Observational Study

Medicine®

OPEN

Correlation analysis and clinical significance of CA125, HE4, DDI, and FDP in type II epithelial ovarian cancer

Li Qiao, Bachelor[a], Xinhua Chen, MD[a], Xuxia Xi, Bachelor[a], Xueqin Chen, Bachelor[a], Pengpeng Zhang, MM[a], Hua Dong, MM[a], Xiaohua Wu, MD[b], Xiaojun Chen, MD[b,*]

Abstract

Ovarian cancer is one of the common female malignant tumors. The early diagnosis and treatment of ovarian cancer has been a research hotspot. Therefore, we aimed to investigate the correlations between the levels of carbohydrate antigen 125 (CA125), human epididymis protein 4 (HE4), D-dimer (DDI), and fibrinogen degradation product (FDP) in patients with type II epithelial ovarian cancer.

From January 2018 to January 2019, a total of 952 patients who underwent initial surgery for epithelial ovarian cancer were enrolled in this study. Peripheral venous blood was taken before operation, and the levels of CA125, HE4, DDI, and FDP were tested. The correlations between the levels of CA125, HE4, DDI, and FDP and other clinical indicators (such as presence or absence of chemotherapy, surgical conditions) were analyzed.

The level of DDI or FDP was statistically associated with age, chemotherapy, Figo staging, surgical procedure, HE4 level, and CA125 level, respectively. Moreover, the Figo staging was statistically correlated with the levels of HE4 and CA125. Besides, we found the levels of CA125 and HE4 were positively correlated with the levels of DDI and FDP.

The levels of CA125 and HE4 are the traditional detection indexes for patients with type II epithelial ovarian cancer, and these 2 indicators reflected the degree of disease and prognosis. The levels of DDI and FDP were closely related to the levels of CA125 and HE4 in type II epithelial ovarian cancer, and they also helped to assess the prognosis of epithelial ovarian cancer. Further larger-scale prospective cohort studies are warranted to determine these associations in the future.

Abbreviations: CA125 = carbohydrate antigen 125, DDI = D-dimer, DIC = disseminated intravascular coagulation, DVT = deep vein thrombosis, FDP = fibrinogen degradation product, HE4 = human epididymis protein 4, HE4 = Human epididymis protein 4, IQR = interquartile range, medians, OS = overall survival, PTE = pulmonary embolism, SD = standard deviation, SE = standard error, TFS = tumor-free survival.

Keywords: CA125, D-dimer, FDP, HE4, type II epithelial ovarian cancer

1. Introduction

Ovarian cancer is the seventh most common cancer and the eighth leading cause of cancer death in women worldwide.[1] In female malignant tumors, the incidence of ovarian cancer is second only to breast cancer and cervical cancer, but the mortality rate is the highest.[2] The pathogenesis of ovarian cancer is concealed, and about 70% of the patients were at the late stage at the time of discovery.[3] The incidence of epithelial ovarian cancer accounts for 85% to 90%, and about 70% epithelial ovarian cancer recurs within 2 years.[4] For all the patients, 30% patients with the early stage ovarian cancer have a 5-year survival rate of 92%, however, 70% of the patients with advanced ovarian cancer only have a 5-year survival rate of about 29%.[5] Thus, the early diagnosis and treatment of epithelial ovarian cancer has been a research hotspot. At present, the treatment methods mainly consist radical surgery and cytoreductive surgery, supplemented by platinum-based chemotherapy and targeted therapy.[6] The thoroughness of the initial surgery is closely related to the long-term prognosis.

According to clinical pathology and molecular genetics, the epithelial ovarian cancer is divided into 2 types, type I and type II.[7] Type I tumors show a slow growth and, generally, have a good prognosis. Histological types for Type I tumors include low-grade serous carcinoma, low-grade endometrioid carcinoma, mucinous carcinoma, and clear cell carcinoma.[8] However, the

Editor: Girijesh Patel.

This study was approved by the ethics committee of the Shanghai Fudan University Cancer Hospital. All the participants (or legal guardians) in this study provided written informed consent.

There are no potential conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

The datasets generated during and/or analyzed during the current study are publicly available.

[a] Department of Gynaecology, Wuhu First People's Hospital, Wuhu, Anhui Province, [b] Department of Gynecological Oncology, Affiliated Cancer Hospital of Fudan University, Shanghai, China.

