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Research Article

Assessment of Prognostic Factors in Epithelial Ovarian Cancer

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Abstract

Objectives: Ovarian cancer is the second most common gynecological cancer, and has a 5-year survival rate of about 40% to 45%. This ratio ranges from 15% to 95%, based on prognostic factors. There are numerous clinical, pathological and biological factors related to prognosis. The aim of this study was to assess prognostic factors in advanced epithelial ovarian cancer.

Methods: A total of 119 stage III and stage IV ovarian cancer patients were evaluated. The patient's age, menopausal status, age of menarche, number of children, height and weight values, surgery, tumor histopathological features, presence of metastasis, residual tumor volume, presence of ascites, abdominal lavage cytology, chemotherapy regimen, number of chemotherapy cycles, the first and last chemotherapy dates, relapse, and recent status were evaluated.

Results: The median age of the study patients was 54 years (minimum: 34, maximum: 79 years). The pathological stages were 10 (8.6%) patients with IIIA, 6 (5%) patients with IIIB, 76 (63.9%) patients with IIIC, and 27 (22.7%) patients with stage IV. In multivariate analysis, age of diagnosis (hazard ratio [HR]: 0.44; 95% confidence interval [CI], 0.22-087; p=0.01), postoperative tumor residual status (HR: 0.32; 95% CI, 0.14-0.71; p<0.01), number of adjuvant chemotherapies (HR: 0.48; 95% CI, 0.23-0.98; p=0.04), and platinum sensitivity (HR: 0.37; 95% CI, 0.18-0.74; p<0.01) were found to be independent variables related to longer survival. Notably, a patient treated with more than 6 cycles of chemotherapy had a worse prognosis.

Conclusion: Independent indicators of a poor prognosis in our study were determined to be advanced age at diagnosis, a residual tumor more than 2 cm in size, more than 6 cycles of chemotherapy, and the presence of platinum-resistant disease. A multidisciplinary approach is needed to improve prognosis.

Keywords: Chemotherapy, mortality, ovarian cancer, prognosis, residual tumor

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Ovarian cancers constitute 4% of female cancers. Ovarian cancer is the second most common gynecological cancer.[1] About 95% of the ovarian malignancies are epithelial tumors. Serous ovarian cancer is the most common epithelial ovarian cancers. Its treatment modalities include surgery, adjuvant chemotherapy, and supportive therapy. It has a rather poor course of prognosis. 5-year survival rate of ovarian cancer is about 40–45%. This ratio ranges from 15% to 95% based on various factors affecting prognosis.[2–7]

There are numerous clinical, pathological and biological prognostic factors. Clinical factors affecting prognosis include age, performance status, menarche age, menopausal status, and parity; pathologic factors include stage, pathologic grade, cytologic findings, the presence of ascites and residual disease after surgery and biological factors comprise various gene expressions. Furthermore, the che-

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motherapy periods, combination and dosages are factors which affect prognosis.[8–12]

The 5-year survival for ovarian cancer is 40% in patients under the age of 50 years while it is around 15% in elderly patients. 40%, 20%, and 5–10% survival is observed in grade 1, grade 2 and grade 3 diseases respectively. 5-year survival is 40–75%, 30–40% and 5% in microscopic residual diseases, optimal cytoreduction, and suboptimal cytoreduction respectively.

The factors affecting the prognosis of the disease in advanced epithelial ovarian cancer patients who applied between 1998 and 2013 to Medical Oncology Department of Trakya University's Medical Faculty were examined in our study.

Materials and Methods

Patient Selection

All epithelial ovarian cancer patients who admitted to medical oncology outpatient clinic of Trakya University's Medical faculties between 1998 and 2013 were included in this retrospective study. Data included in files of 119 stage III and stage IV ovarian cancer patients were incorporated into the study. Approval of Ethics Committee of Trakya University's Medical Faculty was received prior to the study.

The patient's age, menopausal status, age of menarche age, number of children, height and weight values, surgery, tumor histolopathological features and presence of metastasis, residual tumor volume, ascite, abdominal lavage cytology, chemotherapy regimen, number of chemotherapy cycles, the first and last chemotherapy dates, relapse and recent status of patients were evaluated. The relapse location and date, disease-free and overall survival of patients were obtained from tha patient file.

The tumor residue was divided into 3 groups as no residual tumor, less than 2 cm and 2 or more than 2 cm. Patients were also divided into three groups in terms of operation, as complete cytoreduction, optimal cytoreduction and suboptimal cytoreduction. Optimal cytoreduction and suboptimal cytoreduction distinction were determined with a limit of 1 cm.

The time between the first pathological diagnosis and the first relapse defined as disease-free survival (DFS) while the time between the first diagnosis and the date of death defined as overall survival (OS) time. Follow-up times were determined by considering the time between the first diagnosis date and the last control or death date.

Statistical Analysis

Univariate and multivariate analyses were carried out. Comparisons of parametric variables between groups were conducted by independent t test. Nonparametric variables were evaluated by Chi-square test. Kaplan Meier method was employed in order to obtain survival curves with general survival and disease free survival analyses. Comparisons of survival curves were performed by virtue of the Long-rank test. Prognostic factors with a p-value less than 0.15 were also taken to multivariate analysis through the long-rank test. Multivariate analysis was performed by Cox-regression test. The confidence interval was accepted as 95% and p value was accepted as <0.05 for statistical significance. All data were analyzed with SPSS 16.0 package program by coding.

