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ORIGINAL RESEARCH

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Evaluation of the relationship of the amount of ascites as measured quantitatively using computed tomography with chemotherapy toxicity in patients with ovarian cancer

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Abstract

In this study, it was planned to investigate the effects of ascites and sarcopenia on treatment toxicity, disease free survival (DFS) and disease specific survival (DSS) times in a population of patients with stage 3–4 ovarian cancer. In this retrospective study that include 80 patients treated and followed-up for advanced stage ovarian cancer in a university hospital between 2012–2019, ascites volumes and sarcopenia indices of the patients were calculated by computed tomography from medical patient records, and their clinico-pathologic characteristics as well as laboratory variables were reviewed. The median survival was 30.10 $\pm$ 2.85 months for the patients with ascites and 54.26 $\pm$ 4.16 months without ascites ($p < 0.001$). The duration of DSS was found to be negatively affected in patients with ascites (Hazard Ratio (HR): 3.048), prognostic nutritional index (PNI) <47.5 (HR: 2.528), platelet (PLT) >338,000 (HR: 1.936), lactate dehydrogenase (LDH) value >320 (HR: 1.624), albumin value <4 (HR: 1.849). When factors that are found to have a significant relationship with DSS were assessed according to multivariate Cox regression analysis, the presence of ascites was identified as an independent risk factor associated with DSS (p: 0.004). The risk of developing grade 2 or 3 neutropenia, anemia and thrombocytopenia is significantly increased following the first chemotherapy course in patients with ascites when compared to those without ascites (p: 0.006). The presence of ascites in patients with ovarian cancer is a risk factor associated with chemotherapy toxicity and reduced survival.

Keywords

Ascites; Chemotherapy toxiticy; Ovarian cancer; Sarcopenia

1. Introduction

Epithelial ovarian cancer (OC) is the fifth most frequent cause of death in the female population in developed countries [1]. The standard current treatment for OC is the complete resection of the macroscopic disease using cytoreductive surgery followed by adjuvant platinum-based chemotherapy. Cytoreduction may be chosen following neoadjuvant therapy in case sufficient primary cytoreduction cannot be achieved or the patient is not suitable for surgery [2]. The rationale for chemotherapy dosing in adjuvant and neoadjuvant therapy is based on the balance between optimal treatment effectiveness and drug toxicity that may lead to treatment delays or early treatment discontinuation.

Dosing for most chemotherapeutic agents is based on body surface area (BSA) to minimize the variability between individuals. It is thought that determining the dose based on BSA may lead to errors in obese or cachectic patients as well as those with ascites. On the other hand, sarcopenia, characterized by the loss of mass and function in skeletal muscles, is frequently observed in patients with cancer as part of cancer cachexia syndrome [3]. Although there are studies that investigate the effect of sarcopenia on chemotherapy-associated toxicity and survival, studies investigating the effect of the presence of ascites on chemotherapy toxicity are very scarce [4]. However, ascites is observed in approximately one third of all patients with newly diagnosed ovarian cancer and in almost all patients with recurrent disease [5]. Diagnosing cachexia may be difficult in patients with ovarian cancer since it may be masked by ascites collection. Therefore, measuring the amount of ascites and skeletal muscles during tomography follow-ups instead of weight loss is considered more reliable in this group of patients. It was planned to investigate the effect of ascites and sarcopenia on treatment toxicity as well as disease free survival (DFS) and disease specific survival (DSS) in a population of patients with ovarian cancer selected with the target of eliminating the confusing effect of gender.

2. Materials and methods

2.1 Identification of the study population from the cohort of ovarian cancer

Two hundred and thirty-two, International Federation of Gynecology and Obstetrics (FIGO) stage III–IV patients older than 18 years of age were analyzed who were diagnosed with high-grade serous ovarian cancer between January 2010 and December 2019 and treated in our center. Among 232 retrospectively screened patients, 152 patients who underwent primary cytoreduction, had an Eastern Cooperative Oncology Group performance status (ECOG PS) 2, 3 or 4, did not have their disease staging done by computed tomography at the time of diagnosis, did not receive chemotherapy or follow-up in our center-up were not included in the study. In order to create a homogeneous study group, 80 patients who were staged as stage 3c and stage 4 at the time of diagnosis (40 with ascites and 40 without).