[*] Correspondence: Xiaojun Chen, Department of Gynecological Oncology, Affiliated Cancer Hospital of Fudan University, No. 270 Dong'an Road, Xuhui District, Shanghai 200000, China (e-mail: chen_xiaojun19@outlook.com).

How to cite this article: Qiao L, Chen X, Xi X, Chen X, Zhang P, Dong H, Wu X, Chen X. Correlation analysis and clinical significance of CA125, HE4, DDI, and FDP in type II epithelial ovarian cancer. Medicine 2020;99:49(e23329).

Received: 2 January 2020 / Received in final form: 18 August 2020 / Accepted: 20 October 2020

http://dx.doi.org/10.1097/MD.0000000000023329

type II tumors grow rapidly and the prognosis were bad. Histological types type II tumors include high-grade serous carcinoma and high-grade endometrioid carcinoma.[8]

D-dimer (DDI) is a specific product of fibrin degradation, and the determination of DDI can determine whether fibrin has formed.[9] In the case of secondary fibrinolysis, high values of DDI can be exhibited in diseases such as disseminated intravascular coagulation (DIC), thrombotic diseases, infectious diseases, and malignant tumors.[10] Therefore, DDI is an important indicator of deep vein thrombosis (DVT), pulmonary embolism (PTE), and DIC.

Fibrinogen degradation product (FDP) mainly reflects the solubilizing function of fibrin (original).[11] When the primary fibrinolysis caused by the decomposition of fibrinogen occurs, the FDP content also significantly increased. The FDP level also increased in hypercoagulable state, pulmonary embolism, malignant tumor, venous thrombosis, thrombolytic therapy, and secondary hyperthyroidism.[12] It can be seen that FDP is a sensitive indicator of the reaction of fibrinolysis, and its level increased in the case of primary fibrinolysis.

Serum carbohydrate antigen 125 (CA125) is the most widely used tumor marker in the field of gynecology in the past 20 years, and the levels of serum CA125 elevated in about 85.0% patients with advanced ovarian cancer.[13] Human epididymis protein 4 (HE4) is a newly discovered tumor marker.[14] Thus the combined detection of serum CA125 and HE4 could further improve the sensitivity and specificity of tumor diagnosis. In this study, we examined the correlations between DDI and FDP and its correlations with CA125 and HE4, and also the correlations between clinical pathological staging and prognosis in patients with type II ovarian cancer. We hope these results can help to improve the diagnosis of ovarian cancer, which is of great significance for the diagnosis of early ovarian cancer.

2. Materials and methods

2.1. General data

From January 2018 to January 2019, 952 cases of ovarian cancer patients who admitted to the Department of Gynecologic Oncology, Shanghai Fudan University Cancer Hospital, were enrolled in this study. Using the Figo Staging, pathological stages include I-IV, and the pathological types consist of high-grade serous cancer, endometrioid carcinoma, clear cell carcinoma, mucinous carcinoma, metastatic cancer. For Figo Staging: Stage I showed that the tumor is confined to the ovary; Stage II showed that the lesions involved one or both ovaries with pelvic metastasis; Stage III showed that The tumor invaded 1 or both ovaries, with extrapelvic peritoneal implantation or retroperitoneal or inguinal lymph node metastasis, and liver surface metastasis; Stage IV showed that

1. the tumor invaded 1 or both ovaries and had distant metastasis,
2. malignant cells should be found in pleural effusion;
3. liver metastasis involves liver parenchyma.

There was no difference in age and nutritional status. This study was approved by the ethics committee of the Shanghai Fudan University Cancer Hospital. All the participants (or legal guardians) in this study provided written informed consent. All analyses and data handling were performed under the guidelines of the NIH and in accordance with the Declaration of Helsinki and its later amendments.

2.2. Research methods

Peripheral venous blood was taken before surgery or before chemotherapy and after chemotherapy. The levels of CA125 and HE4 were measured with the Commercial kits (Elabscience Biotechnology Co., Ltd., Wuhan, China; Shanghai toujing Life Technology Co., Ltd., Shanghai, China) by chemiluminescence method in accordance with the manufactures protocol. The levels of DDI and FDP were measured with the Commercial kits (Chongqing xinsaiya Biotechnology Co., Ltd., Chongqing, China; Shanghai Yubo Biotechnology Co., Ltd., Shanghai, China) by automated coagulation analyzer (Turbidimetry) under the conditions recommended by the manufacturer. All blood samples were detected within 2 hours after blood collection. The reference value of CA125 is 0–35 U/ml, the reference value of HE4 is 0–84.4 pmol/L, the normal value of DDI is 0–0.5 μg/ml, and the normal value of FDP is 0–5 μg/ml. And the levels above normal are considered abnormal.

