Am J Transl Res 2024;16(8):3614-3625
www.ajtr.org /ISSN:1943-8141/AJTR0157477

Original Article

Effects of TP regimen combined with intraperitoneal hyperthermic perfusion chemotherapy on immune function, quality of life and prognosis of patients with advanced ovarian cancer

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Received April 28, 2024; Accepted June 26, 2024; Epub August 15, 2024; Published August 30, 2024

Abstract: Objective: To evaluate the effect of paclitaxel and cisplatin (TP regimen) combined with intraperitoneal hyperthermic perfusion chemotherapy on immune function and quality of life in patients with advanced ovarian cancer. Methods: This retrospective study involved 107 patients with advanced ovarian cancer who were treated in Baoji Central Hospital between March 2016 and March 2020. The control group was treated with the TP regimen alone (n=48), while the observation group received additional intraperitoneal heat infusion chemotherapy containing 60 mg of cisplatin on the 8th day following the final chemotherapy (n=59). Immunoglobulin (IgG, IgA, IgM) levels, quality of life, tumor marker levels, incidence of adverse effects, and 3-year survival were compared between the two groups. Besides, factors affecting patients' prognosis were detected by unifactorial and multifactorial analyses. Results: Before treatment, there was no significant difference between the two groups in terms of IgG, IgA, and IgM levels (all P>0.05). After treatment, the observation group showed significantly higher levels of IgG, IgA, and IgM than those in the control group (all P<0.05). There were no significant differences in pre-treatment Kamofsky (KPS) score, carcinoembryonic antigen (CEA), and carbohydrate antigen 125 (CA125) between the two groups (all P>0.05). However, after treatment, the KPS score was significantly increased in the observation group as compared to pre-treatment or control group (both P<0.05), while CEA and CA125 significantly decreased in the observation group as compared to pre-treatment or control group (all P<0.05). Nevertheless, the incidence of gastrointestinal reactions in the observation group was higher than that in the control group (P<0.05). The survival rate of the observation group was significantly higher than that of the control group (P<0.05). The AUC of post-treatment IgG for predicting 3-year survival of patients was 0.743. The 3-year survival rate of patients with IgG≥10.950 g/L was significantly higher than that of patients with IgG<10.950 g/L (P<0.05). Multifactorial Cox regression analysis revealed that higher FIGO stage, presence of ascites, higher post-treatment IgG level, and higher post-treatment CEA and CA125 levels were independent risk factors for patients' 3-year mortality. Conclusion: TP regimen combined with intraperitoneal hyperthermic perfusion chemotherapy significantly improves immune function and quality of life in patients with advanced ovarian cancer, although it increases the incidence of gastrointestinal reactions. Higher FIGO stage, presence of ascites, higher IgG after treatment, higher CEA, and higher CA125 were independent risk factors for patients' 3-year mortality.

Keywords: TP regimen, intraperitoneal heat infusion chemotherapy, ovarian cancer, immune function, quality of life, prognosis

Introduction

Ovarian cancer, ranking the third most common gynecologic cancer following uterine and cervical cancers [1], poses a significant burden on global health. In 2020, it accounted for 3.7% of all cancer cases and 4.7% of all cancer-related deaths [2]. With approximately 314,000 new cases and 207,000 deaths reported annually worldwide, ovarian cancer stands as the deadliest gynecologic malignancy [3]. Although it accounts for only 2.5% of all malignant tumors in women, its lethality contributes to 5% of all cancer-related deaths [4]. The disease's insidi-

https://doi.org/10.62347/BFTN7014

ous progression and often symptom-free early stages frequently lead to late diagnoses, thereby diminishing survival rates and worsening prognoses [5, 6]. Early-stage ovarian cancer (stages I-II) has a five-year survival rate of up to 70%, but this figure drastically decreases to between 10-25% for stage III disease [7]. Epithelial ovarian cancer accounts for approximately 90% of all cases, making it the predominant type [8]. Ovarian cancer primarily affects middle-aged and elderly individuals, with the majority of patients being around 63 years old at the time of diagnosis [9].

In cases of advanced ovarian cancer, surgical treatment often falls short in its effectiveness due to widespread metastasis within the abdominal cavity [10, 11]. As a result, chemotherapy becomes the primary approach for extending patient survival. Platinum-based chemotherapy has demonstrated high sensitivity in the treatment of advanced ovarian cancer [12]. The most commonly utilized chemotherapy regimen is a combination of paclitaxel and cisplatin (TP), which effectively targets and kills cancer cells, ultimately improving patient prognosis [13]. Paclitaxel functions as a microtubule inhibitor, impeding cell division, while cisplatin damages tumor cell DNA and inhibits its growth [14]. Despite the application of TP chemotherapy, the prognosis for patients with advanced ovarian cancer remains unfavorable [15]. The TP regimen is associated with common side effects such as nausea, vomiting, myelosuppression, and neurotoxicity. Prolonged utilization of the TP regimen can also result in drug resistance, diminishing its therapeutic efficacy [16]. Therefore, developing strategies to enhance the effectiveness of chemotherapy for advanced ovarian cancer, while minimizing toxic side effects and prolonging patient survival is currently a critical challenge for the medical community.

