

MPV, NLR, and platelet count: new hematologic markers in diagnosis of malignant ovarian tumor

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Summary

Objective: Evaluation of mean platelet volume (MPV), neutrophil to lymphocyte ratio (NLR), and platelet count in the detection of malignant and benign ovarian tumors. **Material and Methods:** Sixty-six patients admitted to the present clinic over three years were included in the study. Patients diagnosed with ovarian cancer were grouped into the areas of epithelial and granulosa cell tumor diagnosis. The values were compared to patients with benign cystic structure. Patients' preoperative hematologic parameters and their values four weeks postoperatively were analyzed. Statistical analyses were performed with SPSS software. **Results:** MPV, NLR, and platelet count were observed at a higher rate as statistically significant in patients diagnosed with malignant ovarian cancer, compared to those with benign adnexal mass. **Conclusion:** The hematological parameters such as MPV, NLR, and platelet count in the detection of malignant ovarian tumors have been evaluated as useful new markers.

Key words: Malignant; MPV; NLR; Ovarian tumors.

Introduction

Although ovarian tumors are the second most frequent tumors in gynecological cancer, they are the most common female genital tract cancer causing death [1]. Primary germ cell tumors of the ovary originate from sex cord stromal and epithelial cell surfaces. Epithelial ovarian tumors constitute 95% of the entire group [2]. Epithelial ovarian cancer is especially diagnosed at an advanced stage, resulting in distant metastases in this stage. This situation delays the treatment of disease and draws it below the expected survival time [3].

Serum CA125 values of a glycoprotein was started to be used at the beginning of the 1980s, particularly for the early detection of epithelial ovarian cancer. However, due to the low sensitivity and specificity, its use for this purpose today is not accepted [4]. Tests such as ROMA, RMI, OVA1, and LR2 with which the combination of serum markers are evaluated, or the malignancy risk of adnexal cystic structure is calculated by evaluating the serum values and ultrasound parameters together, are, today, among the examinations used in the early detection of ovarian cancer. [5].

The inflammation in cancer tissue pathophysiology is the most important reason. The mediators released into the environment as a result of inflammation cause cellular DNA damage, inhibition of apoptosis, and the growth of angiogenesis, and this situation causes the growth, progression, and metastasis of the tumor cells [6]. The platelets play an

important role in the release of these mediators; through these agents released into the environment, the growth and progression of the tumor cell accelerate [7].

Mean platelet volume (MPV) is the most reliable predictor of platelet function and is most easily measured parameters in hematology laboratories. It is known that large platelets are more metabolically active than the smaller ones [8].

In this study, the authors aimed to assess the serum MPV and inflammation parameters of patients diagnosed with ovarian cancer and patients with benign cystic adnexal structures, and they have also aimed to analyze the differences between the groups.

Materials and Methods

Sixty-six patients who applied to Inonu University, Medical Faculty, Turgut Ozal Medical Center, Department of Obstetrics and Gynecology, between the years 2011-2014, were included in the present study. Patients diagnosed with ovarian cancer were grouped into two; one with epithelial and the other with granulosa cell tumor diagnosis. The values were compared to patients with benign cystic structure. Preoperative hematological parameters of the patients and their values four weeks after the operations were analyzed. Routinely, in the present hospital, complete blood counts (CBC) are measured by -ADVIA 2120i and blood samples are measured with potassium ethylene diamine tetra-acetic acid and are analyzed one hour after venepuncture. Normal MPV values in the present laboratory range between 6.8 and 10.8 fl.

Statistical analyses were performed with SPSS software. All parameters are expressed as mean \pm standard deviation (SD). Para-

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Table 1. — *Patients' distributions.*

Surgical procedures		Number of patients
Benign	• Cyst excision	19
	• TAH+BSO	10
	• USO	4
Malign	• TAH+BSO+PPLND+ Omentectomy+appendectomy	21
	• TAH+BSO+debulking	11
	• TAH+BSO+PPLND+ Omentectomy+apendectomy + colon resection+anastomosis	1

TAH+BSO: total abdominal hysterectomy+ bilateral salpingo-oophorectomy,
USO: unilateral salpingo-oophorectomy,
PPLND: pelvic para-aortic lymphadenectomy.

