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Original Article

Diagnostic role of NLR, MLR and PLR in patients with lipoma and liposarcoma

Lipom ve liposarkomlu hastalarda NLR, MLR ve PLR'nin tanısal rolü

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Abstract

Aim: The aim of this study is to investigate the diagnostic role of Neutrophil-to-lymphocyte ratio (NLR), Monocyte-to-lymphocyte ratio (MLR) and Platelet-to-lymphocyte ratio (PLR) in patients with lipoma and liposarcoma.

Material and Methods: Patients operated for lipoma and liposarcoma at our institution between 2015 and 2019 were included in this retrospective study. A total of 92 patients with 44 lipoma and 48 liposarcoma were included in this study. The results of the complete blood count before treatment were retrospectively analyzed. 94 patients with complete blood count results admitted to the same center for reasons other than fracture, infection or tumors with similar age and sex to the aforementioned study group were included as healthy controls.

Results: The average age of lipoma, liposarcoma and control groups included in the study was 55.3 ± 11.6, 48.9 ± 14.7 and 52.1 ± 11.7, respectively. While 50% of lipomas are located on the thigh and 40.9% are on the shoulder, 72.9% of the liposarcomas are located on the thigh. NLR values of the liposarcoma group were significantly higher than the control group. It was observed that PLR values did not differ significantly between groups. It was noted that MLR values were statistically significantly higher in the liposarcoma group than in the lipoma group. A significant but weak AUC value (AUC = 0.620, p = 0.020) was obtained for NLR. When the cut-off value and sensitivity, specificity, + LHR, PPV and NPV values of these cut off values are examined, NLR 1.83 and above values; It pointed out that his predictability was poor in the diagnostic approach for liposarcoma.

Conclusion: Consequently, lipoma and liposarcoma are the most common forms of benign and malignant soft tissue tumors. NLR and MLR may be valuable in the diagnosis of liposarcoma, but more studies are needed in this regard.

Keywords: Lipoma, Liposarcoma, Neutrophil-to-lymphocyte ratio; Monocyte-to-lymphocyte ratio; Platelet-to-lymphocyte ratio

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ÖZ

Amaç: Bu çalışmanın amacı, lipoma ve liposarkomlu hastalarda Nötrofil / lenfosit oranının (NLR), Monosit / lenfosit oranının (MLR) ve Trombosit-lenfosit oranının (PLR) tanısal rolünü araştırmaktır.

Gereç ve Yöntemler: 2015-2019 yılları arasında kurumumuzda lipom ve liposarkom nedeniyle opere edilen hastalar bu retrospektif çalışmaya alındı. Bu çalışmaya 44 lipoma ve 48 liposarkomlu 92 hasta dahil edildi. Tedaviden önce tam kan sayımı sonuçları geriye dönük olarak analiz edildi. Yukarıda belirtilen çalışma grubuna benzer yaş ve cinsiyete benzer kırık, enfeksiyon veya tümörler dışındaki nedenlerle aynı merkeze kabul edilen tam kan sayımı sonuçları olan 94 hasta sağlıklı kontroller olarak dahil edildi.

Bulgular: Çalışmaya dahil edilen lipom, liposarkom ve kontrol gruplarının yaş ortalaması sırasıyla 55.3 ± 11.6, 48.9 ± 14.7 ve 52.1 ± 11.7 idi. Lipomların% 50'si uylukta,% 40.9'u omuzda bulunurken, liposarkomların% 72.9'u uylukta bulunur. Liposarkom grubunun NLR değerleri kontrol grubundan anlamlı olarak yüksekti. PLR değerlerinin gruplar arasında anlamlı farklılık göstermediği gözlendi. Lipozarkom grubunda MLR değerlerinin lipoma grubuna göre istatistiksel olarak anlamlı derecede yüksek olduğu kaydedildi. NLR için anlamlı fakat zayıf bir AUC değeri (AUC = 0.620, p = 0.020) elde edildi. Bu kesme değerlerinin kesme değeri ve duyarlılığı, özgüllüğü, + LHR, PPV ve NPV değerleri incelendiğinde NLR 1.83 ve üzeri değerler; Liposarkom için tanısal yaklaşımda öngörülebilirliğinin zayıf olduğuna dikkat çekti.