2.3. Statistical methods

All results are expressed as percentages for categorical variables and as the means (standard error, SE, or standard deviation, SD) or medians (interquartile range, IQR) for continuous or discrete variables. Proportions were compared using the χ^2 test or Fisher exact test, and ANOVA followed by Bonferroni *post hoc* tests or Kruskal–Wallis H tests, two-tailed *t* tests or nonparametric Mann–Whitney *U* tests were used to compare continuous or discrete variables among groups, as appropriate. Spearman correlation or uni-/multivariate logistic regression was used to analyse relationships between the variables. Two-tailed *P* values $<.05$ represent statistically significant differences. All statistical analyses were performed using the SPSS 20.0 software.

3. Results

3.1. Patient characteristics

From January 2018 to January 2019, a total of 952 patients were consecutively enrolled in this study. The median age of the study participants was 55 years (range, 17–80). In which, 879 (92.33%) cases were diagnosed with serous carcinoma, 8 (0.84%) cases with endometrioid carcinoma, and 65 (6.82%) cases with other types. Of all the patients, 630 (66.2%) cases underwent direct chemotherapy without surgery, and 322 (33.8%) cases underwent surgery after neoadjuvant chemotherapy. Among them, 320 (33.6%) cases received the satisfactory cytoreductive surgery (R0), 434 (45.6%) cases underwent the satisfactory tumor reduction (R1), and 198 (20.8%) cases underwent the unsatisfactory cytoreductive surgery (R2). For all the patients, the median levels of CA125, HE4, DDI, and FDP were 443.9 (102.17,1290.0), 271.4 (113.8,711.7), 2.85 (0.92,7.94), and 8.5 (3.6, 23.8), respectively. Each index was divided into normal group and abnormal group according to the corresponding level, and the detailed grouping information was listed in Table 1.

3.2. Correlation analyses between DDI, FDP, and other clinical indicators

The correlation analysis showed that the level of DDI was statistically associated with age, chemotherapy, Figo staging, surgical procedure, HE4 level, and CA125 level ($P=.01$ for all

Table 1

Patient clinical basic indicator description.

Indicators	Composition ratio
Figo staging	
I–II	114 (12.0%)
III–IV	838 (88.0%)
Surgery	
R0	320 (33.6%)
R1	434 (45.6%)
R2	198 (20.8%)
HE4	
Normal	154 (16.2%)
Abnormal	798 (83.8%)
CA125	
<600	548 (57.6%)
≥600	404 (42.4%)
DDI	
Normal	137 (14.4%)
Abnormal	815 (85.6%)
FDP	
Normal	368 (38.7%)
Abnormal	584 (61.3%)
Chemotherapy	
No	630 (66.2%)
Yes	322 (33.8%)

analysis) (Table 2). Similarly, our results showed that the level of FDP was statistically associated with age, chemotherapy, Figo staging, surgical procedure, HE4 level, and CA125 level ($P=.01$ for all analysis) (Table 3).

3.3. Correlation analyses of Figo staging and the levels of HE4 and CA125

The results showed that the Figo staging was statistically correlated with the levels of HE4 and CA125 ($P=.03$, $P=.01$, respectively). Moreover, the higher Figo staging, the higher levels of CA125 and HE4 (Table 4).

Table 2

Correlation analyses between DDI and clinical indicators.

	DDI grouping			
	Normal (%)	Abnormal(%)	χ^2	*P*
Chemotherapy				
no	35 (5.65)	584 (94.35)	96.64	.01
yes	87 (29.19)	211 (70.81)		
Figo staging				
I–II	28 (27.18)	75 (72.82)	19.71	.01
III–IV	93 (11.45)	719 (88.55)		
Surgery				
R0	58 (19.08)	246 (80.92)	19.78	.01
R1	54 (12.82)	367 (87.17)		
R2	10 (5.21)	182 (94.79)		
HE4				
Normal	64 (45.71)	76 (54.28)	150.47	.01
Abnormal	58 (7.46)	719 (92.54)		
CA125				
<600	111 (21.60)	403 (78.40)	69.71	.01
≥600	11 (2.73)	392 (97.27)		
Age				
<55	87 (18.51)	383 (81.49)	22.66	.01
≥55	35 (7.83)	412 (92.17)		

Correlation analyses between DDI and clinical indicators were performed by Chi-Squared test. Two-sided test was used, inspection level $\alpha=0.05$.