Advanced ovarian cancer within the abdominal cavity also presents challenges for the conventional intravenous drug delivery method to effectively reach the tumor site, primarily due to the plasma-peritoneal barrier [17]. To overcome this limitation, a novel therapeutic approach, known as intraperitoneal thermal perfusion, has been developed, combining local chemotherapy and thermotherapy to enhance treatment efficacy. Intraperitoneal thermal perfusion offers several advantages. Firstly, it promotes local drug absorption, leading to increased drug concentration in the tumor site and improved drug sensitivity. Secondly, intraperitoneal thermal perfusion helps flush out detached tumor tissues from the abdominal cavity, reducing the risk of metastasis and local recurrence. By eliminating these residual tumor cells, the treatment can potentially improve long-term outcomes for patients [18, 19]. Overall, intraperitoneal thermal perfusion holds promise as an effective adjuvant treatment for ovarian cancer, addressing the challenges associated with drug delivery and providing potential benefits such as increased drug concentration at the tumor site and reduced risk of metastasis and local recurrence. Despite these advantages, there have been few studies on the impact of TP chemotherapy combined with hyperthermic intraperitoneal chemotherapy on the immune function and quality of life of patients with advanced ovarian cancer.

To fill in this gap, this study aims to investigate the clinical efficacy and safety of combining peritoneal hyperthermic perfusion chemotherapy based on a TP chemotherapy regimen in patients with advanced ovarian cancer, and to observe the changes in the patient's immune function and quality of life.

Materials and methods

Clinical data

We retrospectively analyzed the medical records of 107 patients with advanced ovarian cancer admitted to Baoji Central Hospital between March 2016 and March 2020. Of the included 107 patients, 48 patients who received the TP regimen alone were assigned into the control group, and the other 59 patients who were treated with the TP regimen combined with intraperitoneal hyperthermic perfusion chemotherapy were classified as the observation group. This study was approved by the Baoji Central Hospital Medical Ethics Committee.

Inclusion criteria: 1) patients with pathologically conformed diagnosis of ovarian cancer and at stage III-IV according to FIGO staging [20]; 2) patients who received satisfactory tumor cytoreduction with residual tumor foci of no more

