

## Original Article

# Comparison of differences between neoadjuvant chemotherapy and conventional chemotherapy for ovarian cancer in application, CA125 and prognosis

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**Abstract:** Objective: To compare the application of neoadjuvant chemotherapy and conventional chemotherapy in the treatment of ovarian cancer and the changes of CA125 and the prognosis in patients after treatments. Methods: A retrospective analysis was made on 384 cases of ovarian cancer patients in the department of gynaecology and oncology in Yantai Yuhuangding Hospital Affiliated to Qingdao University from April 2008 to September 2013. Patients were randomized to the test group (192 patients with neoadjuvant chemotherapy) and the control group (192 patients receiving conventional chemotherapy) according to the way of treatments. The clinical efficacy in two groups of patients and the detection results of CA125 were compared, and all patients were followed up for a period of three years. Results: The response rate of the test group was 94.79%, which was prominently higher than that of the control group (77.09%,  $P < 0.01$ ). The incidence of adverse reactions in the test group was 16.15%, remarkably better than that in the control group (42.70%,  $P < 0.01$ ). There was no noted difference in bone marrow suppression between the two groups (18.23% and 23.96%,  $P = 0.17$ ) and no notable difference in serum concentration of CA125 between the two groups before chemotherapy was observed ( $P = 0.541$ ). The concentration of CA125 in the test group decreased markedly after three weeks and five weeks of chemotherapy, which was obviously lower than that in the control group (all  $P < 0.01$ ). The rates of survival at first, second and third years in the test group were 94.69%, 84.35%, 67.64%, respectively, while those in the control group were 81.43%, 66.05%, 49.60% respectively. Marked differences in the survival rates between the two groups were noted ( $P < 0.05$ ). Conclusion: Neoadjuvant chemotherapy can effectively improve the survival rate of ovarian cancer patients and reduce the incidence of different reactions during the treatment. Hence, it is worth generalization and application in clinical practice.

**Keywords:** Neoadjuvant chemotherapy, conventional chemotherapy, ovarian cancer, prognosis, CA125

## Introduction

Ovarian cancer, whose incidence ranks second only to cervical cancer and uterine corpus cancer, is a malignant tumor with an extremely high incidence in female patients [1]. Oza et al. reported that the average global newly increased number of ovarian cancer patients was more than 245 thousand per year [2]. The study by Hamanishi et al. also showed that the incidence of ovarian cancer was outstandingly increased with the opening up of the social system [3]. At present, the incidence of ovarian cancer shows an upward trend year by year, and age of onset has the youth-oriented tendency [4]. According

to the study by Falconer et al., in 2025, ovarian cancer would be the highest incidence of malignancy in gynecologic diseases if current situations developed [5]. Although the incidence of ovarian cancer is not the highest, the mortality rate of ovarian cancer in 5 years is up to 72.8%, which is the greatest mortality in gynecologic diseases [6]. Surgical removal is the main treatment for ovarian cancer, and is usually combined with chemotherapy after operation because traditional surgical resection cannot completely remove tumor lesions [7]. Considering the high mortality of ovarian cancer, new breakthroughs are constantly being sought in clinic practice to improve the survival of the

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**Table 1.** Evaluation of efficacy in ovarian cancer

Evaluation	Detail information
Excellent	Complete tumor regression
Good	50% or higher tumor volume reduction
Mediocre	50% or lower tumor volume reduction
Poor	No improvement or deterioration of tumor

patients. With the development of medical technology, neoadjuvant chemotherapy has gradually begun to be widely used in cancer treatment; however, compared with traditional chemotherapy, it is not yet clear which of the two is most suitable for ovarian cancer treatment. Therefore, through a retrospective analysis of ovarian cancer patients, the purpose of this article is to provide reference and guidance for the treatment of ovarian cancer in future clinical practice.

## Materials and methods

### *Patients' database*

A total of 384 patients aged from 30 to 60 years, with an average age of (44.17±8.67) years and ovarian cancer in the department of gynaecology and oncology in Yantai Yuhuangding Hospital Affiliated to Qingdao University from April 2008 to September 2013 were enrolled. Patients were randomized to the test group (192 patients with neoadjuvant chemotherapy) and the control group (192 patients receiving conventional chemotherapy) according to the way of treatments. Inclusion criteria: Patients older than 20 years of age were recruited. All patients were diagnosed with ovarian cancer by pathological biopsy. Patients received a series of treatments in Yantai Yuhuangding Hospital Affiliated to Qingdao University after diagnosis. Patients were obedient to arrangements of Yantai Yuhuangding Hospital Affiliated to Qingdao University. Patients with enough case data were selected. Exclusion criteria: Patients suffered from cardiovascular and cerebrovascular diseases, upper respiratory tract diseases, or lower gastrointestinal diseases. Patients had prolonged immobilization in bed. Patients were pregnant. Patients were transferred during the study. Patients had physical disabilities. Patients were unauthorized to accept any treatments from other hospitals. Informed consents were obtained, and this study was approved by the Hospital Ethics Committee.

