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Original Research

Can the Combination of Magnetic Resonance Imaging, Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Predict the Mass Origin in Ovarian Masses?

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ABSTRACT

Objective: Evaluate the effectiveness of magnetic resonance imaging (MRI), blood parameters, and tumor markers to determine the role of objective criteria in distinguishing malignant, borderline, and benign masses and to minimize unnecessary surgical interventions by reducing interpretation differences.

Methods: The histopathological and clinical–laboratory results of the patients who underwent surgery for the initial diagnosis and whose ovarian masses were confirmed were retrospectively reviewed. Between groups, age, cancer antigen 125, mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), the presence of ascites, the ovarian-adnexal reporting and data system MRI scores, mass characteristics, and lymphocyte count were compared.

Results: The study comprised a total of 191 patients. These patients were categorized into three groups: Benign (n=113), borderline (n=26), and malignant (n=52). No noteworthy correlation was detected between the unilocular or multilocular nature of solid, cystic, or mixed masses and the rates of NLR, PLR, or MPV. However, a notable correlation was identified between NLR and the presence of acidity (p=0.003). In ovarian cancer patients, there was no significant difference in NLR and MPV between malignant epithelial and malignant sex cord-stromal types (p>0.05), whereas a significant difference emerged in the PLR ratio (p=0.013).

Conclusion: In ovarian masses with malignant potential, laboratory parameters such as NLR and PLR can guide the diagnosis process. In the future, various studies such as the development of different tests, markers, and imaging methods, the use of blood tests such as NLR, PLR, and MPV in cancer diagnosis will be possible. The results of these studies may contribute to the development of new methods for the diagnosis of ovarian cancer and the improvement of treatment protocols.

Keywords: Mean platelet volume, neutrophil-to-lymphocyte ratio, ovarian-adnexal reporting and data system, platelet-to-lymphocyte ratio

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Ovarian cancer is a gynecological cancer that remains important, with 2.1% of all cancer deaths in 2022.[1] Ovarian masses can cause symptoms such as abdominal pain, bloating, menstrual irregularities, pelvic pain, and a feeling of fullness. It is difficult to distinguish between malignant and benign ovarian masses with only one test or approach. For this reason, many different methods are often used, and the results are evaluated together. These factors include mass size, imaging features, tumor markers, patient's age and menopausal status, family history, symptoms, and histopathological features of the mass tissue.[2] Differentiation of malignant and benign ovarian cysts is significant in terms of establishing an accurate diagnosis and treatment plan. For this reason, the search for developing new methods, examinations, and technologies always continues.

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are ratios measured during blood tests and are used to determine inflammatory responses and infections in the body.[3] An average NLR rate is below 2.5, whereas a high rate may indicate the presence of inflammatory diseases or conditions. A standard PLR rate is below 150, whereas a high rate may indicate the presence of an inflammatory response or infection in the body. Both ratios are generally used to determine inflammatory responses and diseases in the body. However, high NLR and PLR rates may also indicate infections and other inflammatory conditions such as cancer.[4] Some studies have shown that high NLR and PLR ratios may indicate the presence of a cancerous mass.[5] Studies have focused more on differentiating malignant and benign.[6] There are few studies, including borderline ovarian masses.[7-9] Mean platelet volume (MPV) is a parameter measured during a blood test and indicates the mean volume of platelets.[10] Platelets are cells involved in blood clotting. MPV is used to evaluate the activation levels and functionality of platelets. It is stated that there is a relationship between cancer types and high MPV.[11] For example, some studies show a link between cancer types such as liver cancer, lung cancer, and breast cancer and high MPV.[12] However, high MPV is not a determining factor that can be used alone in the diagnosis of cancer and should be evaluated together with other tests and markers.

The ovarian-adnexal reporting and data system (ORADS) is a classification system used to evaluate the ovaries and adnexa with ultrasonography and/or magnetic resonance imaging (MRI). This system is used to determine whether ovarian masses are benign or malignant.[13] ORADS classification divides ovarian masses into five different classes according to the results of ultrasonography. These classes are determined by size, internal structure, borders of the masses, and doppler blood flow characteristics. Each of these classes has different features that determine the probability of the masses being benign or malignant. However, the accuracy of this classification is not sufficient for a definitive diagnosis of ovarian cancer.[14] The ORADS classification can be used as a starting point to determine the probability of a mass being benign or malignant. It should be evaluated in conjunction with other tests and imaging modalities.

The aim of our study is to evaluate the MRI, blood parameters, and tumor markers that can be used in the diagnosis of ovarian cancer to develop more accurate and effective methods for the diagnosis and treatment of ovarian cancer, to determine the role of the masses in the differentiation of malignant, borderline and benign with objective criteria and to interobserver. It is to reduce the number of unnecessary surgical interventions by minimizing the difference in interpretation.