And who received paclitaxel and carboplatin chemotherapy without primary cytoreduction and no ascites drainage were included in the study. Thus, our aim was to determine the effect of ascites amount on chemotherapy-related toxicity while minimizing confounding factors as much as possible.

Chemotherapy-related hematological toxicity degrees were determined as a result of the evaluation after the first course of chemotherapy.

2.2 Description of ascites volume and the degree of sarcopenia by analysing tomography images

For measuring ascites, reviews of transverse computed tomography (CT) slices sections from three levels were used. For fluid measurement across subphrenic areas, the level at which the superior mesenteric artery leaves the aorta was chosen to determine cross sections, the lower pole level of the left kidney to measure the fluid in paraaortic areas, and the femoral head level for the measurement of the fluid in front of the bladder. Ascites thickness measurement was made in centimeters as indicated in the literature, from a total of 5 points that are bilateral subphrenic and paracolic areas and the front area of the bladder [6]. The mean ascites thickness was found by calculating the arithmetic mean of these 5 measurements and the total amount of ascites was calculated in millimeters using the formula given in the literature (mean ascites thickness $\times$ 200 mL) [6]. Patients were included in the ascites group in the presence of at least 300 mL of ascites. The level of sarcopenia was determined using the skeletal muscle index obtained by dividing the total skeletal muscular area (cm^2) by the height squared (m^2) at the third lumbar vertebra (L3) level in the cross-sectional axial plane tomography images of all the subjects included in the study [7].

2.3 Data collection

The clinicopathological characteristics of the subjects were collected including age, comorbidities, FIGO stage, ECOG PS, adjuvant chemotherapy regimens and cycles. The body mass index (BMI) values of the subjects before treatment were calculated by dividing the body weight at diagnosis (kg) by the height squared (m^2). Based on the BMI criteria suggested by the World Health Organization (WHO), the subjects were categorized into three groups as normal ($\geq$18.5 kg/m^2 and $<$25 kg/m^2), overweight ($\geq$25 kg/m^2 and $<$30 kg/m^2) and obese ($\geq$30 kg/m^2) [8]. In addition, body surface areas (BSAs) of the subjects were calculated based on Dubois formula which received acceptance in the literature. (DuBois formula: BSA (m^2) = 0.007184 $\times$ (subject's height in cm) 0.725 $\times$ (subject's body weight in kg) 0.425) [9]. Data collection also includes the levels of cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), albumin, lactate dehydrogenase (LDH), and blood counts including hemoglobin (HGB), neutrophils (NEUT), lymphocytes (LYM) and platelets (PLT) at the time of diagnosis or before starting chemotherapy. Prognostic nutrition index (PNI) as the pre-treatment nutritional index was calculated as follows: 10 $\times$ serum albumin (g/dL) + 0.005 $\times$ peripheral blood lymphocyte count (/μL) [10]. DSS was defined as the time from the date of diagnosis of the primary tumour to the date of disease-specific death or follow up for patients remaining alive. In the course of surveillance, routine CT scans were performed every three to four months during the first two years, every six months during the following two years and every year thereon, or whenever symptoms or examination findings suggested a relapse. DFS was defined as the time interval between the starting date of the primary treatment and the date disease progression was confirmed with imaging as assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [11]. Anemia, leucopenia and thrombocytopenia that subjects developed following the first course of chemotherapy were graded according to the Common Terminology Criteria for Adverse Events (CTAE.5).

2.4 Statistical analysis

The mean standard deviation, median, minimum and maximum values were used for definitive statistics for continuous data and number percent values were provided for categorical data. Shapiro-Wilk test was utilized to examine the suitability of continuous data for normal distribution. For the comparison of continuous variables between subjects with and without ascites, *t*-test and Mann-Whitney U test were used for data that is and is not suitable for normal distribution, respectively. Chi-squared test and Fisher's exact test were used for group comparisons of nominal variables (in crosstabs). Kaplan-Meier analysis was used for survival analyses, and log rank method was used to examine the differences in survival between independent groups. Additionally, Cox Regression Analysis method was used to identify the factors that are effective on survival. IBM SPSS Statistics 20.0 (Armonk, NY, USA) software was used for the assessments and statistical significance limit was considered as $p < 0.05$.