Table 2: — *Pathologic findings.*

	Histopathology	Number of patients
Benign	Serous cystadenoma	15
	Endometrioma	9
	Mature cystic teratoma	8
	Mucinous cystadenoma	1
Malignant	Serous carcinoma	18
	Granulosa cell tumor	13
	Mucinous carcinoma	2

metric or non-parametric tests were applied to data with normal or non-normal distributions, respectively. The paired sample test was used to compare the preoperative and postoperative variables. The Mann–Whitney U test was used to compare the parameters of preoperative ovarian cancer patients and control subjects. The results are expressed as mean \pm SD. A value of $p < 0.05$ was considered statistically significant.

Results

Sixty-six patients diagnosed with a cystic adnexal structure between the years 2011-2014 were included in the present study. Of these patients, 33 with benign ovarian cystic diagnosis and 33 with the diagnosis of malignant ovarian tumor were operated. The mean age of the patients was $45.87 \pm 16:19$ (min. 17, max. 80) years, the average cyst size was 9.15 ± 4.91 (min. 4, max. 25) cm. Surgical methods performed in patients are summarized in Table 1. Fifteen of the patients who were operated due to benign reasons were diagnosed with simple cyst adenomas, eight of them with endometrioma, eight with mature teratoma, and one with mucinous cystadenoma. Eighteen of the patients who were operated due to malignant reasons were diagnosed with serous carcinoma, 13 with granulosa cell tumor, and two with mucinous carcinoma (Table 2).

The platelet count of the patients diagnosed with ovarian cancer before the operation was 338,550, their MPV value was 8.93 ± 2.09 fl, and their neutrophil/lymphocyte ratio (NLR) was found to be 10.79 ± 4.75 . These values were

Table 3. — *MPV, PLT, and NLR results in malign and benign adnexial mass.*

	Ovarian cancer	Benign ovarian cysts	<i>p</i>
MPV*	8.93 ± 2.09	5.86 ± 3.27	< 0.05
PLT**	$338,550 \pm 88,714$	$224,060 \pm 58,323$	< 0.05
NLR***	10.79 ± 4.75	6.99 ± 1.41	< 0.05

* Mean platelet volume. ** Platelet to lymphocyte ratio.

*** Neutrophil to lymphocyte ratio.

Table 4. — *Preoperative and postoperative MPV, PLT, and NLR results.*

	Preoperative	Postoperative	<i>p</i>
MPV*	8.93 ± 2.09	7.55 ± 1.14	< 0.05
PLT**	$338,550 \pm 88,714$	$255,270 \pm 59,707$	< 0.05
NLR***	10.79 ± 4.75	5.72 ± 3.57	< 0.05

* Mean platelet volume. ** Platelet to lymphocyte ratio.

*** Neutrophil to lymphocyte ratio.

224,060, 6.99 ± 1.41 , and 5.86 ± 3.27 , respectively, in the control group. A statistically significant difference was found between the two groups in each of the three values ($p < 0.05$) (Table 3).

Statistically significant results were obtained when the hematological parameters, before and after surgery, were examined in patient groups operated due to ovarian tumor. While MPV values in the study group before surgery were 8.93 ± 2.09 fl, this value declined to 7.55 ± 1.14 fl after the surgery. PLT before the surgery was $338,550 \pm 88,714$ whereas it was $255,270 \pm 59,707$ after surgery. NLR before the surgery was 10.79 ± 4.7 , while it was 5.72 ± 3.57 after the surgery (Table 4).

Discussion

Ovarian cancer is the most lethal gynecological cancer in developed countries, and in spite of recent advances in surgical treatment, the prognosis remains poor. Because of vague symptoms and lack of reliable screening methods, ovarian cancer is commonly diagnosed at an advanced stage [9]. That there is a lack of an effective screening method in other ovarian tumors, particularly in epithelial ovarian cancer, is the best explanation for the delay in diagnosis and treatment of this cancer. The studies conducted in recent years indicate that infection and inflammation in the etiology of ovarian cancer is one of the most important factors [6]. In particular, chronic inflammation can play a key role in ovarian cancer development [7]. The monthly ovulation cycles occurring in the ovarian tissue cause damage in the ovarian tissue, regeneration in the epithelium, and as a result, cause the induction of the inflammation [10]. Epidemiological evidence shows the lower incidence of ovarian cancer in the case of the absence of ovulation (such as pregnancy, oral contraceptive use) or in the case of

