



Original Article

Mean platelet volume, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as prognostic factors in the differentiation of uterine leiomyoma and sarcoma

 Fazıl Avcı,  Ahmet Bilgi,  Çetin Çelik,  Mehmet Kulhan

Selçuk University, Faculty of Medicine, Department of Obstetrics and Gynecology, Konya, Turkey

Abstract

Objective: While uterine leiomyoma (LM) is frequently detected in women of reproductive age, uterine sarcoma is detected in the postmenopausal period and is diagnosed postoperatively. Inflammatory markers that facilitate the diagnosis of uterine sarcoma can be used predictively. We aimed to investigate the use of mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) as prognostic factors in differentiating preoperative uterine LM and sarcoma.

Methods: In this study, we retrospectively evaluated cases diagnosed with uterine sarcoma and LM between January 2011 and December 2021. The clinicopathological features of 51 cases (group 1) diagnosed with uterine LM and 50 cases (group 2) diagnosed with uterine sarcoma were compared.

Results: The mean ages of the patients in group 1 and group 2 were 49.1 ± 5.4 and 60.1 ± 14.0 years, respectively ($p=0.001$). The age range of the cases, menopause status, gravida, parity, preoperative hemoglobin level, platelet levels (PLT), neutrophil levels, PLR, MPV and tumor mass size were not significant ($p>0.05$). The lymphocyte levels and NLR were significant between the groups ($p<0.05$). In the regression analysis, only the age variable was determined to be a significant risk factor.

Conclusion: Age, NLR and lymphocyte level were found to be significant factors in the differentiation of uterine LM and sarcoma, while MPV and PLR were not significant factors. Large randomized controlled studies are needed for definitive evidence-based results.

Keywords: Inflammation, hematological parameters, leiomyoma, uterine sarcoma.

INTRODUCTION

Uterine LM is a frequent benign gynecological tumor that affects 40–60% of women of reproductive age, although uterine sarcoma is uncommon. Uterine sarcoma, which accounts for 1-2% of all uterine cancers and has a poor prognosis, is the most prevalent type of uterine sarcoma (1). The postmenopausal period is when uterine sarcomas are clinically most prevalent, and the median age upon diagnosis is 60 (2). According to Hosh et al., women aged over 50 years had an approximately 4-times higher incidence of sarcoma than individuals who were younger (3). During a diagnosis, uterine sarcomas are frequently incidentally found when hysterectomy or myomectomy tissue is examined (4). Most uterine sarcomas have a poor prognosis and exhibit aggressive behaviors (5, 6). However, there are no reliable preoperative diagnostic techniques for uterine sarcoma. The study proposed that computed tomography (CT) and magnetic resonance imaging (MRI) might be useful for identifying uterine sarcoma (7); however, due to their cost, these diagnostic technologies cannot be feasible for everyone. Clinically, uterine sarcoma can be treated with laparoscopic tumor removal and morcellation but it is frequently misdiagnosed as benign uterine disease (LM or adenomyosis). This misdiagnosis can play a significant role in trocar site metastases (8).

Recent studies have found a strong relationship between inflammation and the development of cancer. The following hematological abnormalities have been discovered, with a hypothesis that they indicate unfavorable outcomes in patients with different forms of cancer: decreased lymphocyte count/function, decreased eosinophil count/function and increased neutrophil count (9-11). Particularly, the NLR is a valuable marker for the diagnosis and prognosis of several types of malignancies (9, 10, 12-14). Inflammatory indicators are also useful in the diagnosis of gynecological cancers (15, 16). There are articles that demonstrate how some hematological disorders can be diagnosed and their severity can be determined through criteria such as PLT count, MPV, platelet distribution width, neutrophil count and red cell distribution width (17-19).

The objective of this retrospective case–control study is to investigate how MPV, NLR, and PLR can be used as predictive markers in the preoperative differentiation of LM and sarcoma.