Methods

The study was an observational case–control study and was planned retrospectively. Patients who underwent surgery due to a mass in the pelvic region in the gynecological oncology clinic between June 2020 and December 2022 were included. The clinic functions as a tertiary oncology center where average of 1000 oncology cases are treated per year. The study was carried out by the Declaration of Helsinki, and the study protocol was approved by the hospital's Local Ethics Committee with the acceptance number 2021.06.217.

Patients who applied to the gynecological oncology clinic and underwent surgery with the indication of suspected adnexal mass in the pre-operative period were included in the study. In the preliminary evaluation, patients with pathological diagnoses of ovarian cancer and patients with other malignancies were excluded.

Complete blood count, clinical features, tumor markers, and MRI images of all patients were evaluated. In total blood count, neutrophil count, lymphocyte count, platelet count, NLR and PLR ratios, MPV (femtoliter), cancer antigen-125 (U/mL), the carcinoembryonic antigen (CEA) (µg/L), and cancer antigen 19-9 (CA-19-9) (U/L) mL) values were noted. MRI images were evaluated together by two experienced urogenital radiologists and scored from 1 to 5 according to the O-RADS MRI system.[15] In addition, benign findings such as dermoid cyst, endometrioma, simple cyst, hydrosalpinx, low T2W signal and low diffusion signal, and wall enhancement were noted. All these features were compared between malignant, benign, and borderline ovarian tumor groups.

Statistical Analysis

Data analysis was performed using SPSS (version 23.0; SPSS Inc., Chicago, IL, USA). All data were prepared as mean ± stan-

dard deviation or median ± minimum-maximum. The normal distribution of the data was analyzed according to Skewness and Kurtosis. Mann Whitney U Test and Independent Samples Kruskal–Wallis Test were used to compare parametric variables. Spearman Correlation Analysis was used to estimate the relationships between the variables. A $p<0.05$ was considered statistically significant in all calculations.

Results

One hundred and ninety-one patients were included in the study. The patients were evaluated in 3 different groups benign (n=113), borderline (n=26), and malignant (n=52) (Table 1). The mean age of all patients was 48.2 (min–max: 19–85). The mean age of the benign patient group was 47.4,

Table 1. General data of the study population

Pathology	Benign (%)	Borderline (%)	Malign (%)
Benign epithelial tumor	73 (64)	2 (7.7)	1 (1.9)
Benign germ cell tumor	23 (20.7)	1 (3.8)	1 (1.9)
Benign sex cord-stromal tumor	10 (9)	0	0
Borderline epithelial tumor	1 (0.9)	23 (88.5)	0
Malign epithelial tumor	0	0	40 (76.9)
Malign sex cord-stromal tumor	0	0	10 (19.2)
Tubo ovarian abscess	6 (5.4)	0	0
Mass			
Solid	13 (11.7)	11 (42.3)	4 (7.7)
Cystic	63 (55)	0	5 (9.6)
Mixt	37 (33.3)	15 (57.7)	43 (82.7)
Septa			
Available	41 (36)	18 (69.2)	40 (76.9)
None	72 (64)	8 (30.8)	12 (23.1)
Septa Thickness			
Thin	26 (23.4)	8 (30.8)	11 (22.2)
Thick	13 (11.7)	10 (38.5)	27 (51.9)
Papillary structure			
Available	9 (8.1)	8 (30.8)	17 (32.7)
None	104 (91)	18 (69.2)	35 (67.3)
Peritoneal implant			
Available	0	0	4 (7.7)
None	113 (100)	26 (100)	48 (92.3)
Ascites			
Available	3 (2.7)	4 (15.4)	16 (30.8)
None	110 (97.3)	22 (84.6)	36 (69.2)
Solid texture			
Available	58 (53.2)	11 (42.3)	36 (69.2)
None	54 (46.8)	15 (57.7)	16 (30.8)
Wall contrast involvement			
Available	49 (42.3)	12 (46.2)	34 (65.4)
None	64 (57.7)	14 (53.8)	18 (34.6)
Low T2/Low DWI*			
Yes	19 (18)	5 (19.2)	5 (9.6)
No	94 (82)	21 (80.8)	47 (90.4)
ORADS MRI**			
1	2 (1.8)	1 (3.8)	1 (1.9)
2	32 (28.8)	6 (23.1)	5 (9.6)
3	29 (24.3)	11 (42.3)	14 (26.9)
4	27 (24.3)	5 (19.2)	16 (30.8)
5	23 (20.7)	3 (11.5)	16 (30.8)

*DWI: Diffusion-Weighted Imaging; **ORADS MRI: The Ovarian-Adnexal Reporting and Data System Magnetic Resonance Imaging.