3. Results

The study included 80 patients with ovarian cancer. They were placed into one group or the other based on the presence of ascites. No differences were found between patients with ascites and without ascites in terms of age, disease stage, BMI

level and sarcopenia index ($p > 0.05$). An interval debulking surgery was performed in 14 patients with ascites and 16 patients without ascites ($p > 0.05$). The PNI values were lower with ascites compared to the without ascites ($p < 0.01$). The rate of relapse was higher with ascites ($p < 0.05$). Lymphocyte counts were lower ($p < 0.05$) and platelet counts were higher ($p < 0.001$) with ascites. CA-125 levels were higher with ascites ($p < 0.05$) while albumin levels were lower ($p < 0.05$). No differences in hemoglobin, absolute neutrophil, CEA and LDH levels were identified between patients with ascites and without ascites ($p > 0.05$). The clinical characteristics and laboratory variables are summarized in Tables 1 and 2.

A chemotherapy-related hematologic toxicity assessment was performed between the groups. No differences were found in the rates of primary and secondary use of granulocyte colony-stimulating factor (G-CSF) between the groups ($p > 0.05$). However, the rate of Grade 2 neutropenia was higher and that of Grade 0 was lower with ascites ($p < 0.05$). Furthermore, the rates of thrombocytopenia of Grade 1 and Grade 3 were higher, while the rates of Grade 0 were lower for the patients with ascites ($p < 0.01$). The rates of Grade 2 and Grade 3 anemia were found to be higher with ascites, while the rates of Grade 1 were lower ($p < 0.01$) (Table 3).

The mean survival was 34.50 ± 3.39 months and the median survival was 30.10 ± 2.85 months for subjects with ascites, while the mean survival was 65.25 ± 6.00 months and the median survival was 54.26 ± 4.16 months for subjects without ascites ($p < 0.001$). Mean survival was 36.71 ± 3.82 in subjects with a PNI index <47.5 while it was 62.26 ± 5.98 in those with a PNI index >47.5 ($p < 0.001$). The mean survival was 59.74 ± 6.19 in subjects with PLT <338,000 and 39.46 ± 3.92 in subjects with PLT >338,000 ($p < 0.01$). The mean survival was 57.24 ± 6.03 in subjects with an LDH value <320 and 41.81 ± 4.11 in subjects with an LDH value >320 ($p < 0.01$). The mean survival was 39.78 ± 4.21 in subjects with an albumin value <4 and 59.46 ± 6.09 in subjects with an albumin value >4 ($p < 0.05$). No association was found between survival and sarcopenia index, hemoglobin, neutrophil, lymphocytes, CEA, CA-125 and BMI ($p > 0.05$) (findings are summarized in Table 4).

When factors (ascites, PNI, PLT, LDH, albumin) showing significant correlation with DSS were evaluated according to univariate Cox regression analysis, it was found that patients with ascites affected DSS in a 3.048-fold negative way ($p < 0.001$). Patients with PNI <47.5 were found to affect DSS 2.528 times negatively ($p < 0.001$). Patients with a PLT value >338,000 were found to affect DSS 1.936 times negative ($p < 0.01$) (Fig. 1). Patients with a LDH value >320 were found to affect DSS 1.624 times negative ($p < 0.05$). Patients with albumin value <4 were found to affect DSS by 1.849 times negative ($p < 0.05$) (findings are summarized in Table 5).

When factors (ascites, PNI, PLT, LDH, albumin) showing significant correlation with DSS were evaluated according to multivariate Cox regression analysis, the presence of ascites was found to be a factor that is correlated with DSS. The median DFS was 13.93 ± 1.17 months for patients with ascites and 18.66 ± 3.20 months for patients without ascites ($p < 0.01$). The mean DFS was 16.73 ± 1.73 months for patients with a PNI index <47.5 and 31.03 ± 5.25 months for patients with a PNI index >47.5 ($p < 0.05$). When factors (ascites, PNI) that had a significant correlation with DFS were evaluated according to univariate Cox regression analysis, it was found that patients with ascites affected DFS in a 2.307-fold negative way ($p < 0.001$). Patients with PNI <47.5 were found to affect DFS by 1.774 times negative ($p < 0.001$). When factors (ascites, PNI) that had a significant correlation with DFS were evaluated according to multivariate Cox regression analysis, the presence of ascites was found to be a factor associated with DFS (findings are summarized in Tables 6 and 7).