MATERIALS AND METHODS

The ethics committee of this study was approved by the Selçuk University Faculty of Medicine Ethics Committee with decision no. 2022/304. Retrospective data on patients with uterine sarcoma and LM were collected between January 2011 and December 2021. Comparable clinicopathological characteristics were found in 51 cases (group 1) diagnosed with uterine leiomyoma (LM) and 50 cases (group 2) diagnosed with uterine sarcoma. The exclusion criteria were endometriosis, adenomyosis, ovarian cyst, other gynecological cancers, cancer history, signs of infection, diagnosis of hematological malignancy and inflammatory disease. The inclusion criteria were uterine sarcoma or LM, which were pathologically diagnosed.

Preoperative laboratory values of hemoglobin level, PLT level, neutrophil level, MPV level, NLR, PLR and the size of the tumor mass (largest diameter in mm) were recorded for the patients. Other information included the patients' age, age range (<50 and ≥50), gravida, parity and menopause status (premenopause and postmenopause). The formulas $NLR = \text{neutrophil count (} 10^3 \text{ L) / lymphocyte count (} 10^3 \text{ /L)}$ and $PLR = \text{platelet count (} 10^3 \text{ /L) / lymphocyte count (} 10^3 \text{ /L)}$ were used to calculate NLR and PLR, respectively. Statistical analyses were used to compare the demographic, clinicopathological, and laboratory characteristics of cases identified as uterine sarcoma and LM.

Statistical analysis

The statistical analysis was performed using SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA). Descriptive statistical tests were used to assess descriptive parameters (mean, standard deviation) in the study. The independent t test was used to compare groups for parameters with a normal distribution, while the Mann–Whitney U test was used to compare groups for nonnormal distribution. Pearson's chi-square test and Fisher's exact test were used to compare categorical parameters. Regression analysis was used to determine risk factors (OR) among group variables. ROC analysis was performed for the cut-off, sensitivity and specificity of the data. The confidence interval was 95% and the significance was taken as $p < 0.05$.

RESULTS

In the study, the mean ages of 101 patients in group 1 and group 2 were 49.1 ± 5.4 and 60.1 ± 14.0 , respectively and were statistically significant ($p = 0.001$) (Table 1). The cases' age range, menopause status, gravida, parity, preoperative complete blood count (CBC), PLT level, neutrophil level, PLR, MPV and the size of the tumor mass were not statistically significant ($p > 0.05$). Lymphocyte levels and NLR were significant between the groups

($p < 0.05$). In the regression analysis, age was determined to be a significant risk factor (Table 2).

The most important factor in the ROC analysis of diagnostic factors was age, which was statistically significant ($p = 0.001$) (Table 3, Figure 1). Other diagnostic factors, such as the NLR and lymphocyte level, were not statistically significant.

Table 1. Comparison of the cases' characteristics

	Leiomyoma (n=51)	Sarcoma (n=50)	p value
Age (year)	49.1±5.4	60.1±14.0	0.001
Age range			0.408
	<50 16 (31.4%)	12 (24.0%)	
	≥50 35 (68.6%)	38 (76.0%)	
Menopause status			0.153
	Pre 18 (35.3%)	12 (24.0%)	
	Post 33 (64.7%)	38 (76.0%)	
Gravida (n)	3.8±1.6	3.7±2.0	0.446
Parity (n)	3.0±1.5	3.4±2.0	0.445
Hemoglobin (g/dL)	11.3±1.9	11.5±1.6	0.524
PLT (K/uL)	277.4±67.4	273.4±88.0	0.801
Lymphocyte (K/uL)	1.6 ±0.9	1.5±2.7	0.026
Neutrophil (K/uL)	8.5±4.5	10.2±4.9	0.074
NLR ratio	9.6 ±9.1	11.7±7.6	0.032
PLR ratio	251.8±164.5	308.3±198.9	0.089
MPV (fL)	8.3±1.3	8.7±2.0	0.225
Mass size (mm)	80.3± 36.8	72.2±40.2	0.295

Abbreviations: PLT: Platelet, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, MPV: Mean platelet volume

Table 2. Regression analysis of diagnostic factors

Diagnostic factors	p value	Exp (B)	95% CI
Age (year)	0.001	1.115	1.056-1.176
NLR	0.370	1.026	0.970-1.086
Lymphocyte	0.338	1.115	0.892-1.394