## Methods

Neoadjuvant chemotherapy used in the test group was performed with paclitaxel/platinum-based chemotherapy for 3 courses (20 d/course) before surgery. After a series of evaluations by the gynecologists in Yantai Yuhuangding Hospital Affiliated to Qingdao University, it was decided when to carry out cytoreduction surgery after chemotherapy; and another 5 courses of chemotherapy were performed 30 days after the operation. In the control group, the traditional chemotherapy was performed as PT chemotherapy (paclitaxel combined with cisplatin), and the surgical resection was performed after 5 courses of chemotherapy. The use of the methodology in chemotherapy was strictly conducted in accordance with the practice guideline for radiotherapy operation of 2010 [8]. The clinical efficacy of patients in two groups was compared and all patients were followed up for a period of 3 years. Two milliliters of venous blood were extracted for the concentration of CA125 in serum by chemiluminescence immunoassay (ADVIA Centaur XP, Siemens, Germany) before chemotherapy, 3 weeks after chemotherapy and 5 weeks after chemotherapy in patients of two groups.

### *Evaluation criteria*

To evaluate the efficacy of ovarian cancer, the study was performed according to the guidelines for safety of gynecological oncology in 2017 [9]. See **Table 1**. The postoperative adverse reactions and bone marrow suppression were both recorded, and the classification criteria were based on the International Encyclopedia of Adverse Drug Reactions in 2015 and the study of bone marrow suppression by Jabbour et al. in 2015 [10, 11]. The response rate was excellent or good. The follow-ups were done by telephone, letter or reexamination in Yantai Yuhuangding Hospital Affiliated to Qingdao University. The treatment cutoff time and event were May 30<sup>th</sup>, 2017 and death or lost contact of the patient, respectively. Then the survival rate of the patient within 3 years was calculated.

### *Statistical analysis*

All statistical analyses were performed with SPSS22.0 software. Efficacy assessment, clinical data, adverse reaction and bone marrow

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**Table 2.** Clinical data in patients of two groups (n, %)

Items	Test group (n=192)	Control group (n=192)	$\chi^2$	P value
Age (years)			1.29	0.26
<45	87 (45.31)	76 (39.68)		
≥45	105 (54.69)	116 (60.42)		
Ethnicity			3.70	0.05
Han	184 (95.83)	190 (98.96)		
Minority	8 (4.17)	2 (1.04)		
Maternity			0.93	0.34
Yes	164 (85.42)	157 (81.77)		
No	28 (14.58)	35 (18.23)		
Marital status			1.35	0.51
Married	154 (80.21)	162 (84.38)		
Single	30 (15.63)	25 (13.02)		
Windowed	8 (4.17)	5 (2.60)		
Place of residence			0.95	0.33
Urban region	124 (64.58)	133 (69.27)		
Rural region	68 (35.42)	59 (30.73)		
Tobacco smoking			2.35	0.13
Yes	109 (56.77)	94 (48.96)		
No	83 (43.23)	98 (51.04)		
Alcohol consumption			0.83	0.36
Yes	49 (25.52)	57 (29.69)		
No	143 (74.48)	135 (70.31)		
Level of education			0.76	0.38
Below university degree	126 (65.63)	134 (69.79)		
University degree or above	66 (34.38)	58 (30.21)		
Exercise habit			1.36	0.24
Yes	75 (39.06)	64 (33.33)		
No	117 (60.94)	128 (66.67)		
Weight			0.87	0.35
<60 kg	84 (43.75)	75 (39.06)		
≥60 kg	108 (56.25)	117 (60.94)		
Pathological stage			0.40	0.53
Stage I and II	74 (38.54)	68 (35.42)		
Stage III and IV	118 (61.46)	124 (64.58)		

suppression in two groups were expressed in terms of rate, and the chi-square test was adopted. The survival rates were calculated by Kaplan-Meier method while the survival rates were compared using Log-rank test. *P* values were judged significant if they were less than 0.05.

