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Prognostic value of pre-operative neutrophil/lymphocyte ratio, monocyte count, mean platelet volume, and platelet/lymphocyte ratio in endometrial cancer

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ABSTRACT

Objective: Cancer-related inflammation is associated with poor long-term outcomes in various solid tumors. The aim of this study is to investigate the prognostic significance of pre-operative neutrophil lymphocyte ratio (NLR), monocyte count (MC), mean platelet volume (MPV), and platelet lymphocyte ratio (PLR) in endometrial cancer.

Study Design: In this study, 763 patients with endometrial cancer were evaluated, who were followed between January 1996 and February 2016. Preoperative values of NLR, MC, MPV, and PLR were evaluated in terms of clinico-pathologic prognostic factors and overall survival (OS).

Results: NLR, MC, and PLR were detected to be statistically significant with regard to advanced stage of the disease ($p = 0.001$, $p = 0.02$, and $p = 0.001$, respectively), but only MC was significant in terms of grade ($p = 0.035$). Higher NLR and PLR values were found to be associated with advanced stage of the disease, deep myometrial invasion, cervical involvement, lymphovascular space invasion (LVSI), and nodal involvement. When the cut-off value was considered as 3, sensitivity and specificity for NLR were found to be 68% and 69%, respectively, to predict lymph node metastasis. NLR was found as a prognostic factor for survival ($p = 0.01$). Age, the presence of comorbidity, stage, and cervical involvement were determined to be independent prognostic factors for OS in our cohort.

Conclusion: NLR was detected to be a prognostic factor for survival. Moreover, NLR and PLR are a predictive value for lymph node involvement and also for cervical invasion in endometrial cancer.

Introduction

Endometrial cancer is the most common type of gynecological cancer with increasing prevalence in developed countries. Age, co-morbidities, histopathologic subtype, stage, grade, the degree of myometrial invasion, the presence of cervical stromal invasion, lymphovascular space invasion (LVSI), lymph node involvement, and the need for adjuvant therapy are well-known prognostic factors for endometrial cancer [1].

Systemic immune and coagulation responses, as well as alterations in the tumor microenvironment play an important role in the initiation, progression, and control of cancer [2]. The interaction of coagulation, inflammation, and carcinogenesis is not precisely understood. Angiogenesis, invasion, and metastasis-linked inflammation processes promote the recruitment of T lymphocytes. Chemokines, different responses to growth factors and resistance to chemotherapies are suggested theories for the effect of inflammation on carcinogenesis. The most common alterations in human cancers include leukocytosis, neutrophilia, thrombocytosis, and lymphocytopenia.

It has been demonstrated that some hematologic parameters reflecting an inflammatory response, such as neutrophil/lymphocyte ratio (NLR), monocyte count (MC), mean platelet volume (MPV), and platelet/lymphocyte ratio (PLR), are associated with poor outcomes in some solid tumors including breast, ovarian, cervical, gastric, colorectal, and oesophagal carcinomas [3]. Complete blood count (CBC) is routinely performed during the preoperative assessment of patients with endometrial cancer. NLR, PLR, MPV, and MC represent simple, robust, and convenient parameters for the inflammatory and procoagulant state in cancer. Elevated platelet count and aggregation may facilitate tumor

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escape from the immune response [4]. Although the prognostic importance of these parameters has been studied for many cancer types, there are limited and unclear data for endometrial cancer. In literature, NLR and PLR have been suggested to be independent prognostic factors and to be associated with the risk of cervical involvement in patients with endometrial cancer [5,6]. However, no association has been shown between the NLR and lymph node involvement [7]. Thus, it was aimed to investigate the association NLR, PLR, MPV, and MC and defined prognostic clinicopathologic factors in endometrial cancer in this study.

Methods

This study was performed on 763 patients with endometrial carcinoma, who were operated and followed up in our clinic between January 1996 and February 2016. All the specimens were evaluated by a gynecologic pathologist. The study was performed after receiving approval from the local ethics committee.

Demographic variables including age, parity, menopausal status, and family history of cancer, and clinicopathologic variables including symptoms, comorbidity, stage, grade, histopathologic type, the degree of myometrial invasion, lymph node involvement, lymphovascular space invasion, peritoneal cytology, choice of adjuvant therapy, and survival outcomes were evaluated. The staging was performed according to the FIGO 2009 guidelines. The main surgical procedures were total laparotomic or laparoscopic hysterectomy- bilateral salpingo-oophorectomy (TH + BSO) and pelvic and para-aortic lymphadenectomy with or without omentectomy in patients with intermediate and or high-risk endometrial cancer.

