

# The association of preoperative thrombocytosis with prognostic factors in malign ovarian tumor

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## Summary

**Purpose:** We assessed the association of preoperative thrombocytosis with prognostic factors in malign ovarian tumor. **Methods:** Over a five-year period, cases treated for ovarian cancer were randomly assigned. The data were collected from gynecological oncology, radiation oncology, medical oncology and pathology departments. Statistical analyses were carried out by using the statistical packages for SPSS 12.0 for Windows (Chicago, IL, USA). Survival was analyzed by the method of Kaplan and Meier, using log-rank (Mantel-Cox) analysis. **Results:** 51 cases with ovarian cancer were evaluated. Cases with thrombocytosis were found to have greater CA-125 levels, more advanced stage disease, more ascites and shorter periods of survival. **Conclusion:** Thrombocytosis is a poor prognostic factor in ovarian cancer. As reported previously, it is associated with aggressive tumor biology. Thus, preoperative thrombocytosis can be used as a marker of poor outcomes.

**Key words:** Thrombocytosis; Ovarian cancer; Prognosis.

## Introduction

Thrombocytosis in cancer was first reported by Reiss in 1872. Thrombocytosis has been reported in a variety of solid tumors including lung, renal, gastric, breast, pancreatic, and colon. In gynecological malign tumors such as endometrial, vulvar, and cervical cancers thrombocytosis has also been reported, and it is considered to be a poor prognostic factor in ovarian cancer [1, 2].

In the literature there are several reports on prognosis of ovarian cancer in patients with thrombocytosis [3-5]. In rat models and human beings, in malignant situations thrombocytosis has been related to the activation of megakaryocytes by granulocyte-macrophage colony-stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF), macrophage colony-stimulating factor (M-CSF), interleukin 1 (IL 1), IL 3, IL 4, IL 11, leukemia inhibitor factor (LIF), erythropoietin and thrombopoietin [6].

Platelets release thrombospondin (adhesive glycoprotein) and platelet-derived growth factor (PDGF) (potent mitogen for different cell types). PDGF is related with tumor growth and thrombospondin with metastases [7-9].

In this study, we evaluated the association between preoperative thrombocytosis and prognostic factors in malign ovarian tumors.

## Material and Methods

This retrospective study was conducted at Dicle University, School of Medicine, Department of Obstetrics and Gynecology between June 2005 and June 2009. A total of 51 cases with a malign ovarian tumor diagnosis were treated. The cases were

divided into two groups according to their platelet count. Group 1 included cases with thrombocytosis and Group 2 cases with normal platelets. Thrombocytosis was considered when platelet count was greater than  $400 \times 10^9/l$  [5]. The data of the cases were collected from gynecological oncology, radiation oncology, medical oncology and pathology departments. For each woman, categorical data were collected concerning age, gravidity, parity, preoperative thrombocytosis, tumor markers, stage, grade, ascites, operation types, chemotherapy, radiotherapy, and overall and disease-free survival.

The mean and standard deviation (SD) were calculated for continuous variables. The normality of the variables was analyzed by the Kolmogorov-Smirnov test. The chi-square test and Student's t-test evaluated associations between the categorical and continuous variables. Two-sided  $p$  values were considered statistically significant at  $p < 0.05$ . Statistical analyses were carried out by using the statistical packages for SPSS 12.0 for Windows (Chicago, IL, USA). Survival analysis of two distributions (according to platelet count) were analyzed by the method of Kaplan and Meier, using log-rank (Mantel-Cox) analysis.

## Results

In this study, we evaluated 51 cases with malign ovarian tumors. The cases were divided into two groups according to platelet count. Group 1: cases with platelets  $\geq 400 \times 10^9/l$  ( $n = 26$ ), group 2: platelet  $< 400 \times 10^9/l$  ( $n = 25$ ). The mean platelet counts in group 1 and 2 were:  $311.56 \pm 38.45 \times 10^9/l$  (211 to 399), and  $488.07 \pm 42.26 \times 10^9/l$  (416 to 610), respectively.

The mean age of the cases in group 1 and 2 were  $50.07 \pm 14.42$  and  $47.44 \pm 19.19$  ( $p = 0.581$ ). The cases had cytoreductive surgery and staging including total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal washing fluid samples, infracolic omentectomy, pelvic and paraaortic lymph node sampling, and appendectomy. A total of 27 cases underwent adjuvant

chemotherapy (47.05% had carboplatin/paclitaxel for 6 courses, and 0.6% bleomycin/etoposide/paclitaxel for 3 courses). The majority of the cases were found to have advanced stage disease. Fifteen (29.42%) were diagnosed with Stage I or II, and 36 (70.58%) with Stage III or IV disease. The most common histopathological type was papillary serous in 33 (64.7%) cases followed by borderline in five (9.80%), dysgerminoma in four (7.84%), endometrioid in four (7.84%), granulosa cell in three (5.88%), clear cell in one (1.96%), and yolk sac tumor in one (1.96%), respectively.