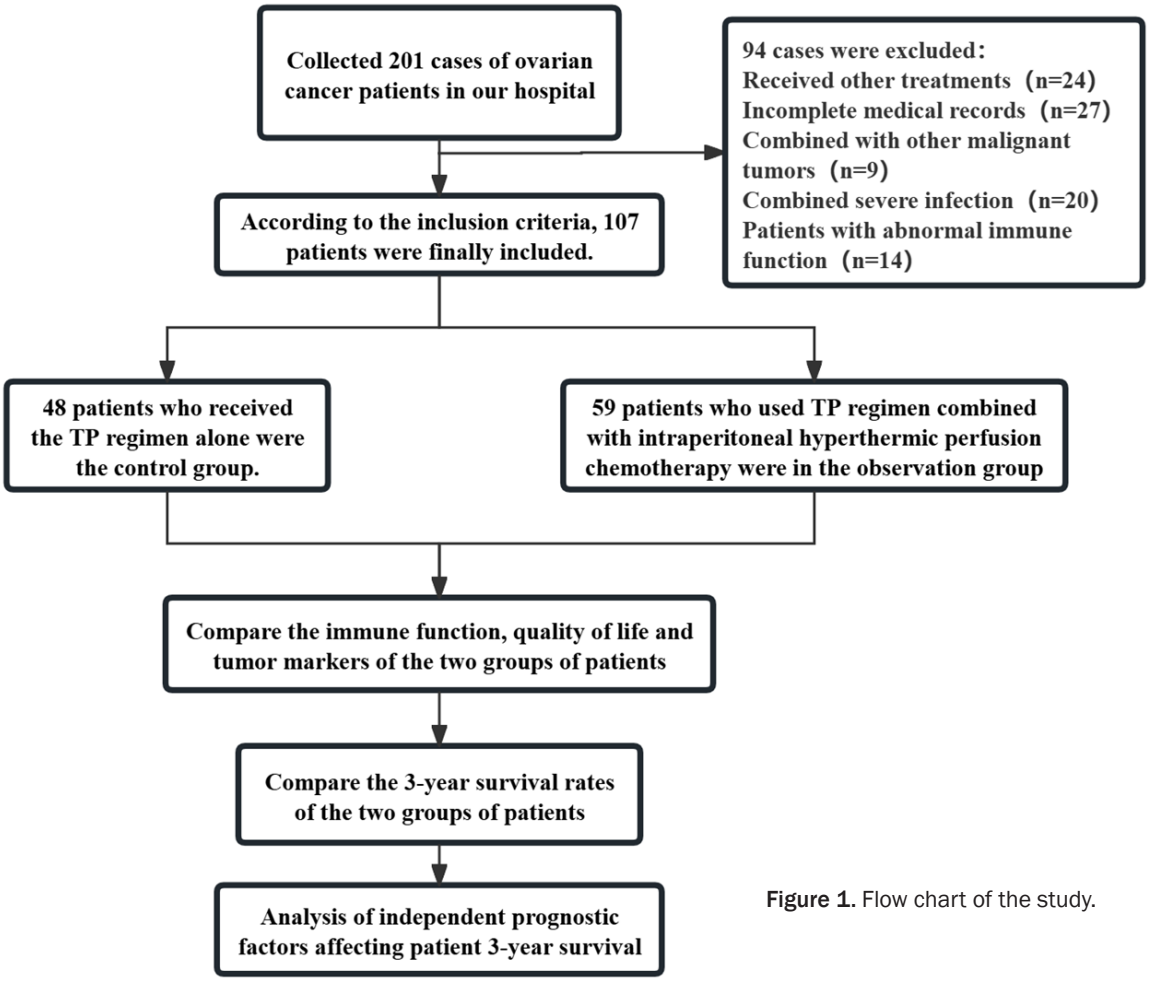

Figure 1. Flow chart of the study.

than 1 cm in size; and 3) patients with an age of 18 years or older. Exclusion criteria: 1) patients who had received any form of treatment other than the specified modalities; 2) patients with incomplete medical records; 3) patients with other malignant tumors; 4) patients with severe infections; and 5) patients with abnormal immune function such as autoimmune diseases or immunosuppressants. The flow of the study is shown in **Figure 1**.

Collection of information

The collected data encompassed demographic information, pathological data, pre- and post-treatment Karnofsky Performance Status (KPS) scores, adverse events during treatment, tumor marker levels before and after treatment, immune function indicators, and survival data. Demographic factors included age, weight, and menopausal status. Pathological data consisted of International Federation of Gynecology and Obstetrics (FIGO) staging, degree of tissue differentiation, pathological type, presence of ascites, and distant metastasis status. The FIGO stage was primarily determined based on clinical examination results, including gynecological, radiological, and histopathological assessments [21]. KPS score was used to evaluate the quality of life before and after treatment, with a maximum score of 100, where higher scores indicate better quality of life [22]. The incidence of adverse reactions among all patients was observed and analyzed, including gastrointestinal reactions, myelosuppression, hepatic insufficiency, and cardiac adverse reactions. The collected tumor markers include carcinoembryonic antigen (CEA) and carbohydrate antigen 125 (CA125). Immune function indicators encompassed immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM).

Chemotherapy and follow-up

After 3 weeks of postoperative recovery, patients in both groups commenced a TP chemotherapy regimen. This regimen included intravenous paclitaxel (150 mg/m^2) on day 1 and intravenous cisplatin (150 mg/m^2) on day 2, administered weekly over three consecutive weeks. Each patient underwent a total of six chemotherapy cycles, with one course every three weeks.

For the patients in the observation group, in addition to intravenous chemotherapy, additional combined abdominal heat infusion chemotherapy was performed on the 8th day following the last chemotherapy session. The procedure was performed by inserting 2 peritoneal puncture placements over a central venous catheter, with each in the left and right abdomen. In patients with the presence of ascites, efforts were made to eliminate the fluid accumulation as much as possible. The catheters were connected to a thermocycling perfusion machine with a circulating fluid volume of 3,000 to 5,000 mL and a dose of cisplatin of 60 mg. The circulating flow rate was set at 300 to 500 mL/min, and the duration of the hemoperfusion chemotherapy was 90 minutes. Courses were administered every 2 weeks for a total of 3 cycles.

Patients were followed up with regular pelvic exams after the initial procedure, including ultrasound, computed tomography, magnetic resonance imaging, or positron emission tomography, as well as evaluation of tumor markers. Patients were followed every 3 months for the first 2 years and every 6 months thereafter. Survival was counted for all patients up to 3 years after surgery.

Statistical methods

Statistical analysis was performed using R software (4.2.1) and SPSS 26.0. The count data were expressed as n (%), and compared using chi-square test. The measurement data conforming to a normal distribution were expressed as mean ± standard deviation and compared using independent t test between groups. The post-treatment levels of IgG, IgA, and IgM for predicting patient 3-year survival was examined using receiver operator characteristic (ROC) curves, and patients were categorized into high and low level groups according to the calculated optimal threshold. Patient's 3-year survival was statistically assessed by Kaplan-Meier (K-M) curves, and compared by log-rank tests. Survival data were analyzed in a multivariate setting based on Cox regression models. A *p*-value of <0.05 was considered statistically significant.