### Results

#### Clinical data

The clinical data of the two groups were compared. There was no prominent difference

between the two groups in age, ethnicity, maternity, marriage, place of residence, smoking, drinking, educational level, exercise habits, weight and pathological stages, which further enhanced the accuracy of test results (all  $P > 0.05$ ). See **Table 2**.

#### Comparisons of efficacy

Patients whose efficacy achieved excellent in the test group were 46.35%, which was markedly higher than those in the control group (29.69%). In the test group, patients whose efficacy achieved mediocre and poor were 4.17% and 1.04% respectively, also superior to those in the control group (16.67% and 6.25%). The response rate of the test group was 94.79%, which was remarkably higher than that of the control group (77.09%,  $P < 0.01$ ). See **Table 3**.

#### Prognosis

The prognosis of the two groups was compared. The adverse reactions I, II, III and IV occurring in the test group were 8.33%, 4.69%, 3.13%, 0.00%, respectively; the overall incidence of adverse reactions was 16.15%. The adverse reactions I, II, III and IV occurring in the control group were 20.31%, 10.94%, 8.85%, 2.60% respectively, and the overall incidence was 42.70%.

The overall incidence of adverse reactions in the control group was outstandingly higher than that in the test group ( $P < 0.01$ ) and no noted difference in bone marrow suppression between the test group and the control group was observed ( $P = 0.17$ ). See **Tables 4** and **5**.

#### Detection results of CA125

There was no significant difference in serum concentration of CA125 between the two groups before chemotherapy ( $P = 0.54$ ). After 3 weeks of chemotherapy, the concentration of CA125 in the test group was notably decreased

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**Table 3.** Comparisons of efficacy in patients of two groups (n, %)

Group	Excellent	Good	Mediocre	Poor	Response rate (%)
Test group (n=192)	89 (46.35)	93 (48.44)	8 (4.17)	2 (1.04)	94.79
Control group (n=192)	57 (29.69)	91 (47.40)	32 (16.67)	12 (6.25)	77.09
$\chi^2$					26.69
P value					<0.01

**Table 4.** Adverse reactions in patients of two groups (n, %)

Items	Test group (n=192)	Control group (n=192)	$\chi^2$	P value
Adverse reaction				
I	16 (8.33)	39 (20.31)		
II	9 (4.69)	21 (10.94)		
III	6 (3.13)	17 (8.85)		
IV	0 (0.00)	5 (2.60)		
Overall incidence (%)	16.15	42.70	32.62	<0.01

**Table 5.** Bone marrow depression in patients of two groups (n, %)

Items	Test group (n=192)	Control group (n=192)	$\chi^2$	P value
Adverse reaction				
I	24 (12.50)	30 (15.63)		
II	8 (4.17)	11 (5.73)		
III	3 (1.56)	5 (2.60)		
IV	0 (0.00)	0 (0.00)		
Overall incidence (%)	18.23	23.96	1.89	0.17

to  $152.8 \pm 18.2$  U/mL, which was remarkably lower than that in the control group ( $207.5 \pm 19.8$  U/mL,  $P < 0.01$ ). The concentration of CA125 in the test group was outstandingly lower than that in the control group after 5 weeks of chemotherapy as well ( $P < 0.01$ ). See **Table 6**.

### Survival curves

A total of 384 patients with ovarian cancer were followed up for a period of 3 years and the success rate of follow-up was 98.18% (377/384), including 3 cases in the test group and 4 cases in the control group losing contact. There were 62 deaths in the test group and the rates of survival at first, second and third years were 94.69%, 84.35%, 67.64%, respectively; while 97 cases of deaths in the control group were documented and the rates of survival at first, second and third years were 81.43%, 66.05%, 49.60%, respectively. The survival rates of the test group in the first, second and

third years were prominently higher than those of the control group (all  $P < 0.05$ ). See **Figure 1**.

### Discussion

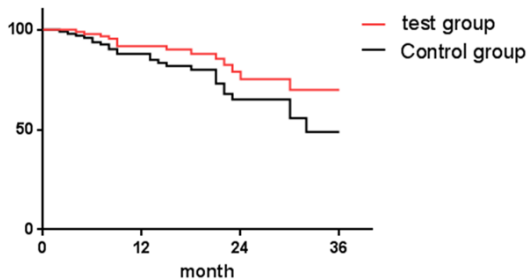
Due to the high incidence and high mortality of ovarian cancer, it has become a critical subject in gynecological clinic practice, which urgently needs to seek a breakthrough [12]. According to the study by Walker et al., cytoreduction surgery was effective in the treatment of ovarian cancer [13]. However, because of the specificity of female body structures, an ovarian lesion is often unable to detect in time because of its large space and strong disguise. In addition, there is no prominent feature in the early stage of ovarian cancer. As a consequence, most of the patients are diagnosed with middle or terminal stage of ovarian cancer at their visits to physicians [14]. Cytoreduction surgery cannot be