tubal ligation where ovaries' less exposure to inflammatory agents occur [11]. For this reason, serum neutrophil count and NLR, which is a sign of acute and chronic inflammation, is considered as a marker used in the diagnosis of malignancy. Similarly, MPV, another marker, can reflect platelet stimulation and the rate of platelet function. Strong evidence indicates that MPV is an important biological variable and that larger platelets are more metabolically and enzymatically active than smaller platelets [12]. Platelets play a metabolic role in cancer through angiogenic, metastatic, and proteolytic activities. Malignant cells produce cytokines, such as interleukin-1 and other growth factors, which induce platelet production [11]. Additionally, many *in vivo* and *in vitro* studies show that platelets play a key role in the development of ovarian cancer. Interleukin-6 release is the mediator which has been best-proven [13]. Additional studies show that the increasing platelet function has the effect of facilitating the metastasis, and it helps the adhesion and extravasation of the tumor cells [14]. Recent studies have shown that the number of platelets, neutrophils, and lymphocytes with median platelet volume are markers of inflammation, and that serum values increase in gynecological and non-gynecological malignancies.

In a study performed by Chen *et al.*, 1,501 patients diagnosed with nasopharyngeal cancer were grouped into three as low, medium, and high platelet count and at the end of the study, in the group with high platelet count, their metastasis rate was higher, and their five-year-survival time was found to be lower and statistically significant compared to other patients in other groups [15].

In another study in 321 patients diagnosed with pancreatic cancer, platelet and neutrophil count, and NLR of the patients with their survival time were evaluated and in the patients with more platelet and neutrophil count with high NLR rates, the mean survival time was found to be significantly shorter than that of control group [16]. Similarly, in patients diagnosed with esophageal cancer, high neutrophil and NLR rates were shown to be associated with decreased survival time [17]. In the study in 308 patients diagnosed with adenocarcinoma cancer, Zhang *et al.*, have shown that distant organ metastasis increase in direct proportion to platelet count and NLR rates before the treatment, and that in particular, the incidence of bone metastases in the presence of thrombocytosis was greater [18]. In a study of 268 patients diagnosed with lung cancer, it was shown that high platelet count and decreased MPV/PC rates had a negative effect on disease-free survival time [19]. Many similar studies have also been carried out in gynecological cancers.

In a study carried out in 113 patients diagnosed with epithelial cancer, MPV and NLR values were compared with those of healthy patient population; MPV and NLR values in patient group were found to be significantly higher in proportion to healthy population [7]. In a study of 100 pa-

tients diagnosed with early- and advanced-stage ovarian tumor cancer, Kokcu *et al.* found that platelet count and NLR were significantly higher in patients diagnosed with advanced stage ovarian tumor cancer; however, they also found that MPV values in both groups were not different [20]. In another study of 569 patients by Yıldırım *et al.*, it was indicated that NLR values had a high sensitivity in the differential diagnosis of benign and malignant ovarian masses [21]. In another study where platelet count and NLR values were compared in differential diagnosis of adnexal masses, the platelet count was found to be statistically significant and higher in malignant patients, and NLR values were found to be higher but not statistically significant in malignant patient group [22]. Particularly in advanced stage endometrial cancer, MPV has been suggested as an important marker, and this result has been shown in a study in Turkey. In the present study of 310 patients diagnosed with endometrial cancer, especially in those diagnosed with advanced stage endometrial cancer, MPV values were found to be statistically significant and higher in proportion to normal patients [23]. As a result, adnexal masses are an important issue for women in both premenopausal and postmenopausal stages. For years, by using blood parameters and ultrasound images, it has been attempted to identify whether masses are benign or malignant. However, even with today's technology, high sensitivity tests have not been found and thus the search for new parameters has already begun. MPV, platelet count, and NLR values have shown to be remarkable values with hard work in recent years. These values, which are increased in gynecological and non-gynecological tumors in literature, in the present study, have also been found to be statistically significant and higher in malignant patient group.

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