

The influence of platelet counts on the postoperative outcome of patients with advanced stage ovarian cancer

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ABSTRACT

Introduction: Ovarian cancer represents one of the most aggressive gynecological malignancies which is associated with poor rates of survival especially if surgery with curative intent is not feasible.

Aim: The current paper analyzes the correlation ship between the preoperative number of platelets and the perioperative outcomes of patients submitted to primary cytoreduction for ovarian cancer.

Material and methods: between 2016-2018, 34 patients with advanced stage ovarian cancer were submitted to surgery; among these patients there were 21 cases with a preoperative platelet number lower than 450.000/microliter and 13 cases with higher than 450.000/microliter values.

Results: higher serum levels of platelets were significantly associated with more advanced stages at the time of the diagnostic, higher tumoral burden (defined as a peritoneal cancer index higher than 20) and lower rates of complete debulking surgery. Meanwhile, these patients reported a significantly higher rate of postoperative complications.

Conclusions: patients presenting a platelet number higher than 450.000/microliter are associated with worse perioperative outcomes after debulking surgery for advanced stage ovarian cancer.

Keywords: advanced stage ovarian cancer, platelets, debulking surgery, perioperative complications

INTRODUCTION

Also known as the "silent killer", ovarian cancer represents one of the most important health problems affecting women worldwide, especially due to the fact that most cases remain asymptomatic for a long period of time; therefore, these patients will address to health services only late during their disease, when disseminated lesions are already present

[1]. In such cases, it seems that a radical surgical approach leading to no visible residual disease might improve the long-term outcomes while an incomplete surgical procedure of debulking is associated with a minimal benefit of survival [2-4]. Therefore, attention was focused on identifying which preoperative factors could have a positive predictive value in regard to the completeness of cytoreduction.

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Traditionally it has been considered that laboratory tests revealing a higher level of CA 125 as well as imagistic findings suggestive for tumoral transformation of the omentum (also known as “omental cake”) represent factors which are associated with incomplete debulking surgery; therefore, patients presenting such aspects are rather considered as candidates for neoadjuvant chemotherapy followed by interval debulking surgery [3-5]. Another laboratory test which seems to be associated with poorer outcomes is represented by the preoperative level of the serum platelets [6-8]. The aim of the current paper is to analyze the influence of the preoperative level of serum platelets on the perioperative outcomes of ovarian cancer patients.

MATERIAL AND METHODS

After receiving the Ethics Committee approval no 192/2020, data of patients submitted to primary cytoreductive surgery for advanced stage ovarian cancer between 2016-2018 were retrospectively reviewed. We identified 34 such patients, in all cases surgery representing the first therapeutic options. Furthermore these patients were classified accordingly to the serum level of platelets in two groups: lower than 450.000/microliter platelets (21 cases) and higher than 450.000/microliter platelets (13 cases). Intraoperative and postoperative outcomes were analyzed and compared between the two groups.

RESULTS

The 34 patients diagnosed with advanced stage ovarian cancer were submitted to debulking surgery as first therapeutic option, in all cases, complete cytoreduction being aimed. These patients were classified accordingly the serum number of platelets (which was determined during the preoperative period) into two groups: patients with a serum number of platelets lower than 450.000/microliter – 21 cases – group A - and patients with a higher number of platelets than 450.000/ microliter – 13 patients – group B. There were no significant differences regarding the mean age of the two groups (54 years versus 53 years), $p=0,67$. However, patients in group B trended to be diagnosed with more advanced lesions (based on the computed tomography aspects) and had a significantly higher level of CA125 (2150U/ml versus 1100U/ml), $p = 0,003$. Preoperative and intraoperative details are shown in Table 1.

As it can be seen from Table 1, patients in group A were more commonly diagnosed with the serous histopathological subtype and with a higher degree of differentiation; meanwhile, patients in group A were more likely to be submitted to complete mac-

TABLE 1. Preoperative and intraoperative features of the two groups of patients

Parameter	Group A (21 cases)	Group B (13 cases)	Statistical significance
Mean age	54 years	53 years	$p=0,67$
CA125 level	1100 U/ml	2150 U/ml	$p=0,003$
FIGO stage			
-	n=18	n=6	$p=0,04$
-	n=3	n=7	
Histopathological type:			$p=0,33$
- Serous	n=13	n=6	
- Non-serous	n=9	n=7	
Degree of differentiation:			$p=0,05$
- Low	n=6	n=3	
- High	n=15	n=10	
Residual disease:			$p=0,04$
- Microscopic	n=17	n=4	
- Macroscopic	n=4	n=9	

n= number of cases

rosopic debulking surgery when compared to patients in group B. When it comes to the rates of postoperative complications, patients in the second group developed more frequently thrombotic complications such as postoperative embolism (which was reported in 3 cases in group B and in 2 cases in group A).

DISCUSSIONS

The influence of thrombocytosis in ovarian cancer has been recently studied in both primary and recurrent ovarian cancer; therefore the presence of a higher amount of platelets seems to be associated with the presence of a more aggressive course of the disease, with higher levels of CA125 and with a lower rate of complete debulking surgery [7,9].