Results

Baseline characteristics of the study population

Comparison of the baseline characteristics showed that there was no significant differences between the two groups in terms of age, body weight, FIGO stage, degree of tissue differentiation, type of pathology, presence of ascites, menopause, and distant metastasis (all P>0.05), as shown in **Table 1**.

Comparison of immune function between the two groups

There was no statistical difference in terms of pre-treatment immune function indicators IgG (7.65±0.72 g/L VS 7.77±0.82 g/L), IgA (1.15±0.25 g/L VS 1.09±0.27 g/L), and IgM (1.20±0.11 g/L VS 1.23±0.12 g/L) between the two groups (all P>0.05). After treatment, the IgG, IgA, and IgM levels of the two groups of patients all increased, and the IgG (10.95±1.19 g/L), IgA (10.95±1.19 g/L), and IgM (10.95±1.19 g/L) levels of the observation group were significantly higher than those of the control group [IgG (10.95±1.19 g/L), IgA (10.95±1.19 g/L), IgM (10.95±1.19 g/L)] (all P<0.001), see **Figure 2**.

Comparison of quality of life and tumor marker levels between two groups before and after the treatment

Before treatment, there were no statistical differences in quality of life KPS score (58.90±3.97 g/L VS 57.80±4.49 g/L) and the tumor markers [CEA (58.90±3.97 g/L VS 57.80±4.49 g/L), CA125 (58.90±3.97 g/L VS 57.80±4.49 g/L)] between the two groups (all P>0.05). After treatment, the KPS scores of the two groups significantly increased, while the CEA and CA125 levels decreased; Besides, the KPS score of the observation group was significantly higher than that of the control group (71.30±4.91 g/L VS 64.24±4.54 g/L, P<0.05), and the CEA score (7.42±2.34 g/L VS

Table 1. Demographics and baseline characteristics

	Observation group (n=59)	Control group (n=48)	P
Age (years)	63.78±7.06	63.06±6.05	0.577
Weight (kg)	60.63±8.56	59.65±8.18	0.549
FIGO installments			0.804
Phase III	43 (72.88)	36 (75.00)	
Phase IV	16 (27.12)	12 (25.00)	
Degree of differentiation			0.806
High	49 (83.05)	42 (87.50)	
Medium	7 (11.86)	4 (8.33)	
Low	3 (5.08)	2 (4.17)	
Pathological type			0.731
Serous carcinoma	54 (91.53)	43 (89.58)	
Non-serous carcinoma	5 (8.47)	5 (10.42)	
Ascites			0.384
Yes	45 (76.27)	33 (68.75)	
No	14 (23.73)	15 (31.25)	
Menopause			0.683
Yes	50 (84.75)	42 (87.50)	
No	9 (15.25)	6 (12.50)	
Distant metastasis			0.941
Yes	25 (42.37)	20 (41.67)	
No	34 (57.63)	28 (58.33)	

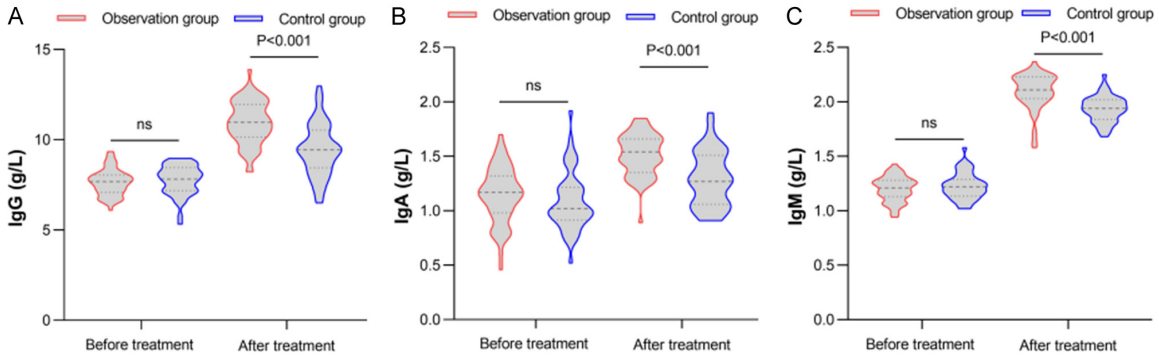

Figure 2. Comparison of immune function indicators between the two groups. A. Changes in IgG levels before and after treatment. B. Changes in IgA levels before and after treatment. C. Changes in IgM levels before and after treatment. IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M.

8.68±2.22 g/L) and CA125 (442.25±244.38 g/L VS 669.96±264.14 g/L) levels were significantly lower than those in the control group (all P<0.001) after the treatment, as shown in **Figure 3**.