Table 2. Comparison of histology parameters and laboratory parameters

	Benign epithelial tumor	Benign germ cell tumor	Malign epithelial tumor	Malign sex cord-stromal tumor
	p			p
NLR*	0.295			0.077
MPV**	0.991			0.264
PLR§	0.145			0.013

*NLR: Neutrophil-to-lymphocyte ratio, **MPV: Mean platelet volume, §PLR: Platelet-to-lymphocyte ratio.

the mean age of the borderline patient group was 47.5, and the mean age of the malignant patient group was 50.4. No significant correlation was found between the solid, cystic, or mixed mass, whether it was uniloculated or multiloculated, and NLR, PLR, or MPV rates. A significant correlation was found between NLR and the presence of acid (p=0.003). The pathologies of the patients were divided into seven different categories, and the Spearman correlation test was performed. When going from benign to malignant, the mass is solid (p≤0.001), multiloculated (p=0.003), septal (p=0.001), papillary structure (p=0.007), and peritoneal implant (p=0.023), presence of ascites (p<0.001) and wall contrast uptake (p=0.036) were significantly increased. There was no significant difference in NLR and MPV between malignant epithelium and malignant sex cord-stromal in ovarian cancer patients (p>0.05), whereas a significant difference was found in the PLR ratio (p=0.013) (Table 2). No significant difference was observed in all three, respectively, (p>0.05) when examining benign epithelial and benign germ cell tumors.

Discussion

Ovarian cancer, like other cancers, is an inflammation-related disease. Therefore, markers of inflammation such as MPV, NLR, and PLR may be associated with ovarian cancer. Some studies have shown that high MPV, high NLR, and high PLR can affect the prognosis of patients with ovarian cancer.[16,17] In addition, MPV, NLR, and PLR may change during ovarian cancer treatment, and these changes may provide information about treatment efficacy and prognosis.[18] For example, decreases in MPV, NLR, and PLR values after treatment indicate that the cancer is in remission and is effective. It was emphasized that NLR and PLR were associated with both overall survival (OS) and progression-free survival (PFS), and as these rates increased, OS and PFS were also associated with shortening.[19] However, it is essential to remember that these markers alone are not sufficient for the diagnosis of ovarian cancer and should be evaluated together with other tests and imaging methods. For this reason, our study evaluates both laboratory parameters and MRI together. In our study, both laboratory parameters, such as NLR, TLR, MPV, and ORADS MRI scores, were evaluated together to provide guidance in the differentiation of malignant benign. Whereas increased TLR rates are warning for malignancy, an ORADS score of 3 and above, as well as the absence of low T2 and low DWI can warn us more in terms of malignancy.

As an example for other cancers, the diagnostic value of NLR and PLR in gastric cancer is higher than the traditional tumor markers CEA and CA19-9.[20] In fact, it has been emphasized in studies that it can predict lymph node metastasis in these patients and may be an independent predictive factor for lymph node metastasis in advanced gastric cancer.[21] In our study, a significant correlation was found with PLR between malignant epithelial and malignant germ cell histology types, but no significant difference was found in NLR and MPV. It seems there is a need for further studies in which parameters such as cancer prognosis and association of lymph node metastases should be evaluated.

NLR and MPV are inflammatory markers and have also been studied in patients with polycystic ovarian syndrome (PCOS). These two values were found to be high in this patient group.[22] In the study of Pergialiotis et al., [23] who wanted to evaluate the relationship of PLR and NLR with hormonal and metabolic parameters in PCOS patients, both PLR and NLR seemed to be associated with some hormonal and metabolic indicators. This relationship was more pronounced with NLR and serum androgens. NLR and PLR were not significantly affected by menstrual cycle disorders or obesity. In our study, a significant relationship was found between the presence of acid and NLR. It is thought that this may be secondary to the inflammation caused by the acid.

In the study of Ghimire et al.,[24] in which the pre-operative neutrophil-lymphocyte ratio was compared with other ovarian cysts in adnexal torsion, it was concluded that NLR may be a predictive marker for torsion. In addition, NLR rates were found to be high in irritable bowel disease, acute surgery, uncontrolled diabetes mellitus, cirrhotic patients, thyroid disorders, and COVID-19.[25-28] Especially in ovari-

an masses with malignant potential such as ORADS 3 and 4, using laboratory parameters such as NLR and PLR may guide us in the diagnosis.

Conclusion

In the future, many different studies can be carried out, such as the use of different tests and markers, the development of ultrasonography and other imaging methods, and the use of blood tests such as NLR, PLR, and MPV in the diagnosis of cancer. In addition, the findings to be obtained as a result of these studies may contribute to the development of new methods that can be used in the diagnosis of ovarian cancer and to the improvement of treatment protocols.

Disclosures

Ethics Committee Approval: The study was approved by the Ethics Committee of Basaksehir Cam and Sakura City Hospital (No: 238, dated 18.10.2021).

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