4. Discussion

In the study by Oriuchi N. *et al.* [6], it was shown that the estimation of ascites using the 5-point method in multislice computed tomography demonstrated good correlation compared to the measurements made using 3-dimensional tomography, particularly for amounts greater than 300 mL. Ascites volume measurements in this study were performed using the 5-point method in computed tomography images of patients obtained before treatment because it is more applicable without interrupting routine practice compared to 3-dimensional tomography. Ascites is seen in approximately one third of all newly diagnosed ovarian cancer patients and in almost all patients with recurrent diseases [5]. Adjusting the chemotherapy dose based on body composition rather than BSA is thought to be more appropriate, since conditions such as large tumor burden or small intestine obstruction frequently accompany ascites in patients with ovarian cancer. For conditions requiring a calculation based on BSA, it is recommended to take into account the excessive weight caused by fluid retention due to ascites or anasarca when calculating the dose. However, because it was not supported by randomized studies, standardization could not be established on this subject. In addition, an important challenge faced during oncology practice is how to optimize the dose of chemotherapeutics [12]. The sizes of parts of the body composition are associated with the distribution of the drug. Hydrophilic drugs are dispersed in non-fatty compartments while lipophilic drugs are dispersed in fatty compartments [13]. How the absorption, distribution and elimination of chemotherapeutics associated with ascites volume are affected in our daily practices and whether an appropriate plasma concentration is achieved or not has been a subject of interest. Similarly, it is considered necessary to investigate whether the toxicity is associated with the volume of the ascites while measurement of drug levels from the ascites fluid and plasma concomitantly may become important, since an increased risk of hydrophilic drug toxicity may emerge as a result of prolonged plasma drug levels. Review of the literature revealed that there was no study evaluating chemotherapy toxicity associated with ascites volume in patients with ovarian cancer. In this study, the entire study population was administered a combination of platinum and taxane as a chemotherapeutic regimen. The risk of developing Grade 2 and Grade 3 neutropenia, anemia and thrombocytopenia after the first course of chemotherapy was found to increase significantly in the ascites group. Based on this conclusion, we believe that it should be further investigated through prospective studies whether the risk of chemotherapy toxicity in patients with

TABLE 1. Comparison of patients with and without ascites.

	Total (n = 80)	Ascites Present (n = 40)	No Ascites (n = 40)	*p* value
Age (yr), Mean ± SD	57.21 ± 10.49	58.00 ± 10.46	56.42 ± 10.59	0.506*
Stage n (%)				
Stage 4	30 (37.5)	14 (35.0)	16 (40.0)	0.644**
Stage 3c	50 (62.5)	26 (65.0)	24 (60.0)	
BMI				
Normal/overweight	45 (56.2)	21 (52.5)	24 (60.0)	0.499**
Obese	35 (43.8)	19 (47.5)	16 (40.0)	
Total ascites volume, Mean ± SD		2379.2 ± 1521.7		
Sarcopenia index, Mean ± SD	50.81 ± 9.67	52.05 ± 11.46	49.57 ± 7.41	0.254*
Sarcopenia index (median 41)				
<41	12 (15.0)	5 (12.5)	7 (17.5)	0.531**
>41	68 (85.0)	35 (87.5)	33 (82.5)	
PNI Mean ± SD	47.10 ± 7.23	44.97 ± 7.01	49.23 ± 6.89	0.008*
PNI (median 47.5)				
<47.5	39 (48.8)	27 (67.5)	12 (30.0)	0.001**
>47.5	41 (51.2)	13 (32.5)	28 (70.0)	
Relapse				
None	6 (7.5)	0	6 (15.0)	0.011**
Yes	74 (92.5)	40 (100.0)	34 (85.0)	

**Independent Samples t-test; **Chi-Square/Fisher's Exact test. BMI: body mass index; PNI: prognostic nutritional index; SD: standard deviation.*

TABLE 2. Comparison of laboratory values in patients with and without ascites.