Abbreviations: NLR: Neutrophil-lymphocyte ratio

Table 3. ROC analysis of diagnostic factors

	AUC	p value	95% CI	Cut off	Sensitivity	Specificity
Age	0.751	0.001	0.643-0.859	52.5	70.0	88.2
NLR	0.624	0.057	0.511-0.736	5.4	78.0	56.9
Lymphocyte	0.372	0.056	0.262-0.481	1.0	50.0	41.2

Abbreviations: AUC: Area under the curve, NLR: Neutrophil-lymphocyte ratio

DISCUSSION

Uterine sarcomas can manifest clinically in a variety of symptoms, including irregular uterine bleeding, abdominal pain and rapid growth (5). However, the same symptoms can also be present in nonmalignant illnesses such as uterine adenomyosis or LM. It is generally known that inflammation and cancer are closely related. The proliferation and survival of malignant cells, angiogenesis, metastasis, poor adaptive immunity and diminished sensitivity to hormonal and chemotherapeutic drugs are all influenced by the presence of inflammation, which is present in high concentrations in the tumor environment (20, 21). Reduced lymphocyte and increased neutrophil counts were identified as predictive indicators in a retrospective study comparing 31 uterine sarcoma and 93 LM cases (10). Preoperative NLR and tumor size were also described as a helpful measure in differentiating sarcoma from uterine LM. Although not the only lesion, the largest lesion measuring >8.0 cm was the sonographic evidence suggesting the presence of uterine sarcoma. In the present study, the age, menopause status and hemoglobin levels of the cases were found to be similar. In the differential diagnosis of uterine sarcoma and LM, increased neutrophil levels, decreased lymphocyte levels and increased NLR align with other studies in the literature. However, our study differed in that both groups had similar numbers. Additionally, body mass index and ultrasound measurements of preoperative uterine mass were not available. However, it was not statistically significant in terms of MPV and tumor size ($p>0.05$). In the regression analysis of the two groups, the test showed a sensitivity of 79.2% and the significant risk factor was identified as age.

Aksakal et al. (22) conducted a retrospective study consisting of 192 cases to differentiate uterine sarcoma and LM, as well as age and gravida reported that neutrophil level, PLT level, MPV parameters were not significant, while NLR, PLR, lymphocyte level, parity and hemoglobin level were found to be statistically significant. Srisutha et al.'s study reported statistically significant differences between uterine sarcoma and LM when comparing increased neutrophil count, increased platelet count and decreased lymphocyte count, respectively. However, age, parity, menopausal status and size of uterine mass were not significant between the two groups (23). In the comparison between cases with uterine sarcoma and LM, Zhang et al. showed that advanced age, menopausal status, parity, increased mass size, increased neutrophil count, NLR and increased PLT count were significant, while gravida and decreased lymphocyte count were insignificant (24). In the current study, gravida, parity, PLT level, neutrophil level and MPV level were not significant ($p>0.05$), while age, lymphocyte level and NLR were significant between the groups ($p<0.05$). Unlike the study, hemoglobin level, parity, and PLR were not significant between the two groups and the lack of measurement of LM and sarcoma may be due to the unequal numbers and heterogeneity of both groups.