Table 3

Correlation analyses between FDP and clinical indicators.

	FDP grouping			
	Normal(%)	Abnormal (%)	χ^2	*P*
Chemotherapy				
no	128 (20.41)	499 (79.59)	262.47	.01
yes	240 (74.53)	82 (25.47)		
Figo Staging				
I–II	79 (71.17)	32 (28.83)	56.09	.01
III–IV	287 (34.33)	549 (65.67)		
Surgery				
R0	169 (52.48)	153 (47.52)	50.97	.01
R1	157 (36.34)	275 (63.66)		
R2	42 (21.54)	153 (78.46)		
HE4				
Normal	131 (85.06)	23 (14.93)	165.90	.01
Abnormal	237 (29.81)	558 (70.19)		
CA125				
<600	321 (58.68)	226 (41.32)	215.53	.01
≥600	47 (11.69)	355 (88.31)		
Age				
<55	197 (40.45)	290 (59.55)	1.18	.28
≥55	171 (37.01)	291 (62.99)		

Correlation analyses between DDI and clinical indicators were performed by Chi-Squared test. Two-sided test was used, inspection level $\alpha=0.05$.

3.4. The correlations between the levels of CA125, HE4, DDI, and FDP

Moreover, we found the levels of CA125 and HE4 were positively correlated with the levels of DDI and FDP. Of all the patients, the level of CA125 was positively correlated with the levels of DDI and FDP ($r=0.676$, 0.659, respectively; $P=.001$). Similarly, the level of HE4 was positively correlated with the levels of DDI and FDP ($r=0.666$, 0.644, respectively; $P=.001$). For patients underwent direct chemotherapy without surgery, the levels of CA125 and HE4 were still positively correlated with the levels of DDI and FDP ($r=0.561$, 0.548, correlations between CA125 and DDI and FDP, respectively; $r=0.576$, 0.563, correlations between HE4 and DDI and FDP, respectively; $P=.001$).

Moreover, for patients underwent surgery after neoadjuvant chemotherapy, our results showed the levels of CA125 and HE4 were still positively correlated with the levels of DDI and FDP ($r=$ 0.509, 0.477, correlations between CA125 and DDI and FDP,

Table 4

Correlations between Figo staging and the levels of HE4 and CA125.

	Figo grouping			
	I-II (%)	III-IV (%)	χ^2	*P*
HE4				
Normal	29 (18.95)	124 (81.05)	9.00	.03
Abnormal	83 (10.41)	714 (89.59)		
CA125				
<600	108 (19.74)	439 (80.26)	78.45	.01
≥600	4 (0.99)	399 (99.00)		

Correlation analyses between DDI and clinical indicators were performed by Chi-Squared test. Two-sided test was used, inspection level $\alpha=0.05$.

respectively; $r = 0.548, 0.506$, correlations between HE4 and DDI and FDP, respectively; $P = .001$).

4. Discussion

Malignant tumors (such as gastric cancer, pancreatic cancer, colon cancer, lung cancer, etc.) patients are always complicated with coagulation abnormalities, mostly manifested as increased DDI, decreased fibrinolysis, increased thrombocytosis, increased clotting factors, etc. Under hypercoagulable state, coagulation function is closely related to tumor invasion, metastasis, and prognosis.[15,16] The increase of DDI and FDP occurs in stage III-IV epithelial ovarian cancer, which is higher than stage I-II,[17] while the reasons were unclear. Our study found that in stage III-IV epithelial ovarian cancer, the levels of CA125 and HE4 increased significantly; however, in stage I-II epithelial ovarian cancer, although the levels of CA125 and HE4 also increased to varying degrees, the degree of elevation was lower than that of stage III-IV. We found the levels of DDI and FDP were correlated with the levels of CA125 and HE4, thus when the levels of CA125 and HE4 were elevated, the levels of DDI and FDP were also elevated. Therefore, the combined test of the levels of CA125, HE4, DDI, and FDP can help to diagnosis the epithelial ovarian cancer.