Comparison of adverse reactions between the two groups

Comparison of the adverse reactions showed that there were no statistical differences in the incidence of bone marrow suppression, hepatic insufficiency, and cardiac adverse reactions (P>0.05) between the two groups; however, the incidence of gastrointestinal reactions in the observation group was significantly higher than that in the control group (P<0.05), as shown in **Table 2**.

Comparison of 3-year survival of patients between the two groups

Of the 59 patients in the observation group, 27 died in three years with a 3-year survival rate of 54.24%. Of the 48 patients in the control group, 33 died in three years, with a 3-year survival

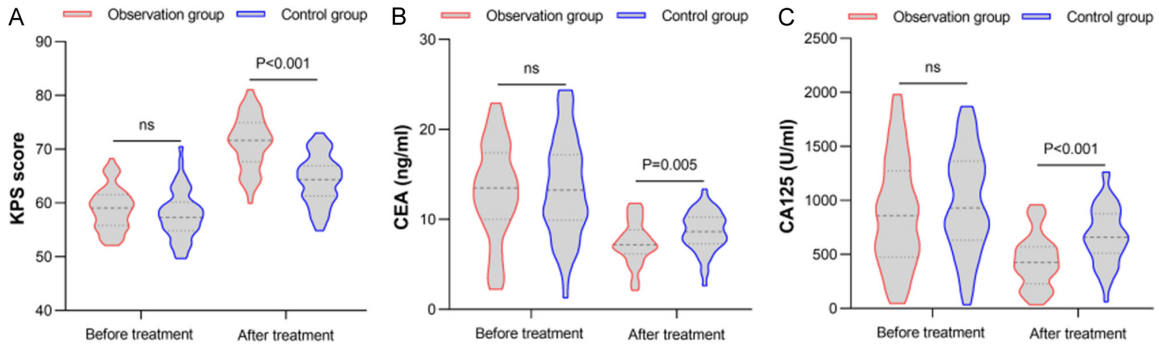

Figure 3. Comparison of quality of life and tumor marker levels between the two groups. A. Changes in KPS scores before and after treatment. B. Changes in CEA levels before and after treatment. C. Changes in CA125 levels before and after treatment. KPS: Karnofsky Performance Status; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125.

Table 2. Comparison of adverse reactions between the two groups

	Gastrointestinal reactions	Myelosuppression	Liver insufficiency	Adverse cardiac reaction
Observation group (n=59)	30 (50.85)	25 (42.37)	8 (13.56)	8 (13.56)
Control group (n=48)	15 (30.61)	13 (57.63)	6 (12.50)	4 (8.33)
P	0.034	0.100	0.872	0.394

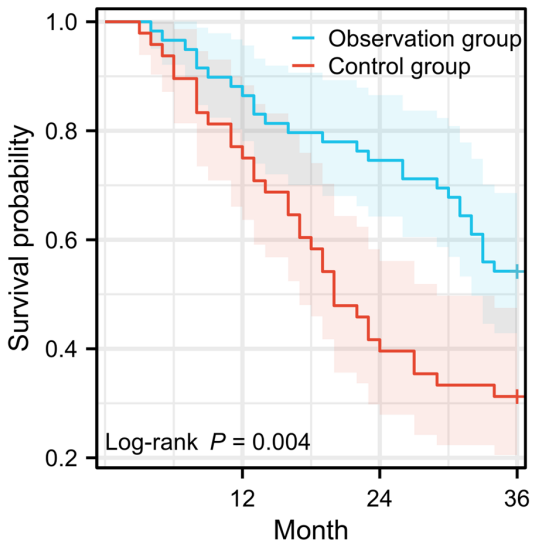

Figure 4. K-M curves for 3-year survival.

rate of 31.25%. The K-M curve analysis showed that the survival rate of the observation group was significantly higher than that of the control group (P<0.05), as shown in **Figure 4**.

Predictive performance of post-treatment immune function indicators for patient survival

The 3-year survival of patients predicted by IgG, IgA, and IgM was assessed using ROC curves, and it was found that the AUC of IgG was the highest at 0.743, which was higher than that of IgA and IgM (0.586 and 0.603), as shown in **Figure 5** and **Table 3**.

Relationship between immune function indicators and patient survival

Patients were stratified according to the cut-off values derived from ROC curve analysis as boundaries. The plotted K-M curve showed that the 3-year survival rate of patients with IgG≥10.950 g/L was significantly higher than that of patients with IgG<10.950 g/L (P<0.05), whereas there was no significant difference in 3-year survival rate between patients with high and low levels of IgA and IgM (all P>0.05), as shown in **Figure 6**.