performed if miss critical time of treatments. In the present clinical practice, the most commonly used treatment for ovarian cancer is chemotherapy in combination with surgery. However, it has been widely proven that the efficacy of traditional chemotherapy combined with surgery is not satisfactory for patients with ovarian cancer, and the survival rates of patients show a trend of decreasing [15, 16]. Moreover, in patients with middle or terminal stage of ovarian cancer, the death rates are more serious because of the larger lesions [17]. With the continuous improvements and popularity of neoadjuvant chemotherapy, many departments have put it into the treatment of cancer. Hence, by comparing the efficacy between neoadjuvant chemotherapy and conventional chemotherapy in the treatment of patients with ovarian cancer, this paper has some vital reference values for the clinical treatment of ovarian cancer.

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**Table 6.** The concentration of CA125 in patients of two groups (U/mL)

Items	Test group (n=192)	Control group (n=192)	t value	P value
Before chemotherapy	354.4±27.5	352.7±26.9	0.61	0.54
Three weeks after chemotherapy	152.8±18.2	207.5±19.8	28.18	<0.01
Five weeks after chemotherapy	72.3±12.7	118.7±15.1	32.59	<0.01



**Figure 1.** Survival curves in patients of two groups after chemotherapy. The rates of survival at first, second and third years in the test group were 94.69%, 84.35%, 67.64%, respectively, while those in the control group were 81.43%, 66.05%, 49.60%, respectively.

The results of this experiment showed that the neoadjuvant chemotherapy was outstandingly superior to the conventional chemotherapy in efficacy and adverse reactions; and the results of 3-year follow-up also indicated that the survival rates of patients with neoadjuvant chemotherapy were notably improved. The reason is that neoadjuvant chemotherapy can largely reduce the range of tumors that needs resection during operation, and it has good regulations on pleural effusion and ascites, resulting in increased tolerance of patients. Besides, neoadjuvant chemotherapy can also intervene tumor metastases. It eliminates distant metastases such as liver and lung, effectively reduces ovarian cancer grade, and further improves the ability of operation [18]. And the study of Plimack et al. demonstrated that neoadjuvant chemotherapy could separate the close links between the tumor and the tissue by reducing the volume of the patient's tumor, so as to avoid the damage to the tissue during the operation to a great extent, and effectively reduce postoperative adverse reactions [19]. Concurrently, in the process of chemotherapy, inhibitions of neoadjuvant chemotherapy on cancer cells can markedly slow down the activity and proliferation of cancer cells, which can greatly prevent the spread of tumor caused by tissue oxidation or mechanical stimulation during the operation. This is consistent with the applica-

tion of neoadjuvant chemotherapy in breast cancer by Wimberly et al., which further confirms the results of this experiment [20]. There was no obvious difference in bone marrow suppression between the two groups, illustrating that compared with the traditional chemotherapy, neoadjuvant chemotherapy was basically the same in the side effects and it could be put into use in clinical practice. As a sensitive cancer marker in ovarian cancer, CA125 is often used as an indicator of the severity of the patient's condition. In this test result, the concentration of CA125 in the test group and the control group decreased greatly before and after the chemotherapy, but the decreasing trend in patients with neoadjuvant chemotherapy was more prominent, which demonstrated that in patients receiving neoadjuvant chemotherapy, tumor lesion reduction was more remarkable and effective, resulting in greatly reducing the burden and damage of patients' health due to long-term chemotherapy. It is much worthy of clinical application.

This study compared the efficacy and prognosis of ovarian cancer patients treated with neoadjuvant chemotherapy and conventional chemotherapy; it was in strict accordance with the inclusion criteria and exclusion criteria for screening study objects, and it compared and analyzed through statistical analyses. Nonetheless, due to the limitation of test conditions, we cannot rule out that there may be some differences in the test results in patients from different countries. In addition, the survival of patients may be different if outcome follow-up time is short. We will conduct a longer period of outcome follow-up and continuously improve the experiment to get the most accurate test results.

In conclusion, neoadjuvant chemotherapy can effectively improve the survival rates of ovarian cancer patients and reduce the incidence of different reactions during the treatment, which is worth generalization and application in clinical practice.

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## Disclosure of conflict of interest

None.

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