma (n=65)		MGCT (n=54)	
	Mean	p	Mean	p
HALP 1	59 (15-133)	0.327*	55 (13-113)	0.510*
HALP 2	57 (12-134)		57.2 (10-111)	
NLR 1	2.95 (1.1-7.7)	0.441**	3.71 (0.8-17.7)	0.008**
NLR 2	2.98 (1-10.9)		2.83 (0.32-11.7)	
PLR 1	129.9 (55-305)	0.953**	152.8 (39.8-376)	0.512*
PLR 2	133.5 (53.6-364)		146.3 (56-390)	

*Paired Samples t-test, **Wilcoxon signed-rank test, MGCT: Mixed germ cell tumor, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, 1: Preoperative, 2: Postoperative

Another comparison was obtained by comparing all tumor patients with the control group. The HALP score of testicular tumor patients was 57.7, but it was 70.8 in the control group (p=0.000). A significant difference was observed when the NLR and PLR values of the tumor group and the control group were compared (p=0.000) (Table 2). Furthermore, ROC curve analysis revealed that the optimal cut-off value for the HALP score was 62 (Table 3) (Figure 1).

When seminoma and MGCT patients were pathologically classified, there was no significant difference in HALP, NLR, and PLR scores pre- and postoperatively (Table 4). If the patients in the MGCT group were classified within themselves, we obtained four groups: 28 embryonal carcinoma, 14 teratoma, 7 seminoma, and 5 Yolk-Sac predominant. In the MGCT group, there was no pathology, with choriocarcinoma predominating. There was no significant difference in HALP, NLR, or PLR values between the groups before and after surgery (Table 5).

All testicular tumor patients were classified according to T staging; there were 37 testicular intraepithelial neoplasia, 67 T1, 14 T2, and 1 T3. According to the T staging of the patients, the HALP, NLR, and PLR values did not differ significantly (Table 6).

Table 2. Comparison of testicular tumor and control group patients

	Testicular tumor (n=119)	Control group (n=100)	p
Age (year)	31.9±9.05	27.9±5.4	0.001*
HALP	57.75±24.8	70.85±21.3	0.001*
NLR	3.29±2.27	1.80±0.68	0.001*
PLR	140±58.3	100.7±29.5	0.001*

*Student's t-test, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

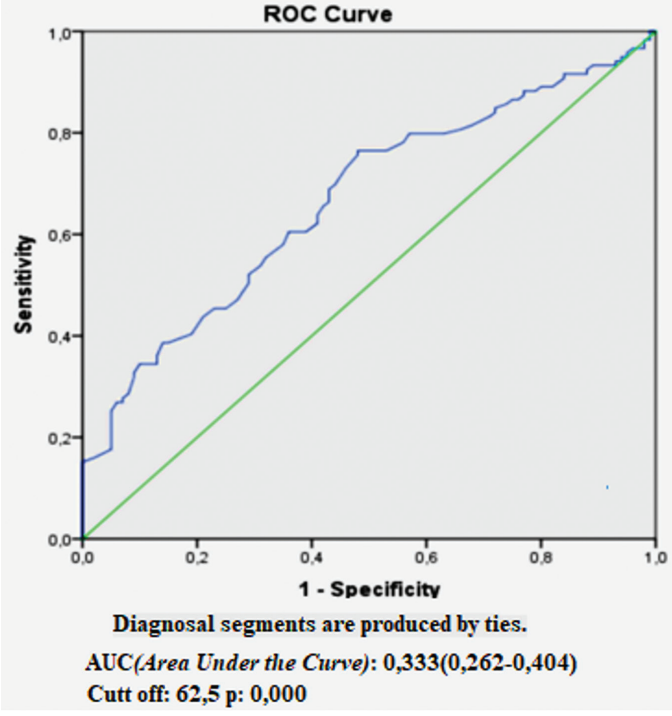

Figure 1. Determination of the optimal threshold value of the HALP score by ROC analysis

HALP: Hemoglobin, albumin, lymphocyte and platelet; ROC: Receiver operating characteristic

Discussion

Hemoglobin and albumin levels are associated with the nutritional status of the body, whereas lymphocytes and platelets are related to the immune system. The HALP score system has typically been used to estimate the prognosis of patients with cancer. This scoring system was initially developed by Chen et al. (8) to determine the prognosis of stomach cancer. The importance of the HALP score as a risk biomarker in various malignancies has also been established. Gao et al. (9), conducted in 2022, suggested that patients with non-metastatic ureteral tumors with a preoperative HALP score below 28 were an independent risk factor for overall survival. We discovered an optimal HALP score of 62 (Figure 1).

In another study by Kaya et al. (10), the HALP score study conducted in 2020 in prostate cancer and benign prostatic hyperplasia patients, the HALP index did not have a diagnostic role.

Unlike previous studies, we aimed to compare HALP, NLR, and PLR scores with the normal population as well as pre- and postoperative pathological diagnosis and stage in our study. In the testicular tumor group, statistical data revealed no significant difference between the seminoma and non-seminoma groups in terms of both pre- and postoperative HALP scores. The most important finding of our study, and the one that most surprised us numerically, is the difference between the HALP scores of the testicular tumor and control groups.

When the data were analyzed according to the pathology and staging, there was no statistical difference between the mean HALP scores. In the foreground, we thought that HALP, NLR, and PLR values would differ before orchiectomy due to tumor burden. However, we noticed no significant difference between the seminoma and MGCT groups regarding both pre- and postoperative HALP scores. We want to note the same result in the "T" staging.