	Total (n = 80)	Ascites (n = 40)	No Ascites (n = 40)	*p* value
Hemoglobin at diagnosis, Mean ± SD	12.13 ± 1.45	11.81 ± 1.58	12.45 ± 1.25	0.051*
Neutrophil at diagnosis, Mean ± SD	5359.0 ± 2010.8	5623.5 ± 2109.7	5094.5 ± 1896.4	0.507**
Lymphocytes at diagnosis, Mean ± SD	1744.7 ± 670.0	1580.5 ± 602.8	1909 ± 700.4	0.031**
Platelet at diagnosis, Mean ± SD	370,762.5 ± 154,493.6	429,825 ± 174,914	311,700 ± 102,946	<0.001**
CEA at diagnosis, Mean ± SD	3.21 ± 8.19	2.15 ± 2.03	4.30 ± 11.45	0.739**
CA-125 at diagnosis, Mean ± SD	1764.4 ± 2796.4	2222.6 ± 3074.7	1306.2 ± 2440.4	0.019**
LDH at diagnosis, Mean ± SD	380.1 ± 257.1	424.6 ± 304.7	334.5 ± 190.1	0.312**
Albumin at diagnosis, Mean ± SD	3.83 ± 0.61	3.70 ± 0.62	3.96 ± 0.59	0.037**

**Independent Samples t-test; **Mann Whitney U test. CEA: carcinoembryonic antigen; CA-125: cancer antigen 125; LDH: lactate dehydrogenase; SD: standard deviation.*

TABLE 3. Comparison of post-chemotherapy toxicity in patients with and without ascites.

	Total (n = 80)	Ascites Present (n = 40)	No Ascites (n = 40)	*p* value
Primary GCSF use n (%)				
Yes	8 (10.0)	5 (12.5)	3 (7.5)	0.712**
None	72 (90.0)	35 (87.5)	37 (92.5)	
Secondary GCSF use n (%)				
Yes	54 (67.5)	30 (75.0)	24 (60.0)	0.152**
None	26 (32.5)	10 (25.0)	16 (40.0)	
Neutropenia grade n (%)				
Grade 1	15 (18.8)	6 (15.0)	9 (22.5)	
Grade 2	13 (16.2)	10 (25.0)	3 (7.5)	
Grade 3	30 (37.5)	16 (40.0)	14 (35.0)	0.033**
Grade 4	16 (20.0)	8 (20.0)	8 (20.0)	
Grade 0	6 (7.5)	0 (0)	6 (15.0)	
Thrombocytopenia grade n (%)				
Grade 1	33 (41.2)	22 (55.0)	11 (27.5)	
Grade 2	12 (15.0)	5 (12.5)	7 (17.6)	
Grade 3	8 (10.0)	6 (15.0)	2 (5.0)	0.006**
Grade 4	3 (3.8)	2 (5.0)	1 (2.5)	
Grade 0	24 (30.0)	5 (12.5)	19 (47.5)	
Anemia grade n (%)				
Grade 1	25 (31.2)	6 (15.0)	19 (47.5)	
Grade 2	45 (56.2)	26 (65.0)	19 (47.5)	0.006**
Grade 3	8 (10.0)	7 (17.5)	1 (2.5)	
Grade 0	2 (2.5)	1 (2.5)	1 (2.5)	