Univariate analysis of variance

We grouped the 107 patients according to their 3-year survival condition into a survival group (n=47) and a death group (n=60), and performed univariate analysis. The results showed that there were statistical differences between the two groups in terms of FIGO stage, ascites, distant metastasis, post-treatment IgG, post-treatment KPS, post-treatment CEA and CA125 levels, and treatment regimen (all P<0.05), as shown in **Table 4**.

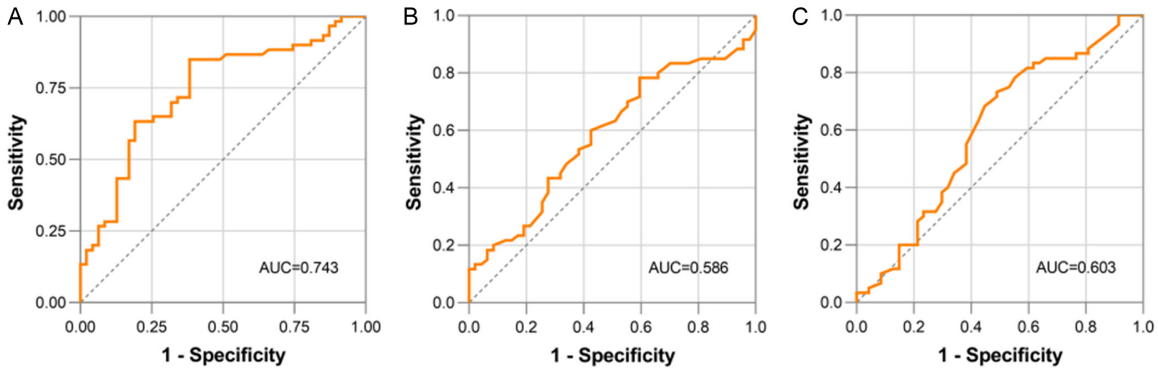

Figure 5. ROC curves of post-treatment IgG, IgA, and IgM for predicting patient survival. A. ROC curves of post-treatment IgG predicting patient 3-year survival. B. ROC curve of post-treatment IgA predicting patient 3-year survival. C. ROC curve of post-treatment IgM predicting patient 3-year survival. ROC: receiver operator characteristic; IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M.

Table 3. ROC curve data

Norm	AUC	95% CI	Cut-off value	Sensitivity	Specificity
IgG	0.743	0.647-0.840	<10.950	85.00%	61.70%
IgA	0.586	0.477-0.695	<1.565	78.33%	40.43%
IgM	0.603	0.491-0.714	<2.085	73.33%	51.06%

IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M.

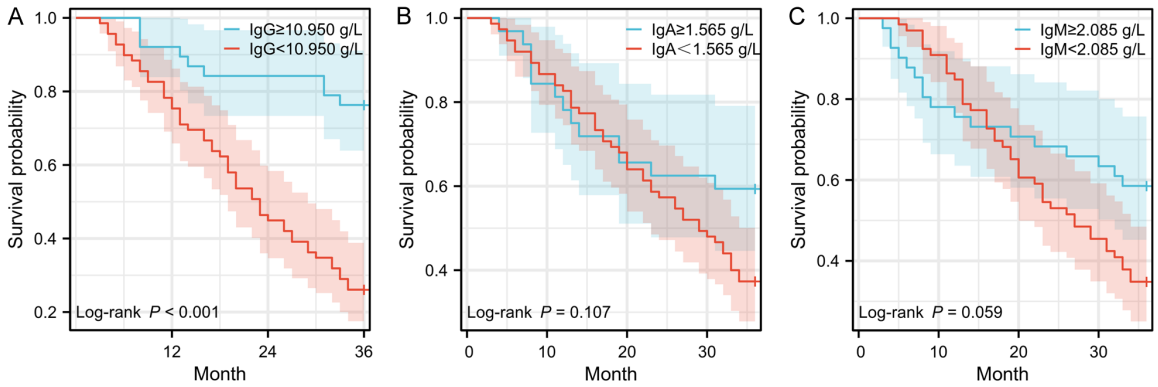

Figure 6. Relationship between immune function indicators and patient survival. A. 3-year survival K-M curves of patients with different levels of IgG after treatment. B. 3-year survival K-M curves of patients with different levels of IgA after treatment. C. 3-year survival K-M curves of patients with different levels of IgM after treatment. K-M: Kaplan-Meier; IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M.

Multifactorial analysis of variance

By multifactorial COX regression analysis, it was found that higher FIGO stage (P=0.001, OR=3.519), presence of ascites (P=0.016, OR=2.359), higher post-treatment IgG (P=0.017, OR=0.783), higher CEA (P=0.032, OR=1.148), and higher CA125 (P=0.001, OR=1.003) were independent risk factors for death 3-years post-treatment, as shown in **Table 5**.