The association between platelet count and clinical characteristics of the cases are shown in Table 1. Cases in group 1 were detected to have higher levels of CA-125 levels, more advanced stage disease, and greater volumes of ascites. We did not find any association of thrombocytosis with age, gravidity, parity, and other tumor markers.

To examine survival analysis, we focused on advanced stage (Stage III/IV). Disease-free survival and overall survival of the cases with advanced stage are shown in Figure 1. Patients with thrombocytosis had a statistically shorter disease-free interval.

Table 1. — Correlation of platelet counts with clinical and characteristics.

	Group 1 (n = 26)	Group 2 (n = 25)	p
Age (years)	50.07 ± 14.42	47.44 ± 19.19	0.581
CA 125	701.73 ± 67.12	469.04 ± 84.33	0.014
CA 15-3	64.734 ± 21.54	36.40 ± 4.23	0.980
Tumor Stage III or IV	22	11	0.046
Ascites	12	4	0.021
Disease-free survival (months)	20.977 ± 1.21	27.465 ± 4.82	0.034
Overall survival (months)	29.077 ± 3.11	36.587 ± 6.39	0.034

p < 0.05 is accepted to be statistically significant.

## Discussion

In spite of new chemotherapeutic, operative techniques and other auxiliary treatment, the 5-year survival is still low in malign ovarian tumors. Thus, early diagnosis and therapy are important to prolong the life and improve the life quality of epithelial ovarian cancer cases. Therefore, investigators are always searching for new markers for early detection of malign ovarian tumors.

Thrombocytosis is a frequent preoperative finding in many solid tumors. Gynecologic malignancies shown to be associated with thrombocytosis are ovarian cancer, vulvar carcinoma, cervical cancer, and endometrial cancer [1, 2]. Levin and Conley [10], reported in 1964 that approximately 40% of cases with inoperable cancers had thrombocytosis (platelets  $\geq 400 \times 10^9/L$ ).

Ziomet *et al.* [11] studied the prognostic factors of thrombocytosis in 130 women with ovarian cancer and reported that the cases that had thrombocytosis (n = 48) had advanced stage disease, higher serum levels of CA-125, and greater volumes of ascites, but they did not detect any differences in survival.

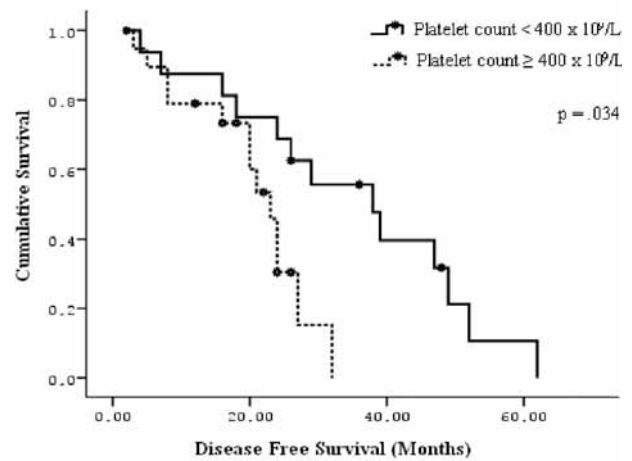


Figure 1. — In patients with Stage III or IV disease, those with thrombocytosis had a statistically shorter disease-free interval. According to the results of log-rank (Mantel-Cox) analysis the survival distribution between groups was significantly different ( $p = .034$ ).

Li *et al.* [12] carried out a study to determine if thrombocytosis is a negative prognostic factor in ovarian cancer. Of 183 women evaluated, 41 (22.4%) had thrombocytosis. They reported the cases with thrombocytosis had greater elevations of CA-125, more advanced stage disease, higher grade tumors, more frequent lymph node metastases, greater volume of ascites, and shorter overall and disease-free survival.

Menczer *et al.* [13] evaluated a series of 70 cases with invasive epithelial ovarian carcinoma in a retrospective study. They also reported thrombocytosis as a poor prognostic factor, such as advanced stage disease and shorter survival periods. Similarly, in a retrospective study in Turkey a total of 292 cases with epithelial ovarian cancer were evaluated, and 42.5% of the cases with thrombocytosis were found to have statistically higher levels of preoperative CA-125 levels, more advanced stage disease, higher grade tumors, and shorter periods of survival [14].

In the present study, we evaluated 51 cases with malign ovarian tumors, 26 of which (50.98%) had thrombocytosis. We did not observe any differences in age of the cases. The cases with thrombocytosis had higher levels of CA-125, more advanced stage, and more ascites. Cases with thrombocytosis had shorter survival periods than patients with platelets  $< 400 \times 10^9/L$ .

In conclusion, preoperative thrombocytosis is a poor prognostic factor in ovarian cancer. It is associated with aggressive tumor biology. Thus, preoperative thrombocytosis can be used as a marker of poor outcome.

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