DDI is one of the specific products of fibrinogen degradation, reflecting the activation of coagulation and fibrinolysis system, high level of DDI is a specific molecular marker reflecting the presence of hypercoagulable state and hyperfibrinolysis in the body.[18] The procoagulant activity of DDI may be related to the expression of cancer tissue facto and the clinical stage of malignant tumor. Besides, the level of DDI is closely related to the possibility of tumor metastasis.[15–17] In this study, we found that the higher levels of CA125 and HE4 in patients with epithelial ovarian cancer, the higher level of DDI was. Previous research has found that overall survival (OS) and tumor-free survival (TFS) were not only related to residual lesions after primary surgery, but also closely related to preoperative blood DDI level.[19] One research reported the relationship between DDI level and overall survival, and considered that high DDI levels were an important risk factor for overall survival.[20] In addition, WACKMANN et al found that the higher the preoperative DDI, the lower overall survival rate and the shorter the survival time.[21] Although these studies have determined the relationship between DDI and OS and TFS, they did not clarify the intrinsic reasons. Our research found the closely correlations between DDI and CA125 and HE4 in patients with epithelial ovarian cancer, thus indicated that high DDI level may be a risk factor for recurrence and poor prognosis of epithelial ovarian cancer.[22]

FDP is a general term for degradation products produced by the decomposition of fibrin or fibrinogen under the action of plasmin produced by fibrinolysis. It can promote the progression of malignant tumors and increase the invasiveness of tumors through various ways.[23] Patients with malignant tumors often have hypercoagulable state. Tumor cells can directly secrete procoagulant substances to activate the coagulation system, and promote coagulation abnormalities through various pathways and mechanisms to form a vicious circle. There is an increase in platelet in patients with malignant tumors.[24] Platelet can release transforming growth factor beta and platelet-derived endothelial cell growth factor, which has a mitogenic effect and promotes the cloning and growth of tumor cells.[25] Platelet secretion is related to coagulation. Proteins, such as fibrinogen and platelet factor IV, cause an increase in FDP, which synergistically promotes tumor infiltration and progression.[26] Our study showed that FDP has a significant correlation with CA125 and HE4, and can reflect the tumor burden of epithelial ovarian cancer to some extent.

There was also limitation in the present study. The positive correlation between CA125, HE4, D-dimer and FDP in type II epithelial ovarian cancer was expounded. However, whether there is statistical significance in type I epithelial ovarian cancer needs further study due to small sample size.

In summary, in patients with type II epithelial ovarian cancer, the levels of serum DDI, FDP, CA125, HE4 were closely related to each other, and the levels of these indicators were correlated with high tumor burden and poor prognosis in epithelial ovarian cancer. The higher levels of DDI and FDP, the lower OS and TFS, the lower survival rate and the worse prognosis. Therefore, it is recommended to use the detection of levels of DDI and FDP to help to assess the tumor burden and prognosis of epithelial ovarian cancer.

Author contributions

Li Qiao is responsible for the study concepts & design, definition of intellectual content, literature research, clinical studies, experimental studies, data acquisition & analysis, statistical analysis, manuscript preparation & editing; Xinhua Chen, Xuxia Xi and Xueqin Chen are responsible for the literature research; Pengpeng Zhang and Hua Dong are responsible for the statistical analysis; Xiaohua Wu is responsible for the manuscript review; Xiaojun Chen is responsible for the guarantor of integrity of the entire study, definition of intellectual content, literature research, manuscript editing & review. All authors read and approved the final manuscript.

Conceptualization: Li Qiao, Xiaojun Chen.
Data curation: Li Qiao.
Formal analysis: Li Qiao, Pengpeng Zhang, Hua Dong.
Investigation: Xiaojun Chen.
Methodology: Li Qiao, Xiaojun Chen.
Project administration: Li Qiao.
Resources: Li Qiao, Xinhua Chen, Xuxia Xi, Xueqin Chen.
Writing – original draft: Li Qiao.
Writing – review & editing: Xiaohua Wu, Xiaojun Chen.