Sonuç: Sonuç olarak, lipom ve liposarkom, benign ve malign yumuşak doku tümörlerinin en yaygın formlarıdır. NLR ve MLR, liposarkom tanısında değerli olabilir, ancak bu konuda daha fazla çalışmaya ihtiyaç vardır.

Anahtar kelimeler: Lipom; liposarkom; nötrofil-lenfosit oranı; monosit-lenfosit oranı; trombosit-lenfosit oranı

Introduction

Lipomas are very common benign neoplastic mesenchymal tumors arising from adipose tissue, while liposarcomas are the most common soft tissue sarcomas in adults and make up about 20% of all soft tissue malignancies.[1] While lipomas are limited masses of mature adipocytes that do not show cellular atypia, liposarcomas originate from primitive mesenchymal cells with much potential rather than mature adipose tissue.[2] Liposarcomas usually originate from the extremities, especially the thigh, retroperitoneum, groin and paratesticular areas.[3, 4] Differential diagnosis is performed clinically, radiologically and pathologically, but the need for a reliable and easily generalizable criteria is evident however there are no specific biomarker available in the clinical setting despite ongoing studies.[5]

The tumor microenvironment and, in particular, the inflammatory response play an important role in cancer development and progression and may be associated with systemic inflammation. [6] Recently, some inflammation parameters, originated from routine complete blood count (CBC), have been investigated as potential biomarkers with mixed results and no consensus so far regarding its accuracy and clinical usefulness: neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR). [7] Therefore, we aimed to investigate the diagnostic role of NLR, MLR and PLR in patients with lipoma and liposarcoma in this study.

Material and Methods

Patients diagnosed with lipoma and liposarcoma in our institution between 2015 and 2019 were included in this retrospective study. Ninety-two patients were identified in the institutional patient database and age, sex, location and type of tumor, pre-treatment complete blood count results were acquired retrospectively. Of 92 identified patients (51 males, 41 females) 44 were diagnosed with lipoma and 48 with liposarcoma. Ninety-four with complete blood count results admitted to the same center for reasons other than fracture, infection or tumors with similar age and sex to the aforementioned study group were included as healthy controls. Patients without necessary information or with high c-reactive protein or procalcitonin were excluded from the study. NLR.MLR and PLR were calculated as the absolute count of neutrophil,monocyte and platelet, respectively, divided by the absolute lymphocyte count. This study was approved

by our Institutional Review Board. Informed consent was obtained from all patients and the principles of the Helsinki Declaration were followed.

Statistical analysis

Statistical analyses were done using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics are presented as numbers and percentages for categorical variables and mean ± standard deviation, median (minimum value – maximum value) for continuous variables. Normal distribution for continuous variables were assessed with visual (histograms and probability graphics) and analytic methods (Kolmogorov-Smirnov and Shapiro-Wilk's test). In the data that do not fit the normal distribution, Mann-Whitney U test was used for comparison analysis between the two independent groups. Comparison analyses for categorical variables between independent groups were done by chi-square test.Diagnostic and prognostic values of pre-treatment NLR was assessed using receiver operating curve (ROC) analysis. The area under the ROC curve (AUC) results were considered excellent for AUC values between 0.9-1, good for AUC values between 0.8-0.9, fair for AUC values between 0.7-0.8, poor for AUC values between 0.6-0.7 and failed for AUC values between 0.5-0.6 (1,2). Results following ROC analysis; area under curve (AUC) and cut-off values, sensitivity and specificity of these cut-offs values, likelihood ratio PPD and NPD are presented. $P < 0.05$ was considered to be statistically significant.[8, 9]