Ovarian cancer cells seem to produce growth factors and interleukines (IL) such as IL -6 which will further stimulate thrombocyte synthesis; therefore, an excess of circulating platelets will develop due to an excessive production and not due to the alteration of platelets' survival [10]. Meanwhile, other studies came to demonstrate that a higher number of circulating platelets will further synthesize growth factors such as platelet derived growth factor which are known to exhibit a mitogen activity on the epithelial surface cells from the ovary or thrombospondin, a glycoprotein which seems to promote the process of tumoral dissemination [11,12].

An interesting study which aimed to investigate if a higher number of platelets is associated with a poorer long-term prognostic was published by Li et al. in 2004; the study included 183 patients with ovarian cancer or primary peritoneal cancer. The

authors demonstrated that a higher number of circulating platelets was significantly associated with a higher stage at the time of diagnostic, higher grades of the tumors, higher rates of lymph node metastases, higher amounts of CA 125 and a higher amount of ascites; meanwhile cases presenting thrombocytosis were more likely to be submitted to incomplete debulking. When investigating the impact of the number of platelets on the overall survival the authors took into consideration only patients diagnosed in advanced stages of the disease and demonstrated that cases with preoperative thrombocytosis reported a significantly poorer disease free and overall survival; moreover, this impact was also observed in multivariate analysis, demonstrating once again the strength of this prognostic factor [9].

A similar conclusion was drawn by Allensworth et al. in 2013; the authors demonstrated that [6] thrombocytosis was associated with a significantly poorer outcome in both early stage and advanced stage ovarian cancer; moreover, the authors demonstrated that the presence of thrombocytosis is also associated with a higher risk of perioperative complications such as postoperative ileus, postoperative wound infection and urinary tract infection. Meanwhile patients with preoperative thrombocytosis

needed a significantly longer hospital in stay. Oppositely to Li's study, Allensworth's study came to demonstrate a significant correlation ship between the serum level of albumin and hemoglobin and the number of circulating platelets; meanwhile, Allensworth's study underlined the fact that a poorer prognostic is to be expected in every stage of the disease if a higher number of platelets is present and underlined the fact that cytoreduction as first intent treatment in such cases should be carefully analyzed [6].

CONCLUSIONS

Preoperative identification of a higher number of circulating platelets seems to be associated with a higher risk of presenting unresectable, disseminated lesions which might impede performing a complete debulking surgical procedure; meanwhile, this parameter seems to be associated with the presence of more aggressive tumors and with a higher rate of postoperative embolic complications; therefore, these patients should be carefully selected for performing per primam surgery, the possibility of performing neoadjuvant chemotherapy being seriously taken into consideration.

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REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013; 63(1):11–30.
2. Mutch DG. Surgical management of ovarian cancer. *Semin Oncol.* 2002; 29(1 Suppl 1):3–8
3. Lheureux S, Braunstein M, Oza AM. Epithelial ovarian cancer: Evolution of management in the era of precision medicine. *CA Cancer J Clin.* 2019;69(4):280-304.
4. Tsonis O, Gkrozou F, Vlachos K, Paschopoulos M, Mitsis MC, Zakyntinakis-Kyriakou N et al. Upfront debulking surgery for high-grade serous ovarian carcinoma: current evidence. *Ann Transl Med.* 2020;8(24):1707.
5. Chiofalo B, Bruni S, Certelli C, Sperduti I, Baiocco E, Vizza E. Primary debulking surgery vs. interval debulking surgery for advanced ovarian cancer: review of the literature and meta-analysis. *Minerva Med.* 2019;110(4):330-340.
6. Allensworth SK, Langstraat CL, Martin JR, Lemens MA, McGree ME, Weaver AL et al. Evaluating the prognostic significance of preoperative thrombocytosis in epithelial ovarian cancer. *Gynecol Oncol.* 2013; 130(3):499–504.
7. Menczer J, Schejter E, Geva D, Ginath S, Zakut H. Ovarian carcinoma associated thrombocytosis. Correlation with prognostic factors and with survival. *Eur J Gynaecol Oncol.* 1998; 19(1):82–84.
8. Naina HV, Harris S. Paraneoplastic thrombocytosis in ovarian cancer. *N Engl J Med.* 2012; 366(19):1840.
9. Li AJ, Madden AC, Cass I, Leuchter RS, Lagasse LD, Karlan BY. The prognostic significance of thrombocytosis in epithelial ovarian carcinoma. *Gynecol Oncol.* 2004; 92(1):211–214
10. Trantum BL, Haut A. Thrombocytosis: platelet kinetics in neoplasia. *J Lab Clin Med* 1974;84:615 – 619.
11. Dabrow MB, Francesco MR, McBrearty FX, Caradonna S. The effect of platelet-derived growth factor and receptor on normal and neoplastic human ovarian surface epithelium. *Gynecol Oncol.* 1998;71:29 – 37.
12. Qian X, Tuszynski GP. Expression of thrombospondin-1 in cancer: a role in tumor progression. *Proc Soc Exp Biol Med.* 1996;212:199 – 207