References

[1] Shetty MK. Imaging and differential diagnosis of ovarian cancer. Semin Ultrasound Ct Mri 2019;40:302–18.
[2] Jelovac D, Armstrong DK. Recent progress in the diagnosis and treatment of ovarian cancer. CA 2011;61:183–203.
[3] Johnson KA. The standard of perfection: thoughts about the laying Hen model of ovarian cancer. Cancer Prev Res 2009;2:97–9.
[4] Nicoletta G, Toom VG, Gabriella P, et al. Ovarian cancer. Oncol Hematol 2006;60:159–79.
[5] Desai A, Xu J, Aysola K, et al. Epithelial ovarian cancer: an overview. World J Transl Med 2014;3:1–8.
[6] Coleman RL, Monk BJ, Sood AK, et al. Latest research and treatment of advanced-stage epithelial ovarian cancer. Nat Rev Clin Oncol 2013;10: 211–24.
[7] Koshiyama M, Matsumura N, Konishi I. Recent concepts of ovarian carcinogenesis: type I and type II. J Biomed Biotechnol 2014;2014:934261.
[8] Kaku T, Ogawa S, Kawano Y, et al. Histological classification of ovarian cancer. Med Electron Microsc 2003;36:9–17.
[9] Clinical value of automated fibrin generation markers in patients with septic shock: A SepsiCoag ancillary study. Bri J Haematol 2018;183: 636–47.
[10] Olson JD. D-dimer: an overview of hemostasis and fibrinolysis, assays, and clinical applications. Adv Clin Chem 2015;69:1–46.

[11] Victor J, Marder MD, Myrtle O, et al. Detection of serum fibrinogen and fibrin degradation products: comparison of six technics using purified products and application in clinical studies. Am J Med 1971;51:71–82.
[12] Planner RS, O'Sullivan EF, Campbell JJ, et al. The hypercoagulable state and pulmonary embolism in patients with ovarian carcinoma. Aust N Z J Obstet Gynaecol 2010;18:209–12.
[13] Zhen S, Bian L, Chang L, et al. Comparison of serum human epididymis protein 4 and carbohydrate antigen 125 as markers in ovarian cancer: A meta-analysis. Molec Clin Oncol 2014;2:559–66.
[14] Speeckaert MM, Speeckaert R, Delanghe JR. Human epididymis protein 4 in cancer diagnostics: a promising and reliable tumor marker. Adv Clin Chem 2013;59:1–21.
[15] Wang Y, Wang Z. Predictive value of plasma D-dimer levels in patients with advanced non-small-cell lung cancer. Onco Targets Ther 2015;8: 805–8.
[16] Antoniou D, Avlakou G, Stathopoulos GP, et al. Predictive value of D-dimer plasma levels in response and progressive disease in patients with lung cancer. Lung Cancer 2006;53:205–10.
[17] Yan YF, Li XQ, Xiao L, et al. Correlation analysis between D-dimer FDP and PLT and prognosis of epithelial ovarian cancer. Anhui Med J 2018;39:1171–5.
[18] Diaz ES, Walts AE, Karlan BY, et al. Venous throm-boembolism during primary treatment of ovarian clear cell carcinoma is associated with decreased survival. Gynecol Oncol 2013;131:541–5.
[19] Chen M, Lin ZQ, Chen W. The role of combined detection of CA125 and D-dimer in the differential diagnosis of ovarian cancer. J Pract Obstetr Gynecol 2007;23:475–7.
[20] Gadducci A, Baicchi U, Marrai R, et al. Preoperative evaluation of D - dimer and CA125 levels in differentiating benign from malignant ovarian masses. Gynecol Oncol 1996;60:197–202.
[21] von Tempelhoff GF, Dietrich M, Niemann F, et al. Blood coagulation and thrombosis in patients with ovarian malignancy. Thromb Haemost 1997;77:456–61.
[22] Nagy Z, Horváth O, Kádas J, et al. D-dimer as a potential prognostic marker. Pathol Oncol Res 2012;18:669–74.
[23] Mackman N, Tilley RE, Key NS. Role of the extrinsic pathway of blood coagulation in hemostasis and thromhosis. Arteroscler Thromb VascBiol 2007;27:1687–93.
[24] Li XQ, Xiao L, Xu XM, et al. Changes and clinical significance of fibrin degradation products and D-dimer in peripheral blood platelet counts in patients with epithelial ovarian cancer. Anhui Med Pharmaceut J 2017;38:288–90.
[25] Iwasaki A, Hamanaka W, Harnada T, et al. Significance of platelet counts in patients who underwent surgical treatment for lung metastasis. Int Surg 2007;92:103–9.
[26] Meng XK, Li H, Wen F, et al. Relationship between patients with advanced ovarian cancer serous papillary cystadenocarcinoma and increased platelet count. China J Modern Med 2010;20:1575–7.