Results

A total of 92 patients with 44 lipoma and 48 liposarcoma were included in this study. While 50% of lipomas are located on the thigh and 40.9% on the shoulder, 72.9% of the liposarcomas are located on the thigh (table 1). All lipomas were removed by excision and all liposarcomas were removed by wide resection. Comparison analysis of the control group included in the study with both patient groups are presented in table 2. While the gender distribution of the control group and lipoma and liposarcoma patients were similar ($p = 0.081$ and 0.314), it was observed that male patients were more frequent in the liposarcoma group than the lipoma group ($p = 0.013$). Age of liposarcoma group was significantly lower than lipoma group ($p = 0.013$). It was observed that the NLR values of the liposarcoma group were significantly higher than the control group ($p = 0.020$). PLR values did not differ significantly between the groups ($p = 0.110$, $p = 0.931$ and 0.159). It was noted that MLR values were statistically significantly higher in liposarcoma group than lipoma group ($p = 0.035$) (table 2).

Table 1. Basal Demografics of Malignancies

Characteristic	Total N=92	Lipoma n=44 (%47.8)	Liposarcoma n=48 (%52.2)
Localization, n (%)			
Thigh	57(62.0)	22(50.0)	35(72.9)
Shoulder	21(22.8)	18(40.9)	3(6.3)
Cruris	4(4.3)	0	4(8.3)
Gluteal Region	3(3.3)	0	3(6.3)
Elbow	2(2.2)	2(4.5)	0
Forearm	2(2.2)	2(4.5)	0
Arm	2(2.2)	0	2(4.2)
Back	1(1.1)	0	1(2.1)
Direction, n(%)			
Right	56(60.9)	28(63.6)	28(58.3)
Left	36(39.1)	16(36.4)	20(41.7)
Surgery, n (%)			
Excision	44(47.8)	44(100)	0
Wide Resection	48(52.2)	0	48(100)

Since NLR showed significant differences in liposarcoma and control group comparison analyzes, we evaluated the diagnostic predictability for liposarcoma with ROC analysis (fig 1). According to Table 3, a significant but weak AUC value (AUC = 0.620, $p = 0.020$) was obtained for NLR. When the cut-off value and sensitivity, specificity, + LHR, PPV and NPV values of these cut off values are examined, NLR 1.83 and above values; It pointed out that his predictability was poor in the diagnostic approach for liposarcoma (Sensitivity = 56.3%, specificity = 60%, + LHR = 1.4, PPV = 41.5% and NPV = 72.7) (Table 3).

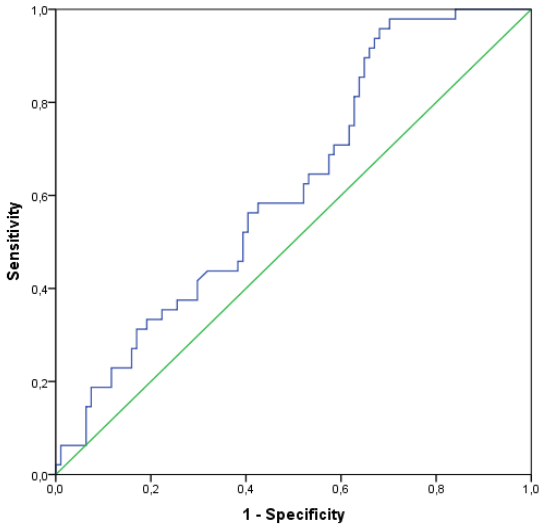

Figure 1. Receiver operating characteristic (ROC) curve for the NLR

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Table 2. Evaluation of Case-Control Groups