Table 1. Demographic characteristics of study subjects

	Median±SD	Minimum–maximum
Age at diagnosis	54±10.8	34–79
The age of menarche	13.2±1.1	11–17
Number of births	3±1.7	0–10
Age at the first birth	21±2.5	16–31
The age of menopause	49±4.6	32–57

SD: Standart deviation.

Results

Clinical Demographic and Pathologic Features

The clinical features of the patients are provided in Table 1. Twenty-three (19.3%) patients had right sided ovarian tumors, 22 (18.5%) had left sided tumors and 74 (62.2%) patients had a bilateral tumor. 10 (8.4%), 6 (5%), 76 (63.9%) and 27 (22.7%) patients were found to had stage 3A, stage 3B stage 3C and stage 4 disease at diagnosis 113 (95%), 4 (3.4%) and 2 (1.6%) patients included in the study were diagnosed with surgery, biopsy and clinically and radiologically, respectively. Fourty-four (37%), 37 (31.1%) and 32 (26.9%) of the patients who were diagnosed with surgery were complete, optimal and suboptimal cytoreduced, respectively. Average of tumor diameters were 8±5.7 cm (mean±SD).

Lymph node dissection was performed in 74 of 119 patients. The number of lymph nodes removed were 20±23.4 (mean±SD) (min=0–max=103). There was an average of 2.01±5.6 (mean±SD) (min=0–max=45) tumor positive lymph nodes in the removed lymph nodes. In the group from which lymph node was removed, 41 (55.4%) patients were positive in terms of lymph node while 33 (44.6%) patients were negative in terms of a lymph node. 12 (29.2%) patients in the group with positive lymph node were observed to have lymph node positivity of 5 and more while 29 (70.8%) patients were observed to have lymph node positivity less than 5 (Data are shown in supplementary material).

Forty (33.6%) patients undergone surgery had residual tumor less than <2 cm while 18 (15.1%) of them had residual tumor equal or more than 2 cm. 54 (45.4%) patients did not have any detectable residual tumors. 56 (47.1%) patients had metastases while 63 (52.9%) patients were not metastatic. 10 (8.4%), 27 (22.8%) and 13 (10.9%) of metastatic patients had liver metastases, peritoneal and diffuse metastases respectively while 6 (5%) of them had metastases distant to other regions. 84 (70.6%) patients had ascite at diagnosis and 35 (29.4%) patients did not have ascite at diagnosis (Data are shown in supplementary material).

It was observed when pathology results were examined, that 96 (80.7%) patients had serous papillary adenocarcinoma and 21 (17.6%) patients had other types of epithelial ovarian cancer and 2 (1.7%) patients had no pathological diagnosis. While malignant cells were detected in abdominal lavage fluid of 84 (70.6%) patients, malignant cells were negative in 27 (22.7%) patients. Abdominal lavage fluid examination had not be done in 8 (6.7%) patients.

Factors Related to Relapse

A relapse rate (p=0.017) was significantly higher in patients diagnosed at the age of 60 and over. Menopausal age was divided into two groups as 46 years and over and under 46 years. Menopausal patients aged 46 years and over were found to have significantly more relapses compared to menopausal patients aged under 46 years (p=0.022). Patients with a first delivery age of 20 years or younger had significantly more relapses (p=0.023). Patients having metastases at the time of diagnosis and those who have ascites prior surgery had statistically significant more relapses (p<0.001, p=0.006) (Data are shown in supplementary material).

Patients without postoperative tumor residuals and patients below 2 cm had significantly less relapse (p=0.011) than patients with tumor residuals bigger than 2 cm. Completely cytoreduced patients were less likely to recur (p=0.011) compared to patients with suboptimally or optimally cytoreduced patients. Stage 3 and stage 4 patients were compared in terms of relapse in our study. Stage 4 patients were more likely to recur compared to stage 3 patients (p=0.007).

Patients received adjuvant 4–6 cycles chemotherapy had statistically significantly less relapse compared to patients received more than 6 cycles (p=0.034).

The demographic characteristics in relation with the other relapse are summarized in Table 2. There were no significant differences between the two groups in terms of other demographic features.

Table 2. Demographic characteristics of patients with recurrence

	Recurrence (+) n=84		Recurrence (-) n=35		p
	n	%	n	%	
Age at diagnosis					
<60	47	56	21	84	0.017*
≥60	37	44	4	16	
Number of births					
0	9	10.7	3	12	1.000*
≥1	75	89.3	22	88	
The age of menarche					
≤13	55	65.5	17	68	1.000*
>13	29	34.5	8	32	
Age at the first birth					
≤20	46	54.8	7	28	0.023*
>20	38	45.2	18	72	
Menopause					
Present	63	75	13	52	0.046*
Absent	21	25	12	48	
The age of menopause					
<46	31	36.9	16	64	0.022*
≥46	53	63.1	9	36	
Body mass index					
<25	36	42.9	14	56	0.263*
≥25	48	57.1	11	44	

*Chi-square; n: count.