***Chi-Square/Fisher's Exact test. G-CSF: granulocyte colony-stimulating factor.*

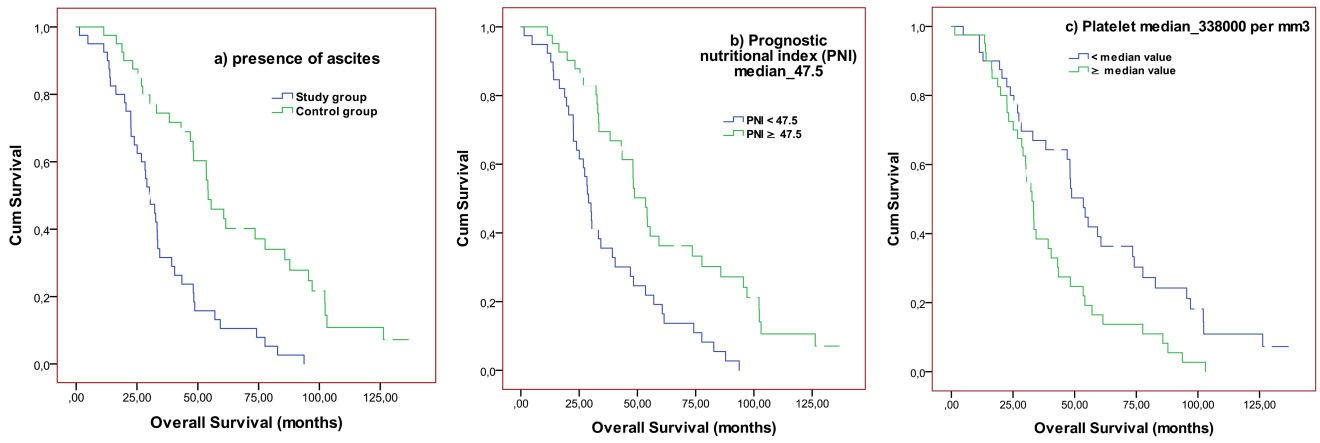

FIGURE 1. Factors affecting on overall survival time (ascites, PNI, PLT).

TABLE 4. Comparison of overall survival durations by patient characteristic.

	n (no of deaths)	Mean survival (months ± SD)	Median survival (months ± SD)	Log rank *p*
Overall	80/71	49.49 ± 3.80	39.26 ± 7.12	
Ascites				
Yes	40/39	34.50 ± 3.39	30.10 ± 2.85	<0.001
None	40/32	65.25 ± 6.00	54.26 ± 4.16	
Sarcopenia index				
<41	12/11	45.72 ± 9.80	46.96 ± 7.08	0.718
>41	68/60	50.16 ± 4.13	38.30 ± 5.77	
PNI				
<47.5	39/38	36.71 ± 3.82	44.21 ± 29.06	<0.001
>47.5	41/33	62.26 ± 5.98	53.53 ± 4.40	
Hemoglobin				
<12.3	40/38	47.92 ± 4.57	34.33 ± 6.27	0.439
>12.3	40/33	51.84 ± 6.36	43.10 ± 8.46	
Neutrophils				
<5100	42/39	50.70 ± 4.94	48.13 ± 2.99	0.703
>5100	38/32	47.83 ± 5.91	32.23 ± 1.84	
Lymphocytes				
<1650	40/37	43.54 ± 4.36	33.26 ± 10.00	0.102
>1650	40/34	55.31 ± 6.09	43.10 ± 5.75	
Platelet				
<338,000	40/33	59.74 ± 6.19	53.53 ± 4.48	0.006
>338,000	40/38	39.46 ± 3.92	32.70 ± 1.82	
CEA				
<1.55	41/36	50.29 ± 5.02	40.46 ± 8.31	0.772
>1.55	39/35	48.32 ± 5.66	33.50 ± 8.57	
CA-125				
<430	40/34	47.48 ± 4.90	48.10 ± 6.83	0.622
>430	40/37	50.61 ± 5.50	33.50 ± 4.02	
LDH				
<320	41/34	57.24 ± 6.03	53.53 ± 7.92	0.043
>320	39/37	41.81 ± 4.11	33.00 ± 4.71	
Albumin				
<4	39/38	39.78 ± 4.21	30.46 ± 2.62	0.010
>4	41/33	59.46 ± 6.09	48.76 ± 6.20	
BMI				
Normal	45/38	51.87 ± 5.52	46.96 ± 5.74	0.412
Obese	35/33	46.26 ± 4.95	33.50 ± 2.74	

PNI: prognostic nutritional index; CEA: carcinoembryonic antigen; CA-125: cancer antigen 125; LDH: lactate dehydrogenase; BMI: body mass index; SD: standard deviation.

TABLE 5. Univariate and multivariate COX regression analysis for overall survival.