Characteristic	Control (G1) n=94	Lipoma (G2) n=44	Liposarcoma(G3) n=48	P (G1 vs. G2)	P (G1 vs. G3)	P (G2vs. G3)
Gender, n(%) Male Female	 55(58.5) 39(41.5)	 18(40.9) 26(59.1)	 33(68.8) 15(31.2)	0.0811	0.3141	0.0131
Age, Years Mean±sd Median(min-max)	 52.1±11.7 54.5(19-74)	 55.3±11.6 57(28-71)	 48.9±14.7 49(20-80)	0.0672	0.0782	0.0132
Hgb Mean±sd Median(min-max)	 14.5±1.5 14.9(10.6-17.1)	 13.7±1.5 13.4(11.2-16.4)	 13.9±1.9 14.7(7.5-16.2)	0.0012	0.0742	0.0582
NLR Mean±sd Median (min-max)	 1.87±0.89 1.73(0.11-6.22)	 2.24±1.1 1.80(0.88-4.26)	 2.44±2.25 1.84(1.13-16.79)	0.1292	0.0202	0.6502
PLR Mean±sd Median(min-max)	 126.6±39.3 116.9(63.7-296.7)	 138.4±45.9 140.9(64.1-244.5)	 132.8±70.7 125.1(30.9-507.6)	0.1102	0.9312	0.1592
MLR Mean±sd Median(min-max)	 4.93±1.47 4.80(1.55-9.13)	 4.84±2.0 4.3(1.79-10.31)	 5.12±1.54 5.03(0.77-7.62)	0.1542	0.2032	0.0352

1Chi-Square Test
2Mann-Whitney U test

Table 3. Diagnostic value of NLR for liposarcoma

	AUC (95% CI)	P	Cut-off	Sensitivity (%)	Specificity (%)	+LHR	PPV (%)	NPV (%)
NLR	0.620 (0.527-0.713)	0.020	≥1.83	56.3	60	1.4	41.5	72.7

+LHR: Positive Likelihood Ratio, PPV: Positive Predictive Value, NPV: Negative Predictive Value

Discussion

Lipoma and liposarcoma are the most common benign and malignant soft tissue tumors, respectively. [1] Our study shows that NLR and MLR can be useful in the differential diagnosis of lipoma and liposarcoma.

The relationship between inflammation and tumors is well established. Inflammation can increase the risk of cancer and promote carcinogenesis. [10] Although it is not clearly understood which mechanisms cause this relationship, some theories have been suggested. Tumor-related inflammation may cause direct or indirect increases in cytokines, inhibition of apoptosis, and increases in angiogenesis. [11] Tumor cells release granulocyte colony-stimulating factor (GCSF) that can trigger neutrophilia. Neutrophils play a role in tumor angiogenesis by producing proangiogenic factors such as vascular endothelial growth factor, matrix metalloproteinase, interleukin-8, and elastases. [12]Based on this information, NLR, MLR and PLR, whose relationship with most cancer has been investigated; We investigated its role in the diagnosis of lipoma and liposarcoma.

Systemic inflammatory biomarkers such as NLR, MLR and PLR in clinical management of cancers have recently begun to emerge as viable alternatives to traditional methods that have been shown to be associated with diagnosis and / or prognosis in different tumor types.[13-16] Current interest in utilizing these ratios seem justified as these are readily available values derived from routine complete blood count with no economic burden. We recorded NLR, MLR and PLR values from the routine complete blood count.

Hu et al. In 2018, they showed increased NLR in hepatocellular cancer patients.[13] Similarly, Li et al. showed that NLR can be used as a diagnostic marker in colorectal cancer.[14] Also Kemal et al. found high NLR and PLR values in lung cancer patients compared to healthy volunteers.[15] Likewise Nikolić et al. In 2016, they showed that NLR and PLR values were significantly higher in patients with lung cancer. [16] In our study, the NLR value of the liposarcoma group was significantly higher compared to the control group.

This study has some limitations. First, a significant but weak cut-off value was found for NLR. Another limitation would be retrospective, single-center nature of the study. We believe that future studies with larger sample sizes are necessary to further explore the characteristics of inflammation and role of systemic inflammatory biomarkers in lipoma and liposarcoma.

Conclusion

Lipoma and liposarcoma are the most common forms of benign and malignant soft tissue tumors. NLR and MLR may be valuable in the diagnosis of liposarcoma, but more studies are needed in this regard.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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