Factors Related to Survival

Median DFS, in the patient having menopause prior to the age of 46 years was 23 months (CI 95%=18.27–29.69) and in the patient having menopause after the age of 46 years was 17 months (CI 95%=15.14–18.04). There was a significant difference between the two groups in terms of disease-free survival (p=0.042). Patients having menopause younger had a DFS of up to 7 months more compared with patients having menopause at a later age. There was no significant difference in disease-free survival in other demographic features (p>0.05) (Data are shown in supplementary material).

When the clinical factors in terms of disease-free survival were examined, median DFS was 16 months (CI 95%=12.72–18.42) in patients with metastatic disease at the time of diagnosis and median DFS was 25 months (CI 95%=14.52–35.80) (p<0.001) in patients without metastatic disease at the time of diagnosis. Median DFS was 17 months (CI 95%=14.88–18.68) in the ascite-positive group and the median DFS was 36 months (CI 95%=15.56–56.97) in the ascite-negative group in terms of ascite status prior to operation (Data are shown in supplementary material).

Median DFS in the patients who underwent complete surgery was 27 months (CI 95%=10.87–43.53) while median disease-free survival was 17 months (CI 95%=12.95–20.61) in suboptimally or optimally cytoreduced patients (P=0,006). In advanced disease patients, median disease-free survival was 42 months (CI 95%=6.55–78.27), 16 months (CI 95%=15:30 to 17:28), 23 months (CI 95%=15.65–30.40) and 14 months (CI 95%=11.47–15.92 in stage 3A, 3B, 3C and 4 patients respectively (p=0.003). 5-year survival rate was found to be 74%, 47%, 51% and 32% in stage 3A, 3B, 3C and 4 patient groups, respectively.

Median DFS was 23 months (CI 95%=17.35–28.70) in patients receiving 4 to 6 cycles adjuvant chemotherapy, while median DFS was 15 months (CI 95%=12.48–15.92) in patients receiving adjuvant chemotherapy more than 6 cycles (P=0.008) (Data are shown in supplementary material).

A significant result could not be achieved although malignant cell-negative patients in the abdominal lavage fluid had significant longer disease-free survival compared to malignant cell-positive patients. In addition, the patients with unilateral tumors had no significant difference compared to patients with bilateral tumors in terms of disease-free survival.

It was observed that OS was significantly longer (p=0.47) in patients diagnosed before age of 60 compared to patients diagnosed after the age of 60 and over. Median OS was 54 months (CI 95%=38.31–68.92) in the non-metastatic patients at the time of diagnosis, while median OS was 34 months (CI 95%=26.78–68.92–41.09) in the metastatic patients (P=0.001). There was a significant difference between the two groups in terms of overall survival. Median overall survival was 75 months (CI 95%=17.09–82.32), 47 months (CI 95%=32.58–61.90), 52 months (CI 95%=36.38–66.78) and 32 months (CI 95%=25.02–39.50) in stage 3A, 3B, 3C and 4 patient groups, respectively (p<0.001) (Data are shown in supplementary material).

Median OS of patients with residual tumor less than 2 cm subsequent to the operation was 47 months (CI 95%=40.48–53.02), while median OS of patients with residual tumor over 2 cm was 32 months (CI 95%=27.40–37.12; p=0, 011). Median OS was 45 months (CI 95%=34.38–56.35) in patients receiving 4 to 6 adjuvant chemotherapies while median overall survival was 38 months (CI%=30.78–44.91) in patients receiving adjuvant chemotherapy more than 6 cycles (p=0.046). No significant difference was detected between overall survival, and tumor location and cytoreduction status. Patients diagnosed under 60 years of age were observed to die significantly less compared to patients over 60 (p=0.001). Patients who gave their first birth over 20 years attained a statistically significantly lower death (p=0.001). Patients who did not have menopause at the time of diagnosis were found to have survived significantly longer compared to the menopausal patients at the time of diagnosis (p=0.015). Patients diagnosed with metastasis at the time of diagnosis had significantly higher survival rates compared to patients without metastasis at the time of diagnosis (p=0.042). The patients who had ascites prior to the operation had significant higher death ratio compared to patients without ascites (p=0.042). Patients without tumor residue after surgery were found to lose their lives less in a statistically significant manner compared to patients with tumor residues over and below 2 cm (p=0.001). In addition, patients whose ECOG performance score of 0–1 lost their lives less in a significant manner compared to the other group (p=0.003). As expected, the patients with stage 4 were observed to have lost their lives more, but no statistically significant relation was observed between the stages of the patients and their death status (Data are shown in supplementary material).

Multivariate Analysis Results

Factors related to overall survival such as the age of diagnosis with the p value below 0.15, tumor residue after surgery, a number of adjuvant chemotherapy cycles, platinum sensitivity, disease stage, preoperative ascites status, tumor location were subjected to uni-and multivariate analysis.