	Univariate			Multivariate		
Factor	HR	95% CI	*p*	HR	95% CI	*p*
Ascites present	3.048	1.820–5.104	<0.001	2.407	1.314–4.411	0.004
PNI <47.5	2.528	1.520–4.169	<0.001	1.313	0.670–2.574	0.427
PLT >338,000	1.936	1.194–3.138	0.007	1.115	0.619–2.010	0.717
LDH >320	1.624	1.010–2.611	0.046	1.502	0.922–2.448	0.103
Albumin <4	1.849	1.150–2.973	0.011	1.319	0.715–2.433	0.376

HR: Hazard Ratio; PNI: prognostic nutritional index; PLT: platelet; LDH: lactate dehydrogenase; CI: confidence interval.

TABLE 6. Comparison of the effect of patient characteristics on disease-free survival.

	n (Progression)	Mean disease free survival (months ± SD)	Median disease free survival (months ± SD)	Log Rank *p*
Disease-Free	73/7	23.89 ± 2.89	14.83 ± 0.82	
Ascites				
Yes	40/38	15.19 ± 1.48	13.93 ± 1.17	0.001
None	40/35	32.48 ± 5.24	18.66 ± 3.20	
Sarcopenia index				
<41	12/10	22.59 ± 5.12	15.83 ± 5.33	0.825
>41	68/63	23.97 ± 3.18	14.80 ± 0.63	
PNI				
<47.5	39/37	16.73 ± 1.73	14.43 ± 1.27	0.017
>47.5	41/36	31.03 ± 5.25	15.83 ± 2.73	
Hemoglobin				
<12.3	40/38	20.87 ± 2.39	14.43 ± 0.97	0.703
>12.3	40/35	26.22 ± 4.94	14.86 ± 0.86	
Neutrophils				
<5100	42/39	22.87 ± 3.36	14.40 ± 1.66	0.784
>5100	38/34	24.05 ± 4.29	14.86 ± 0.67	
Lymphocytes				
<1650	40/36	21.98 ± 2.66	14.80 ± 2.12	0.996
>1650	40/37	25.28 ± 4.69	14.83 ± 0.97	
Platelet				
<338,000	40/37	25.91 ± 3.96	15.63 ± 3.05	0.335
>338,000	40/36	20.60 ± 3.37	14.43 ± 0.64	
CEA				
<1.55	41/36	28.82 ± 2.87	14.86 ± 2.38	0.477
>1.55	39/37	22.89 ± 4.36	14.80 ± 1.20	
CA-125				
<430	40/36	21.47 ± 2.93	14.83 ± 1.69	0.635
>430	40/37	25.45 ± 4.33	14.80 ± 0.89	
LDH				
<320	41/37	24.38 ± 3.50	14.83 ± 2.26	0.581
>320	39/36	22.64 ± 4.18	14.80 ± 1.15	
Albumin				
<4	39/36	19.57 ± 2.99	14.40 ± 0.81	0.161
>4	41/37	27.19 ± 4.39	15.83 ± 2.24	
BMI				
Normal	45/39	25.00 ± 4.36	16.06 ± 2.56	0.695
Obese	35/34	22.16 ± 3.37	14.43 ± 0.61	

PNI: prognostic nutritional index; CEA: carcinoembryonic antigen; CA-125: cancer antigen 125; LDH: lactate dehydrogenase; BMI: body mass index; SD: standard deviation.

TABLE 7. Univariate and multivariate COX regression analysis for progression-free survival.

	Univariate			Multivariate		
Factor	HR	95% CI	*p*	HR	95% CI	*p*
Ascites present	2.307	1.412–3.771	0.001	2.069	1.150–3.723	0.015
PNI <47.5	1.774	1.102–2.856	0.018	1.209	0.686–2.131	0.512

HR: Hazard ratio; PNI: prognostic nutritional index; CI: confidence interval.