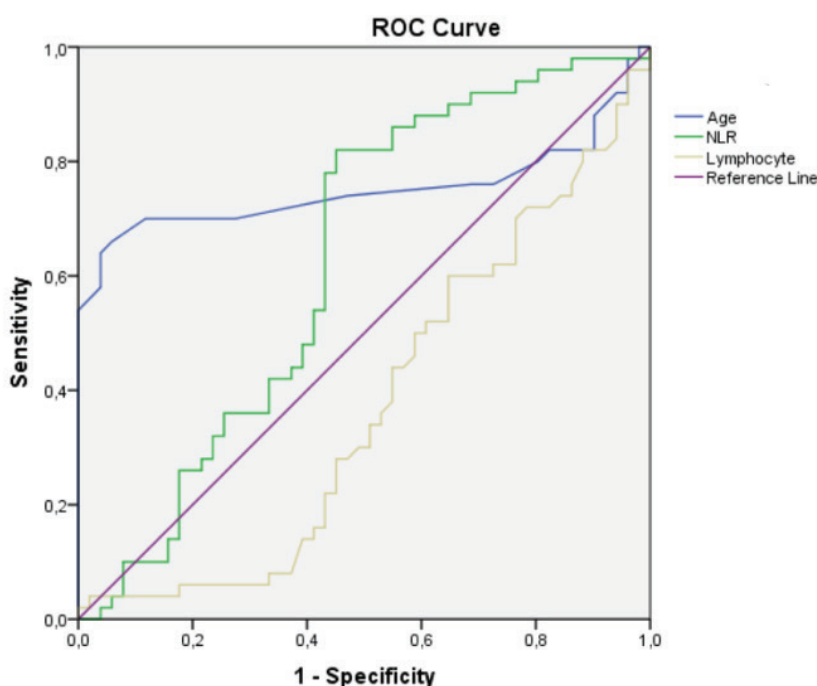


Figure 1. ROC graph of the diagnostic factors

Kim et al. compared the NLR with serum CA-125 as preoperative diagnostic markers for uterine sarcoma in a retrospective series of 55 sarcomas with 330 LM diagnoses, finding that the NLR was more useful as a diagnostic marker. They found that an NLR ≥ 2.12 had 74.5% sensitivity and 70.3% specificity for the preoperative diagnosis of uterine sarcoma (25). Cho et al. conducted a retrospective study of 31 uterine sarcomas with 93 LMs, finding that uterine sarcoma was an important independent factor of NLR > 2.1 . In addition, sensitivity and specificity were 43.2% and 82.8%, respectively (10). Aksakal et al. (22) conducted a retrospective study of 192 cases in the differentiation of uterine sarcoma and LM and calculated the NLR as 2.04 with a sensitivity of 59.4% and a specificity of 59.5% at a PLR of 150.7 with a sensitivity of 65.6% and a specificity of 64.7%. Yoshiko Nishigaya et al. conducted a retrospective study consisting of 336 cases,

where increased white blood cell count and neutrophil count in the postmenopausal period showed that NLR could be used as a marker to differentiate sarcoma (1). NLR sensitivity and specificity rates were reported as 63.5% and 61.7%, respectively. Srisutha et al. reported that the cut-off value of NLR of 2.8 was statistically significant in the differentiation of uterine sarcoma and LM. The sensitivity of the cut-off value of NLR 2.8 was 61.5% and the specificity was calculated as 73.1% (23).

According to the scoring system of Zhang et al., age ≥ 40 years, NLR ≥ 2.8 cut-off value, PLT of 298×10^3 and LDH of 193 U/L have 80% sensitivity and 77.8% specificity (24). In the current study, the sensitivity and specificity of age were 70.0% and 88.2%, respectively. NLR (cut-off=5.4) sensitivity and specificity rates were recorded as 78.0% and 56.9%, respectively. Based on current knowledge, there is still no reliable method to differentiate between LM and uterine sarcomas preoperatively. However, recent developments in artificial intelligence on this subject may help to highlight this issue (26).

This case-control study is a retrospective evaluation of a similar number of cases evaluated over a period of time. A large controlled study with a large number of cases can give a clearer and more generalizable result. This study is important in terms of showing which factors are effective and predictive in the differentiation of LM and sarcoma. The strength of the study lies in the regression and ROC analysis of inflammatory markers of two groups with a similar sample size.

Limitations:

The limitations of the study include its retrospective nature, small sample size and the absence of preoperative ultrasound findings.

CONCLUSION

Age, NLR and lymphocyte level are significant factors in the differentiation of uterine LM and sarcoma. MPV and PLR were not significant factors. Large randomized controlled studies are needed for definitive evidence-based results.

Conflict of interest: The authors declare no conflict of interest.

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Ethical approval: The study was conducted in accordance with the conditions recommended by the Helsinki Declaration. It was approved by the university clinical research ethics committee with the decision number 2022/304 on June 21, 2022.

Author contributions: Concept: FA - Design: FA, AB - Supervision: AB, CC - Materials: AB - Data collection and/or processing: FA, MK - Analysis and/interpretation: FA, MK -Literature review: AB, CC, MK -Writing: FA, CC - Critical review: CC, MK.

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