As a result of the multivariate analysis, age of diagnosis (HR=0.44, CI 95%=0.22 to 087, p=0.01), postoperative tumor residual status (H R=0.32, CI% 95%=0.14–0.71, p<0.01), number of adjuvant chemotherapies (HR=0.48, CI 95%=0.23–0.98, p=0,04) and platinum sensitivity (HR=0.37, CI 95%=0.18–0.74, p<0.01) were found as independent variables related to longer survival. P values of overall survival factors according to univariate and multivariate analysis were compared in Table 3.

Discussion

The major prognostic factors related to ovarian cancer are younger age, low volume of residual disease, good performance status, and serous histology. Our study revealed that older age, advanced stage, residual tumor more than 2 cm, and the presence of platinum-resistant disease were associated with worse prognosis. In addition, patient who treated with more than six cycles of chemotherapy also had worse prognosis.

Some studies have suggested that patients with advanced stage have worse prognosis.[13–15] Satoshi et al. revealed that advanced stage ovarian cancer patients were classified as stage 3A, stage 3B, stage 3C and stage 4, and the 5-year survival rates were found to be 79%, 9%, 46% and 31%, re-

Table 3. Univariate and multivariate prognostic factors related to overall survival (p value)

The prognostic factors, p<0.15	Univariate analysis p	Multivariate analysis p
Age at diagnosis	0.047	0.009
<60		
≥60		
Tumor residual status (cm)	0.101	0.000
<2		
>2		
Absent		
Adjuvan chemotherapy cycles	0.056	0.046
≤6		
>6		
Platinum sensitivity	0.056	0.000
Stages	<0.001	0.444
3A		
3B		
3C		
4		
Ascite prior to surgery	0.098	0.828
Present		
Absent		
Tumor location	0.056	0.603
Unilateral		
Bilateral		
Metastasis status at diagnosis	0.001	0.548
Present		
Absent		

spectively. As the stage progresses, the 5-year survival decreases.[16] We found that as the disease stage progressed, the survival time was shorter and the relapse rate was higher as well. On the other hand overall survival in stage 3 patients had different results; stage 3A patients have shorter survival time compared to stage 3B and 3C patients and stage 3B patients have shorter survival time compared to stage 3C patients.

Tumor grade is also an important prognostic factor in ovarian cancers. Although the importance of tumor grade was related to prognosis in early stage of epithelial ovarian cancers, it was not associated with prognosis in advanced stages of them. Furthermore, response to induction chemotherapy in patients with advanced disease was found to be independent of tumor grade in terms of prognosis.[17, 18] Although significant results have been obtained in numerous studies in patients with advanced disease in univariate analyses, tumor grade prognostic has not been shown as factor in multivariate analysis.[13, 14] Although disease grade was seen as an important prognostic factor clinically on survival, there were not any significant association between grade and relapse and survival in our study (Data are shown in supplementary material).

The main purpose of the surgery in advanced stage is to ensure optimal cytoreduction via removing the primary and all metastatic tumor and decreasing the total tumor load under 1 cm.The more the tumor load is decreased, the greater it provides benefit to the patient's survival. The success of optimal cytoreductive surgery has been shown in numerous studies and maximal effort is spent for the optimal cytoreduction in recent years.[19, 20] As a result of our study, patients who underwent optimal cytoreduction in patients with advanced stage epithelial ovarian cancer relapsed significantly late and had longer survival in both multivariate and univariate analyses as reported in the literature. Survival rates might be increased by targeting optimal cytoreduction with the introduction of new technologies.

It has been revealed that the prognosis of ovarian cancer is better in younger patients. It is important to mention that factors such as diagnosis of younger patients at an earlier stage, acting more radical surgery and completion of chemotherapy in the optimal dose of may be effective on these results. One-year surveillance rate was found as 95.6% in ovarian cancer patients between the ages of 15 and 39 between 2003 and 2009, and this rate decreased to 34.6% in ovarian cancer patients over the age of 85 in a study carried out in the UK. 5-year surveillance rate was 84.2% in ovarian cancer patients between the ages of 15 and 39 while it was 13.7% in ovarian cancer patients over the age of 85 in the same study.[21] Bailey et al. divided the diagnosis age of patients is less than 60, between 60 and 74 and over 75 in their study. The results of the study revealed the fact that patients diagnosed under the age of 60 have longer survival rates compared to other groups.[22] We observed in our study that women over 60 had an increased risk of relapse and death compared to women younger than 60 years of age. The worse prognosis of elderly patients can be explained by differences in tumor biology and immune response and additional comorbid diseases. However, indecision while deciding more aggressive treatments especially for salvage treatment, may contribute to these differences experienced in elderly patients.[23]

There was not a certain agreement in previous studies about the prognostic significance of the histologic type of ovarian cancer. Some studies have suggested that serous tumors have a better course while other studies have suggested that mucinous tumors have a better course.[24–26] Satoshi et al. reported that epithelial ovarian cancer patients were examined in terms of 5-year survival rate and it was

observed that 5-year survival rate of patients with clear cell carcinoma was shorter in a significant association compared to other histologic types.[16] In another study, Tracey et al. suggested that endometrioid and none epithelial tumors were associated with better survival compared to serous tumors.[27] In our study, we divided tumor histology into two groups as serious and other. We could not find any significance association between tumor histology and prognosis in both the univariate and multivariate analyses. This finding is consistent with many other studies in the literature (Data are shown in supplementary material).