Our study is not the first to examine NLR and PLR levels in patients with testicular tumors. There are studies in the literature that show that NLR and PLR values are helpful for testicular tumor diagnosis, staging, and metastasis. Wealso found a significant difference in NLR and PLR values between tumor patients and the control group (11-13). However, there has been no published research on the relationship between HALP score and testicular

Table 3. Receiver operating characteristic curve parameters of positive prognostic factors for testicular cancer

	AUC (95%)	Cut-off	p	Sensitivity (%)	Specifity (%)
Age	0.625 (0.551-0.699)	28.5	0.001	59.7	37
HALP	0.333 (0.262-0.404)	62.5	0.000	39.5	61
NLR	0.782 (0.843-0.722)	2.06	0.000	70	30
PLR	0.723 (0.655-0.790)	110.3	0.000	66.4	32

AUC: Area under the curve, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

Table 4. Comparison of HALP, NLR, PLR values of seminoma and MGCT

Age	Seminoma (19-58)	34	p
	MGCT (18-58)	28	0.001*
HALP 1	Seminoma	59.9	0.283*
	MGCT	55.0	
HALP 2	Seminoma	57.4	0.959*
	MGCT	57.2	
NLR 1	Seminoma	2.95	0.056**
	MGCT	3.71	
NLR 2	Seminoma	2.98	0.193**
	MGCT	2.83	
PLR 1	Seminoma	129.9	0.077**
	MGCT	152.2	
PLR 2	Seminoma	133.5	0.913**
	MGCT	146.3	

*Student's t-test, **Mann-Whitney U test, MGCT: Mixed germ cell tumor, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, 1: Preoperative, 2: Postoperative

Table 5. Pre-op and post-op HALP, NLR, PLR comparison of MGCT patients by dominant Tm type

Dominant pathology type	Number of patients (n=54)	HALP 1	HALP 2	NLR 1	NLR 2	PLR 1	PLR 2
Seminoma	7	46.2	44.4	3.53	2.73	169.6	167.8
Teratoma	14	60.1	66.0	4.13	2.55	140.2	130.9
Embryonal carcinoma	28	51	52.4	3.69	3.11	161.8	156.5
Yolk-Sac	5	75.6	77.2	2.86	2.22	108	102.2
Mean		55	57.2	3.71	2.83	152.2	146.3
p:		0.162*	0.104*	0.852*	0.814	0.302*	0.439

*One-Way ANOVA, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte Ratio, 1: Preoperative, 2: Postoperative

tumors. We would like to emphasize that our study is the first of its kind. We should also mention that our HALP value was higher in both the testicular tumor and non-cancerous groups than in previous studies (5,14).

Study Limitations

Include the fact that it is retrospective, single-center, and the time determined for the postoperative HALP score is limited to the first three months; it is unclear whether the patients will receive chemotherapy or radiation therapy. We also accept that some patients underwent retroperitoneal lymph node dissection (RPLND) during the follow-up period after orchiectomy, and no cancer-specific mortality information that was not reported in the trial.

It is possible that patients who have undergone RPLND have different HALP scores than those who have not. However, if we make an average comment based on T staging, we should state that the results were not statistically significant (p=0.187). Another notable finding was that there was no significant difference in HALP scores between the seminoma group and the non-seminomatous testicular tumor group, which has a worse prognosis.

Table 6. Pre-op and post-op HALP, NLR, PLR scores according to T staging							
TNM	**n=119**	**HALP 1**	**HALP 2**	**NLR 1**	**NLR 2**	**PLR 1**	**PLR 2**
TIN	37	62.8	59.2	2.65	2.39	130.4	122.5
T1	67	57.2	57.6	3.44	3.07	137.1	142.1
T2	14	46.0	51.2	4.38	3.59	181.2	170.7
T3	1	64	52	2.29	2.47	113.3	138.2
Mean		57.7	57.374	3.29	2.91	140	139.3
p		0.187*	0.783*	0.081*	0.219*	0.037*	0.171*

*One-Way ANOVA, HALP: Hemoglobin, albumin, lymphocyte, and platelet score, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, 1: Preoperative, 2: Postoperative, TNM: Tumor node metastasis, TIN: Testicular intraepithelial neoplasia

There is a study in the literature that a new index called "HALPA" is created by combining the HALP score and the anesthesiologists grade of the patient. In a study by Peng et al. (5) in 2018, they stated that the HALPA score is associated with decreased survival after radical cystectomy. Again, Ornaghi et al. (15), in a study conducted in 2020, emphasized that preoperative HALP and HALPA scores are independent risk factors for postoperative complications and mortality in patients who underwent radical cystectomy. In this regard, we accept the lack of data on the mortality status of the patients in our study. There is yet to be a study on the HALPA score and testicular tumor. From this perspective, the absence of a HALPA score in our data is another shortcoming of our study. In the other process, a study on the relationship between the HALPA score and testicular tumor can be planned.

Conclusion

The HALP score of testicular tumor patients is lower than that of the non-cancerous population, according to our findings. However, we should note that the HALP score does not yield significant staging and pathological typing results. It is currently not possible to calculate a standard HALP score and predict whether it is critical for survival. Multicenter and long-term studies with a larger patient population may produce different results.

The HALP score of patients with testicular cancer is lower than that of the non-cancerous population. However, it should be noted that the HALP score does not provide significant results for staging and pathological typing. It is currently not possible to calculate a standard HALP score and predict whether it is critical for survival. Multicenter and long-term studies with a larger patient population may provide different results.

Ethics

Ethics Committee Approval: The study was initiated with the approval of the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (date: 29.09.2021, approval no: 2021/514/210/1).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: A.C., U.C., C.Ç., E.D., Concept: A.C., U.C., Design: A.C., U.C., Data Collection or Processing: A.C., E.D., Analysis or Interpretation: A.C., U.C., C.Ç., Literature Search: A.C., C.Ç., Writing: A.C., U.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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