Discussion

The primary objective in treating advanced ovarian cancer is to improve the survival rate and quality of life for patients [23]. Intraperitoneal hyperthermic perfusion chemotherapy provides a distinct advantage over intravenous chemotherapy by directly targeting the tumor site [24-26]. Some studies have also reported positive effects of peritoneal heat per-

Table 4. Single factor analysis

	Survival group (n=47)	Death group (n=60)	P
Age (years)	62.74±6.60	64.02±6.61	0.322
Weight (kg)	60.60±8.79	59.86±8.07	0.652
FIGO stage			0.005
III	41 (87.23)	38 (63.33)	
IV	6 (12.77)	22 (36.67)	
Degree of differentiation			0.544
High	41 (87.23)	50 (83.33)	
Medium	5 (10.64)	6 (10.00)	
Low	1 (2.13)	4 (6.67)	
Pathological type			0.282
Serous carcinoma	41 (87.23)	56 (93.33)	
Non-serous carcinoma	6 (12.77)	4 (6.67)	
Ascites			0.021
Yes	29 (61.70)	49 (81.67)	
No	18 (38.30)	11 (18.33)	
Menopause			0.429
Yes	39 (82.98)	53 (88.33)	
No	8 (17.02)	7 (11.67)	
Distant metastasis			0.008
Yes	13 (27.66)	32 (53.33)	
No	34 (72.34)	28 (46.67)	
Post-treatment IgG (g/L)	10.97±1.29	9.73±1.45	<0.001
Post-treatment IgA (g/L)	1.46±0.21	1.38±0.26	0.089
Post-treatment IgM (g/L)	2.05±0.18	2.00±0.16	0.132
Post-treatment KPS	69.80±6.49	66.84±5.08	0.009
Post-treatment CEA (ng/ml)	7.16±2.58	8.63±1.96	0.001
Post-treatment CA125 (U/ml)	399.11±217.29	658.21±265.99	<0.001
Treatment plan			0.017
TP alone	15 (31.91)	33 (55.00)	
Combination therapy	32 (68.09)	27 (45.00)	

FIGO: International Federation of Gynecology and Obstetrics; IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M; KPS: Karnofsky Performance Status; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125.

Table 5. Multifactor analysis

Variable	β	Std Error	P	OR Value	95% Lower	95% Upper
FIGO stage	1.258	0.332	0.001	3.519	1.837	6.740
Ascites	0.858	0.357	0.016	2.359	1.172	4.749
Distant metastasis	0.314	0.302	0.298	1.369	0.758	2.472
Post-treatment IgG	-0.244	0.102	0.017	0.783	0.641	0.957
Post-treatment KPS	-0.05	0.027	0.068	0.951	0.902	1.004
Post-treatment CEA	0.138	0.065	0.032	1.148	1.012	1.303
Post-treatment CA125	0.003	0.001	0.001	1.003	1.001	1.004
Treatment plan	-0.424	0.381	0.266	0.655	0.310	1.381

FIGO: International Federation of Gynecology and Obstetrics; IgG: immunoglobulin G; IgA: immunoglobulin A; IgM: immunoglobulin M; KPS: Karnofsky Performance Status; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125.

fusion chemotherapy in patients with significant amounts of ascites and pleural fluid, as well as those with both platinum-resistant and platinum-sensitive ovarian cancer [27].

Chemotherapeutic drugs target not only tumor cells but also have a greater toxic effect on normal cells, including immune cells such as leukocytes and T-cells, leading to impaired immune function [28]. Therefore, it is crucial to find ways to enhance immune function and reduce the adverse effects of chemotherapy to optimize the overall antitumor treatment regimen. Immunoglobulins, including IgG, IgA, and IgM, are indicators of humoral immune function. Chemotherapy can disrupt immune function, as indicated by changes in these immune factors [29]. In this study, after receiving a combination of TP chemotherapy and intraperitoneal hyperthermic perfusion chemotherapy, the immune function markers IgG, IgA, and IgM significantly increased compared to patients treated with TP chemotherapy alone. This suggests that the combined treatment approach can more effectively improve patients' immune function. One possible explanation for this improvement is that intraperitoneal heat infusion chemotherapy increases the concentration of drugs in the abdominal cavity, enhancing their killing effect on intraperitoneal tumors while reducing the inhibitory effect on the systemic immune system. This may help protect the patient's immune function, resulting in increased levels of IgG, IgA, and IgM. Overall, the combination of TP chemotherapy and intraperitoneal hyperthermic perfusion chemotherapy appears to have a positive impact on immune function.