Ascites can be observed in approximately 17% of early stage ovarian cancer patients have ascites, this ratio increases to 90% in patients with advanced disease.[28] Although the prognostic relationship between ovarian cancer and ascites has been investigated in various studies. The ascites status have been evaluated in many studies. The cytological findings should also be evaluated to determine ascite feature. Puls et al. have found that patients without ascite had higher 5-year survival rate compared to patients with ascite.[29] In some of the studies, they found the presence of ascite significant in ovarian cancer in the univariate analysis but they could not detect significance in multivariate analysis.[14, 30] Kosary et al. revealed that patients with negative ascite cytology had higher 5-year survival rate compared to patients with positive cytology.[13] Ayhan et al. showed determined that the ratio of malignant ascite in advanced stage patients (stage III–IV) was significantly higher compared this in early stage patients, but presence of malignant ascite with different tumor grades showed no statistical difference.[31] Although we could not find significant results between presence and absence of ascites in bothe univariate and multivariate analyses. We suggested that patients with ascites had shorter survival. Furthermore, we revealed that patients with epithelial ovarian cancer who had significant ascite recurred more frequently compared to the patient who did not have ascite.

There are some studies about patient performance. It is one of the most important prognostic factors for ovarian cancer.[32, 33] The important 3 scales including Karnofsky, GOG, and ECOG are utilized in terms of patient performance. In a study conducted based on ECOG criteria, the 5-year survival rate in ECOG 0 patients were determined to be highest while 5-year survival rate in patients with ECOG 3–4 was determined to be lowest.[14] Winter et al. revealed that performance status (according to ECOG) was found to be an independent risk factor to predict relapse and survival with a homogeneous and sufficient number of patients. Particularly, it was emphasized that it may be an important determinant to decide treatment for elderly patients.[33] In our study, we divided the patient performances into 2 groups as ECOG 0–1 and ECOG 2–4. In the univariate analysis, we found that ECOG 0–1 patients had significantly longer survival times compared to ECOG 2–4 patients. However, we could not determine any significance in the multivariate analysis. The possible reason to explain this finding is due to fact that our study population is heterogeneous, and the inadequate number of patient groups may have led to this situation.

Primary cytoreduction has been recommended for patients with ovarian cancer for approximately 30 years. The benefits of cytoreductive surgery goal are to reduce the tumor burden, to improve the immune response, and to relieve circulation. Therefore, better penetration of chemotherapeutic agents to lesions can be provided. The correlation among disease, the tumor size, and survival was examined in 52 and 97 studies of the Gynecologic Oncology Working Group (GOG) and it was observed that 4-year survival rate was 60% in microscopic residual disease and 40% in <2 cm residual disease and was reduced to 20% in residual disease >2 cm residual disease.[34, 35] The definition of the optimal surgery according to the remaining residual tumor diameters changed from year to year in the literature. 2 ≤ cm was seen sufficient for an optimal procedure in the 1970s and subsequently optimal surgery was defined as ≤3 cm in early 1980s. At the end of the 1980s residual tumor size was revised as ≤1 cm. Residual tumor diameter after surgery was divided into three groups in the study of Bailey et al. as under 1 cm, between 1 and 2 cm and over 2 cm. It was observed that patients with a residual tumor over 2cm had shorter survival compared to the other group of patients.[22] Residual tumor diameter is considered to be an important prognostic factor in most of the previous studies, but in some studies, no significant difference could be found between residual tumor diameter and ovarian cancer prognosis. Linasmit et al. residual tumor size was divided into two groups as less than 2 cm and over 2 cm. They found no significant result between the ovarian cancer prognosis and residue tumor diameter.[36] In our study, residual tumor diameter after an operation was divided into 2 groups as less than 2 cm and over 2 cm. In the multivariate analysis, patients with tumors over 2 cm residual tumor diameter had significantly shorter survival compared to patients with tumors less than 2 cm. In addition, patients with a residual tumor diameter of 2 cm or more significantly more frequently relapsed in a shorter period compared to patients with a residual tumor diameter of 2 cm or less. Our results are consistent with the literature.

We evaluated the prognostic significance of the number of chemotherapy cycles at first-line. Patients were divided into two groups according to the number of chemotherapy cycle as 4–6 cycles and more than 6 cycles, and the

patients who received chemotherapy more than 6 cycles at first-line were found to have poor DFS and OS than patients who received 4–6 cycles. Literature data emphasize the fact that treatments given more than six cycles do not contribute OS or DFS benefits, but only causes the increase of treatment-related toxicity.[37, 38] Although the complere response to primary treatment is achieved in most patients. Subsequently, many of them were relapsed. The maintenance or consolidation therapy is not standard for ovarian carcinoma.[39] We revealed that DFS and OS of our patients who received more than six cycles of chemotherapy did not provide additional benefit. The shorter survival rate was observed in patients who were treated more than 6 cycles.