In addition, preoperative CBC results and absolute neutrophil, lymphocyte, monocyte, platelet counts, and MPV were evaluated. NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count and PLR as the absolute platelet count divided by the absolute lymphocyte count.

Chemotherapy was administered for systemic control and radiotherapy for locoregional control in high-risk patients. Patients were followed up every 3 months in the first two years and then every 6 months up to 5 years. During the follow-up, the patients were evaluated through gynecological examination, transvaginal sonography, and thoracic and abdominopelvic computed tomography (every 6 months in the first two years and then every year) in our clinic. Overall survival was defined as the time from the diagnosis of disease to death.

Data were analyzed using SPSS software version 20.0 (IBM, Armonk, NY, USA). The variables were tested using visual (histograms, probability plots) and analytical methods (Shapiro-Wilk's test) to determine whether or not they were normally distributed. Descriptive analyses were presented using mean ± SD and propriety data were shown as median and min-max value. Chi-square test or Ficher's exact test was performed for analyzing categorical data. The effect of clinicopathologic variables on survival data was evaluated using the Kaplan–Meier method. Moreover, differences in the survival curves were calculated through the log-rank test. The Cox proportional hazard model was used to assess the significance of multiple variables. ROC was employed to calculate threshold, sensitivity, and specificity.

Results

The analysis was performed in 763 patients. The mean age in the cohort was 57.2 ± 10.5 years and the median age was 58 (27–91) years. The mean body mass index (BMI) was found as 35.4 ± 7.3 kg/m [2]. Half of the patients had many comorbidities. Type 2 endometrial cancer was observed in 25% of the patients. Preoperative mean and median values for NLR were 2.8 ± 1.8 and 2.3(0.3–18), respectively. Absolute mean MC was found to be 544.4 ± 220.7 /μL and the median MC was 510 (94–2400) /μL. The mean and median MPV values were 8.5 ± 1.2 and 8.3 fL (2.4–13), respectively. The mean and median PLR were calculated as

Table 1
Clinical and pathological features of the cohort.

Variables		Status- alive Alive n(%)	Status- exitus Exitus n(%)	p
Age	<40	48(7.2%)	1(1.1%)	<0.001*
n:763	41–50	142(21.3%)	8(8.4%)	
	>51	478(71.6%)	86(90.5%)	
BMI	<30	91(25.9%)	8(22.2%)	0.070
n:387	31–35	99(28.2%)	10(27.8%)	
	36-40	86(24.5%)	4(11.1%)	
	>41	75(21.4%)	14(38.9%)	
Comorbidity	present	300(45.9%)	64(69.6%)	<0.001*
n:745	none	353(54.1%)	28(30.4%)	
Surgical procedure	Laparotomy	401(60.2%)	77(82.8%)	<0.001*
n:759	Laparoscopy	265(39.8%)	16(17.2%)	
Grade	1	330(56.3%)	21(33.9%)	<0.001*
n:648	2	215(36.7%)	29(46.8%)	
	3	41(7.0%)	12(19.4%)	
Stage	Early (1 + 2)	574(87.5%)	52(56.5%)	<0.001*
n:751	Advance (3 + 4)	85(12.5%)	40(43.5%)	
Histopathologic type	Type 1	522(79.2%)	51(54.8%)	<0.001*
n:752	Type 2	137(20.8%)	42(45.2%)	
LVSI	positive	213(32.6%)	56(60.9%)	<0.001*
n:745	negative	440(67.4%)	36(39.1%)	
Cervical invasion	positive	72(11.0%)	28(30.8%)	<0.001*
n:743	negative	580(89.0%)	63(69.2%)	
Lymph node involvement	positive	53(8.1%)	24(26.1%)	<0.001*
n:744	negative	599(91.9%)	68(73.9%)	
Adjuvant therapy	positive	242(37.2%)	64(70.3%)	<0.001*
n:741	negative	408(62.8%)	27(29.7%)	

BMI: Body mass index; LVSI: Lymphovascular space invasion.