In this study, it was observed that patients in the observation group demonstrated more substantial decrease in CEA and CA125 levels and increase in KPS scores as compared to the control group after treatment, indicating enhanced quality of life and more effective tumor suppression. Regarding post-treatment adverse reactions, it was found that the incidence of gastrointestinal reactions in the observation group was significantly higher than that in the control group. This could be attributed to the higher drug concentration in the local area and the impact of elevated temperature, which can stimulate the gastrointestinal mucosa, leading to gastrointestinal discomfort. Xu et al. [30] compared the safety of TP chemotherapy alone with TP combined with hyperthermic intraperitoneal chemotherapy for advanced ovarian cancer and showed that there was no statistical difference in gastrointestinal reactions between the two groups of patients. This outcome was attributed to the high incidence of gastrointestinal reactions - exceeding 80% in both groups - which was likely influenced by adverse effects stemming from cytoreductive surgery, thus masking any potential differences attributable solely to chemotherapy regimens.

Chemotherapy techniques involving the direct administration of chemotherapeutic agents into the peritoneal cavity have become increasingly popular for postoperative maintenance treatment in patients with advanced ovarian cancer, particularly those with peritoneal metastases. This approach enables targeted treatment by allowing the chemotherapeutic agents to directly interact with the tumor. The efficacy of this method has shown promising results. In our study, we observed a significantly higher 3-year survival rate among patients who underwent combined intraperitoneal hyperthermic perfusion chemotherapy compared to those treated with TP chemotherapy alone, as evidenced by the K-M survival curves. Ba et al. also demonstrated the effectiveness of cytoreduction combined with TP chemotherapy in controlling ascites, even in patients with suboptimal cytoreduction outcomes [31].

We constructed ROC curves to explore the predictive performance of IgG, IgA, and IgM for the 3-year survival of patients. The findings revealed that IgG exhibited a stronger predictive value for patients' 3-year survival post-treatment, with an AUC of 0.743, surpassing those of IgA (0.586) and IgM (0.603). Furthermore, we conducted additional analysis by generating Kaplan-Meier survival curves to compare the 3-year survival rates between patients with high and low IgG, IgA, and IgM. The results demonstrated that patients with high IgG level experienced significantly higher survival rates than those with low IgG level; however, the survival rates in patients with high and low levels of IgA and IgM didn't show distinct differences.

Finally, to determine the independent factors influencing patients' 3-year mortality, further analyses using unifactorial and multifactorial Cox regression were conducted. The results indicated that higher FIGO stage, presence of ascites, elevated post-treatment IgG levels, higher CEA and CA125 levels were identified as independent risk factors for 3-year mortality of patients with advance ovarian cancer. These

findings align with the study conducted by Li et al. [32], where they also highlighted that CA125 levels and FIGO stage were independent prognostic factors for complex epithelial tumors of the ovary. Additionally, Li et al. found no association between radiotherapy and prognosis in patients with carcinoma of unknown primary origin, suggesting that surgery may be more beneficial for patients with ovarian epithelial tumor. Similarly, Ayhan et al. [33] conducted a study that emphasized the presence of ascites as an independent risk factor for poor prognosis in patients with recurrent ovarian cancer who underwent tumor cytoreduction plus peritoneal hyperthermic perfusion chemotherapy. Furthermore, our study did not identify the treatment regimen as an independent factor affecting the three-year survival of patients. This may be due to the fact that all patients included in this study underwent satisfactory cytoreductive surgery prior to chemotherapy, leaving residual tumor nodules no larger than 1 cm. This suggests that the similar tumor burden at baseline potentially diminished the independent impact of the treatment modality on prognosis. The residual tumor burden after surgery is itself a powerful prognostic factor, rendering the additional benefits of intraperitoneal hyperthermic perfusion chemotherapy less significant [34]. The study by Dang et al. also conducted a COX analysis on the 3-year mortality of patients with ovarian cancer, but its multivariate analysis results showed that the KPS score was the only indicator significantly related to prognosis. This discrepancy may be due to differences in the sample inclusion criteria or other study-specific factors [35].

The innovation of this study lies in its novel approach to explore the prognosis of patients with TP chemotherapy combined with intraperitoneal hyperthermic perfusion, particularly in assessing how postoperative immune function indicators might influence patient outcomes. However, due to the retrospective nature, it relies on data extracted from existing medical records, and therefore not all contributing factors were available. In addition, it was challenging to account for all other treatment regimens that patients might have received during the postoperative follow-up period, potentially skewing the results. Finally, this study has not yet explored in depth the specific mechanism by which the treatment regimen affect biomarkers such as IgG, IgA, IgM, CEA, and CA125. Future studies will include a detailed analysis of the factors affecting these key indicators in order to reveal their potential mechanisms of action.

In conclusion, TP regimen combined with peritoneal hyperthermic perfusion chemotherapy significantly improves immune function and quality of life in patients with advanced ovarian cancer, despite the elevated incidence of gastrointestinal reactions. Higher FIGO stage, presence of ascites, higher post-treatment IgG level, and higher post-treatment CEA and CA125 levels were independent risk factors for patients' 3-year mortality.

Disclosure of conflict of interest

None.

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