The standard systemic treatment of ovarian cancers cancer is paclitaxel/platinum combination chemotherapy administered prior to and/or subsequent to cytoreductive surgery. The most important agents of ovarian cancer treatment are platinum analogs. Platinum-based treatments cause longer DFS and OS in ovarian cancer patients. The response to platinum and the duration of the response is the most important prognostic factor. Patients who have relapsed after 6–12 months following the completion of first-line treatment are considered to be sensitive to platinum and may benefit from the platinum analogs in the next line of treatment. Patients, who have a relapse before this period, are platinum-resistant. We also divided our patients into two groups as platinum-sensitive and platinum-resistant. We defined our patients who had a relapse after 6 months and those who we did not have a relapse during follow-up as platinum-sensitive and those who had relapsed before 6 months as platinum-resistant. We found that the survival time of patients with platinum sensitivity was statistically longer (Data are shown in supplementary material).

As a result, approximately two-thirds of epithelial ovarian cancer cases are diagnosed at an advanced stage and their prognosis is very poor. The five-year survival rate is unfortunately not at the desired level. Independent poor prognostic indicators were determined as advanced age at diagnosis, to have residual tumor more than 2 cm, more than six cycles of chemotherapy and the presence of platinum-resistant disease in our study. To improve the prognosis by providing optimal treatment with a multidisciplinary approach is more important. Futher larger randomized prospective trials are needed to detect new prognostic markers to predict platinum sensitivite ovarian patients.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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Supplementary Materials

Study subjects related to mortality

	Alive n:53	Death n:66	p
Localization of tumor			
Unilateral	21 (%46.7)	24 (%53.3)	0.849*
Bilateral	32 (%43.2)	42 (%56.8)	
Metastasis at diagnosis			
Present	19 (%33.9)	37 (%66.1)	0.042*
Absent	34 (%54)	29 (%46)	
Ascite prior to diagnosis			
Present	32 (%38.1)	52 (%61.9)	0.042*
Absent	21 (%60)	14 (%40)	
Surgery			
Complete cytoreduction	29 (%38.7)	46 (%61.3)	0.126*
Others**	24 (%54.5)	20 (%45.5)	
Residue tumor			
<2 cm	17 (%42.5)	23 (%57.5)	
≥2 cm	2 (%11.1)	16 (%88.9)	0.001*
Absent	33 (%61.1)	21 (%38.9)	
Histopathology			
Serous	44 (%45.8)	52 (%54.2)	1.000*
Others***	9 (%42.9)	12 (%57.1)	
Abdominal wash fluid			
Positive	37 (%44)	47 (%56)	0.376*
Negative	15 (%55.6)	12 (%44.4)	
Grade			
1	6 (%40)	9 (%60)	
2	23 (%39.7)	35 (%60.3)	0.413*
3	24 (%52.2)	22 (%47.8)	
Stage			
3A	4 (%40)	6 (%60)	
3B	3 (%50)	3 (%50)	0.561*
3C	37 (%48.7)	39 (%51.3)	
4	9 (%33.3)	18 (%66.7)	
Adjuvant Cht cycles			
≤6	48 (%48)	52 (%52)	0.129*
>6	5 (%26.3)	14 (%73.7)	
Performance status			
0-1	50 (%51)	48 (%49)	0.003*
Others****	3 (%14.3)	18 (%85.7)	

N: count, *: Chi-square, **: suboptimal cytoreduction, optimal cytoreduction, biopsi, ***:musinous, endometroid, brenner tumor, mix types, ****: ECOG 2-3-4-5, Cht: Chemotherapy

Clinical characteristics related to overall survival

	Median OS	p
Localization of tumor		
Unilateral	60.32 (38.56-82.07)	0.056*
Bilateral	38.34 (32.56-44.12)	
Surgery		
Complete cytoreduction	50.26 (41.84-58.68)	0.071*
Others**	35.35 (29.43-41.26)	
Metastasis at diagnosis		
Present	33.93 (26.78-41.09)	0.001*
Absent	53.61 (38.31-68.92)	
Ascite prior to diagnosis		
Present	42.97 (34.27-51.67)	0.098*
Absent	58.05 (26.71-89.39)	
Residue tumor		
<2 cm	46.75 (40.48-53.02)	
≥2 cm	32.26 (27.40-37.12)	0.011*
Absent	50.26 (38.51-62.02)	
Histopathology		
Serous	41.75 (34.57-48.94)	0.071*
Others***	70.40 (47.18-93.63)	
Abdominal wash fluid		
Positive	44.81 (36.38-53.23)	0.241*
Negative	50.26 (33.60-66.92)	
Grade		
1	67.77 (15.11-120.44)	
2	45.07 (34.77-55.37)	0.431*
3	40.21 (31.88-48.54)	
Stage		
3A	74.71 (17.09-32.32)	
3B	47.24 (32.58-61.90)	0.000*
3C	51.58 (36.38-66.78)	
4	32.26 (25.02-39.50)	
Adjuvant Cht cycles		
≤6	45.37 (34.38-56.35)	0.046*
>6	37.84 (30.78-44.91)	
Performance status		
0-1	45.37 (38.14-52.59)	0.231*
Others****	34.89 (22.75-47.02)	

*: Long Rank, **: suboptimal cytoreduction, optimal cytoreduction, biopsi, ***:musinous, endometroid, brenner tumor, mix types, ****: ECOG 2-3-4-5, Cht: Chemotherapy