ovarian cancer ascites is affected by inappropriate doses depending on BSA or by prolonged plasma drug levels. In this study, correlation was found between the presence of ascites and a low PNI, and both were associated with shorter DSS times. Furthermore, the presence of ascites was identified as an independent risk factor for shortening DFS. According to the literature, this study demonstrated a positive correlation between serum CA-125 levels and ascites volume [14]. In a clinical study conducted with 372 patients with ovarian cancer who were classified into two groups based on the presence or absence of ascites obtained by intraoperative aspiration, it is reported that no differences were observed in tumor size and disease stage, while an association was observed between the presence of ascites and the spread of intraperitoneal and retroperitoneal tumors. Furthermore, this study reported that an important relationship with the presence and volume of ascites and patient survival was found [15]. In addition to ascites, other factors that could contribute to decreased survival in the patients with ascites are more aggressive disease, resulting in larger disease volume and reduced likelihood of resectability. The study by Quan Q. *et al.* [16] conducted retrospectively on a population of 546 subjects with ovarian cancer evaluated platinum resistance in addition to ascites volume, disease-free survival, and overall survival. In this study, ascites volume was found to be associated with primary platinum resistance, and poorer disease-free and overall survival times were obtained in the group with greater ascites volume [16]. There are articles arguing that the presence of ascites contributes to cancer progression and chemoresistance by forming a tumor microenvironment rich in tumor cells, cytokines, lipid metabolites, proteins and exosomes. The study by Tomer *et al.* [17] demonstrated that molecular features are different in patients with low and high ascites volume and that the strengthened immunoreactive phenotype in the group with lower ascites volume is associated with prolonged overall survival. The authors argued in line with their study results that immunotherapy may be a reasonable approach for the treatment of ascites in the future [17]. From the perspective of sarcopenia, the studies showed that sarcopenia is a prognostic factor associated with poor survival, increased resistance to chemotherapy, and toxicity in patients with various malignancies including breast, small-cell lung and gastric cancers [18]. There are contradictions between the conclusions of studies investigating the effect of sarcopenia on survival in ovarian cancer. Some studies concluded that sarcopenia negatively affects progression-free survival (PFS) or overall survival (OS) in patients, while others did not find a significant relationship between sarcopenia and survival times [19–21]. In another study that evaluated the relationship between body compositions of patients with ovarian cancer calculated by computed tomography and chemotherapy toxicity, visceral fatty tissue thickness and skeletal muscular density were found to be related to delayed chemotherapy, while the presence of sarcopenia was not associated with survival [22]. In the present study, sarcopenia was not found to be associated with chemotherapy toxicity and survival times. Study conclusions should be interpreted with caution due to differences between studies in terms of design, population, disease state and definition of sarcopenia.

5. Conclusions

The presence of ascites in patients with ovarian cancer is a risk factor associated with toxicity of chemotherapy and shorter survival times. As this study was retrospective and non-randomised, the results should be considered hypothesis generating. So far, very few studies have been conducted on body composition in patients with ovarian cancer. There is an urgent need to further study the prognostic value of each component of body composition in ovarian cancer, especially the volume of ascites.

ABBREVIATIONS

ANS, neutrophils; BSA, body surface area; BMI, body mass index; CA-125, cancer antigen 125; CEA, carcinoembryonic antigen; CI, confidence interval; CT, computed tomography; CTAE.5, common terminology criteria for adverse events; ECOG PS, Eastern Cooperative Oncology Group performance status; FIGO, international federation of gynecology and obstetrics; G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio; HGB, hemoglobin; HGSOC, high grade serous ovarian cancer; LDH, lactate dehydrogenase; LYM, lymphocytes; OC, ovarian cancer; OS, overall survival; PFS, progression free survival; PLT, platelet; PNI, prognostic nutritional index; RECIST, response evaluation criteria in solid tumors; SD, standard deviation; WHO, World Health Organization.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from corresponding author.

AUTHOR CONTRIBUTIONS

DBG and MD—idea/concep; DBG and ND—design; MD, DBG and EG—control/supervision; DBG, ND, MD and EG—literature review, writing the article; DBG—critical review.

All authors have read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Before initiating the study that was planned as a retrospective cohort study, local ethics committee approval (Date: 15 June 2021, Decree No: 15, Issue: E-25403353-050.99-201921) was obtained and the Declaration of Helsinki criteria were followed. Patient informed consent was obtained before starting the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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