Demograpical characteristic related to mortality			
	Alive n:53	Death n:66	p
Age at diagnosis			
< 60	34 (%56.7)	26 (%43.3)	0.010*
≥60	19 (%32.2)	40 (%67.8)	
Number of birth			
0	6 (%42.9)	8 (%57.1)	1.000*
>0	47 (%44.8)	58 (%55.2)	
Age of menarche			
≤13	36 (%45.6)	43 (%54.4)	0.846*
>13	17 (%42.5)	23 (%57.5)	
Age at first childbirth			
≤20	17 (%28.8)	42 (%71.2)	0.001*
>20	36 (%60.0)	24 (%40.0)	
Menapouse			
Var	31 (%36.9)	53 (%63.1)	0.015*
Yok	22 (%62.9)	13 (%37.1)	
Age of menapouse			
<46	10 (%66.7)	5 (%33.3)	0.095*
≥46	43 (%41.3)	61 (%58.7)	
Body mass index			
<25	24 (%43.6)	31 (%56.4)	1.000*
≥25	29 (%45.3)	35 (%54.7)	

*: Chi-square, n: count.

Demographical characteristics related overall survival		
	Median OS	p
Age at diagnosis		
< 60	45.37 (35.96-54.78)	0.047*
≥60	36.27 (27.11-45.42)	
Number of birth		
0	45.07 (25.65-64.49)	0.612*
>0	44.81 (35.82-53.80)	
Age of menarche		
≤13	38.34 (29.49-47.18)	0.457*
>13	50.26 (42.53-58.60)	
Age at first childbirth		
≤20	45.07 (33.90-56.24)	0.580*
>20	40.47 (30.34-50.61)	
Menapouse		
Var	41.75 (33.82-49.69)	0.638*
Yok	47.24 (36.60-57.88)	
Age of menapouse		
<46	54.07 (34.52-73.63)	0.264*
≥46	41.75 (33.30-50.20)	
Body mass index		
<25	51.58 (39.12-64.03)	0.166*
≥25	38.37 (32.99-43.74)	

*: Long Rank.

Clinical characteristics related to progression free survival		
	Median PFS	p
Localization of tumor		
Unilateral	27.49 (10.50-44.36)	0.084*
Bilateral	16.59 (14.30-18.88)	
Surgery		
Complete cytoreduction	27.20 (10.87-43.53)	0.006*
Others**	16.78 (12.95-20.61)	
Metastasis at diagnosis		
Present	15.57 (12.72-18.42)	0.000*
Absent	25.16 (14.52-35.80)	
Ascite prior to diagnosis		
Present	16.78 (14.88-18.68)	0.003*
Absent	36.27 (15.56-56.97)	
Residue tumor		
<2 cm	17.67 (13.80-21.54)	
≥2 cm	15.57 (13.74-17.39)	0.085*
Absent	25.52 (16.76-34.28)	
Histopathology		
Serous	17.67 (14.42-20.92)	0.059*
Others***	41.39 (7.13-75.65)	
Abdominal wash fluid		
Positive	17.67 (14.27-21.07)	0.090*
Negative	24.83 (10.08-39.58)	
Grade		
1	22.47 (13.85-31.08)	
2	16.59 (14.31-18.86)	0.640*
3	17.93 (10.42-25.45)	
Stage		
3A	42.41 (6.55-78.27)	
3B	16.29 (15.30-17.28)	0.003*
3C	23.03 (15.65-30.40)	
4	13.70 (11.47-15.92)	
Adjuvant Cht cycles		
≤6	23.03 (17.35-28.70)	0.008*
>6	15.14 (12.48-17.80)	
Performance status		
0-1	17.87 (12.16-23.57)	0.212*
Others****	17.87 (12.88-22.86)	

*: Kaplan-Meier, **: suboptimal cytoreduction, optimal cytoreduction, biopsi, ***:musinous, endometroid, brenner tumor, mix types, ****: ECOG 2-3-4-5, Cht: Chemotherapy.

Demographical characteristics related to progression free survival		
	Median PFS	p
Age at diagnosis		
<60	20.43 (13.12-27.74)	0.573*
≥60	17.67 (16.01-19.33)	
Number of birth		
0	15.04 (11.47-18.61)	0.662*
>0	20.14 (14.61-25.66)	
Age of menarche		
≤13	21.84 (15.65-28.04)	0.603*
>13	15.90 (13.23-18.57)	
Age at first childbirth		
≤20	15.90 (14.49-17.30)	0.063*
>20	24.83 (20.76-28.91)	
Menapouse		
Var	17.08 (15.36-18.80)	0.206*
Yok	23.39 (15.82-30.96)	
Age of menapouse		
<46	23.98 (18.27-29.69)	0.042*
≥46	16.59 (15.14-18.04)	
Body mass index		
<25	17.67 (9.59-25.75)	0.633*
≥25	17.93 (13.53-22.34)	

*: Kaplan-meier.

Clinical characteristics related to recurrence			
	Recurrence (+) n: 84	Recurrence (-) n: 35	p
Localization of tumor			
Unilateral	26 (31%)	13 (52%)	0.062*
Bilateral	58 (69%)	12 (48%)	
Metastasis at diagnosis			
Present	48 (57.1%)	3 (12%)	0.000*
Absent	36 (42.9%)	22 (88%)	
Ascite prior to diagnosis			
Present	64 (76.2%)	11 (44%)	0.006*
Absent	20 (23.8%)	14 (56%)	
Surgery			
Complete cytoreduction	26 (31%)	15 (60%)	0.011*
Others**	58 (69%)	10 (40%)	
Residue tumor			
<2 cm	32 (41.6%)	4 (16%)	
≥2 cm	13 (16.8%)	2 (8%)	0.011*
Absent	32 (41.6%)	19 (76%)	
Histopathology			
Serous	71 (86.6%)	18 (72%)	0.124*
Others***	11 (13.4%)	7 (28%)	
Abdominal wash fluid			
Positive	60 (78.9%)	16 (64%)	
Negative	16 (21.1%)	9 (36%)	
0.181*			
Grade			
1	11 (13.1%)	3 (12%)	
2	41 (48.8%)	10 (40%)	0.668*
3	32 (38.1%)	12 (48%)	
Stage			
3A	5 (6%)	4 (16%)	
3B	3 (3.6%)	2 (8%)	0.007*
3C	49 (58.3%)	19 (76%)	
4	27 (32.1%)	0 (0%)	
Adjuvant Cht cycles			
≤6	66 (78.6%)	24 (96%)	0.034*
>6	18 (21.4%)	1 (4%)	
Performance status			
0-1	69 (82.1%)	25 (100%)	0.020*
Others****	15 (17.9%)	0 (0%)	

N: count, *: Chi-square, **: suboptimal cytoreduction, optimal cytoreduction, biopsi, ***:musinous, endometroid, brenner tumor, mix types, ****: ECOG 2-3-4-5, Cht: Chemotherapy.

Demographical characteristics related to recurrence			
	Recurrence (+) n: 84	Recurrence (-) n: 35	p
Age at diagnosis			
<60	47 (56%)	21 (84%)	0.017*
≥60	37 (44%)	4 (16%)	
Number of birth			
0	9 (10.7%)	3 (12%)	1.000*
≥1	75 (89.3%)	22 (88%)	
Age of menarche			
≤13	55 (65.5%)	17 (68%)	1.000*
>13	29 (34.5%)	8 (32%)	
Age at first childbirth			
≤20	46 (54.8%)	7 (28%)	0.023*
>20	38 (45.2%)	18 (72%)	
Menapouse			
Yes	63 (75%)	13 (52%)	0.046*
No	21 (25%)	12 (48%)	
Age of menapouse			
<46	31 (36.9%)	16 (64%)	0.022*
≥46	53 (63.1%)	9 (36%)	
Body mass index			
<25	36 (42.9%)	14 (56%)	0.263*
≥25	48 (57.1%)	11 (44%)	

*:Chi-square, n: count.

Tumor diameter in patients with ovarian cancer		
Tumor diameter cm	Count	Percentage (%)
<8	55	48.7
≥8	58	51.3

Stages in patients with ovarian cancer	
	n (%)
3A	10 (8.4)
3B	6 (5)
3C	76(63.9)
4	27 (22.7)
Total	119 (100)

Histopathological grades in patients with ovarian cancer	
Grade	n (%)
1	15 (12.6)
2	58 (48.7)
3	46 (38.7)

The residue tumor status	
Tumor residue (+)	n (%)
<2 cm	40 (33.6)
>2 cm	18 (15.1)
Tumor residue (-)	54 (45.4)
Other*	7 (5.9)
Total	119 (100)

*biopsy proven pathology confirmation

Positive nodal status		
Positive Lymph node	n	Percentage (%)
<5	29	70.8
≥5	12	29.2

Lymph node status	
	Mean (min- max)
Lymph node dissection	20.0±23.4 (0-103)
Positive lymph node	2.01±5.6 (0-45)

Metastatic region at diagnosis	
	n (%)
Liver	10 (8.4)
Carcinomatosis peritonei	27 (22.8)
Disseminated metastasis	13 (10.9)
Other*	6 (5)
Metastasis (-)	63 (52.9)
Total	119 (100)

*Colorectal, osseos, lung, bladder, stomach.

Surgery type	
	n (%)
TAH+BSO	16 (13.4)
TAH+BSO+omentectomy	53 (44.5)
TAH+BSO+appendectomy+abdominal wash	10 (8.4)
TAH+BSO+appendectomy+omentectomy	28 (23.5)
Other*	6 (5)

TAH+BSO: Total Abdominal Hysterectomy+Bilateral Salphingooferectomy, *Subtotal Hysterectomy+Bilateral Salphingooferectomy (BSO), right salphingooferectomy+omentectomy+apendectomy, bilateral salphingooferectomy.

Chief complaints of the patients	
	n (%)
Abdominal tendency	57 (47.9)
Abdominal pain	47 (39.5)
Menorrhagia	8 (6.7)
Dysmenorrhea	3 (2.5)
Other*	4 (3.3)
Toplam	119 (100)

* Nausea-emesis, dyspnea, dysuria.