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Metastasis patterns of the spleen and association with survival outcomes in advanced ovarian–tubal–peritoneal epithelial cancer

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Abstract

Purpose To evaluate the significance of parenchymal, hilar and capsular involvement of the spleen with regard to survival.

Methods All patients who underwent primary cytoreductive surgery for advanced ovarian–tubal–peritoneal (OTP) epithelial cancer were reviewed retrospectively. Stage 3C patients who had an upper abdomen involvement and who were optimally debulked were included. Patients who had abdomen-confined disease, but were upstaged to stage 4B due to splenic parenchymal metastases were also included.

Results Seventy four patients eligible with the inclusion criteria who underwent splenectomy and 69 patients who did not undergo splenectomy were included. The median follow-up time was 39.1 months. The median overall survival of the study group was 61.4 months. Patients who underwent splenectomy were grouped according to the involved site of the spleen: parenchyma subgroup, hilus subgroup, capsule subgroup and benign subgroup. The median overall survival of patients in the hilus subgroup was 41.1 months. The median overall survival of patients who were not in the hilus subgroup was 65.5 months. Patients in the hilus subgroup showed significantly shorter survival ($p=0.035$). Hilus subgroup was associated with a statistically significant increase in mortality risk (hazard ratio 1.971; 95% confidence interval 1.1–3.531).

Conclusions Splenic hilus involvement predicts poorer survival outcomes among stage 3C epithelial OTP cancer patients with disease expansion to upper abdomen. According to current study and many published studies, hilar involvement had a higher incidence rate compared to parenchymal involvement. Thus, hilar involvement would be a beneficial clinical predictor of survival for larger number of patients.

Keywords Ovarian cancer · Splenectomy · Surgery · Cytoreduction · Prognosis · Survival

Introduction

Epithelial ovarian cancer is the most common cause of gynecologic cancer death. The majority of patients with epithelial ovarian cancer are diagnosed at an advanced stage [1, 2]. For these patients, the standard initial treatment consists of cytoreductive surgery followed by a combination of taxane- and platinum-based adjuvant chemotherapy [3, 4]. Prior studies have demonstrated a survival advantage for patients who underwent optimal cytoreduction compared with those who did not [5–8] and aggressive surgical resection to minimize residual disease was associated with improved survival outcomes [9]. Splenectomy is a surgical procedure that facilitates tumor removal and optimal cytoreduction in advanced-stage ovarian cancer. Its safety and feasibility have been well described [10–14].

Previous studies have identified three models of splenic involvement in patients with advanced ovarian–tubal–peritoneal (OTP) epithelial cancer: parenchymal, hilar, and capsular [13, 15–17]. The new International Federation of Gynecology and Obstetrics (FIGO) staging guideline for cancer of the ovary, fallopian tube, and peritoneum was approved by the FIGO Executive Board in 2012 and published in 2014. In the new OTP cancer staging classification, FIGO upstaged patients with splenic parenchymal metastases to stage 4B. However, the significance of hilar and capsular involvement has not yet been clearly evaluated.

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In the current study, we report survival outcomes of patients with advanced OTP epithelial cancer who underwent primary cytoreductive surgery and were optimally debulked. The main objective of the study was to evaluate the significance of parenchymal, hilar, and capsular involvement of the spleen with regard to survival.

Materials and methods

We retrospectively reviewed the hospital medical records of all patients who underwent primary cytoreductive surgery for advanced OTP epithelial cancer between June 1, 2002 and June 1, 2018. FIGO stage 3C patients who had upper abdomen involvement (in the spleen, diaphragm, liver capsule, porta hepatis, gastric serosa, omentum minus, lesser sac or Morison's Pouch) during the study period were included to the study. Patients who had abdomen-confined disease, but were upstaged to stage 4B due to splenic parenchymal metastases were also included to the study group.

Optimal cytoreduction was defined as leaving 1 cm of residual disease or less. Exclusion criteria were the receipt of neoadjuvant chemotherapy, suboptimal cytoreduction, the absence of upper abdomen involvement, the presence of any extraabdominal disease, the involvement of the hepatic parenchyma, and death within 30 days of surgery (Table S1). All patients who underwent splenectomy were categorized as the "splenectomy group", and the remaining patients were categorized as the "no splenectomy group" (Fig. 1). All patients were administered platinum- and taxane-based adjuvant chemotherapy, and those who underwent splenectomy were vaccinated postoperatively.

Involvement of the three anatomical sites of the spleen (parenchyma, hilus, and capsule) was noted in the pathology reports for each patient. We grouped patients who underwent splenectomy into four subgroups: parenchyma subgroup, hilus subgroup, capsule subgroup, and benign subgroup. Involvement of more than one anatomical site of the spleen was not rare and these patients were categorized with a clinical approach based on survival outcomes. Given that patients with splenic parenchymal involvement were upstaged to stage 4B in new FİGO's 2014 OTP cancer staging guideline, we categorized patients who had splenic parenchymal involvement into the parenchyma subgroup, although any other site of the spleen could also be involved. In our study group, the median survival of patients with isolated hilar involvement was shorter than that of patients with isolated capsular involvement. Thus, patients who had both hilar and capsular involvement were categorized into the hilus subgroup. Patients with isolated capsular involvement formed the capsule subgroup (Fig. 1).

Splenic İnvolvement		n	Median Survival (Months)
Parenchyma	Only parenchyma	1	33.2
	Parenchyma+hilus	3	
	Parenchyma+capsule	3	
	Parenchyma+hilus+ capsule	0	
Hilus	Only hilus	23	41.1
	Hilus+capsule	6	
Capsule	Only capsule	28	55.1
Benign	Benign	10	NSC
No Splenectomy		69	75.3

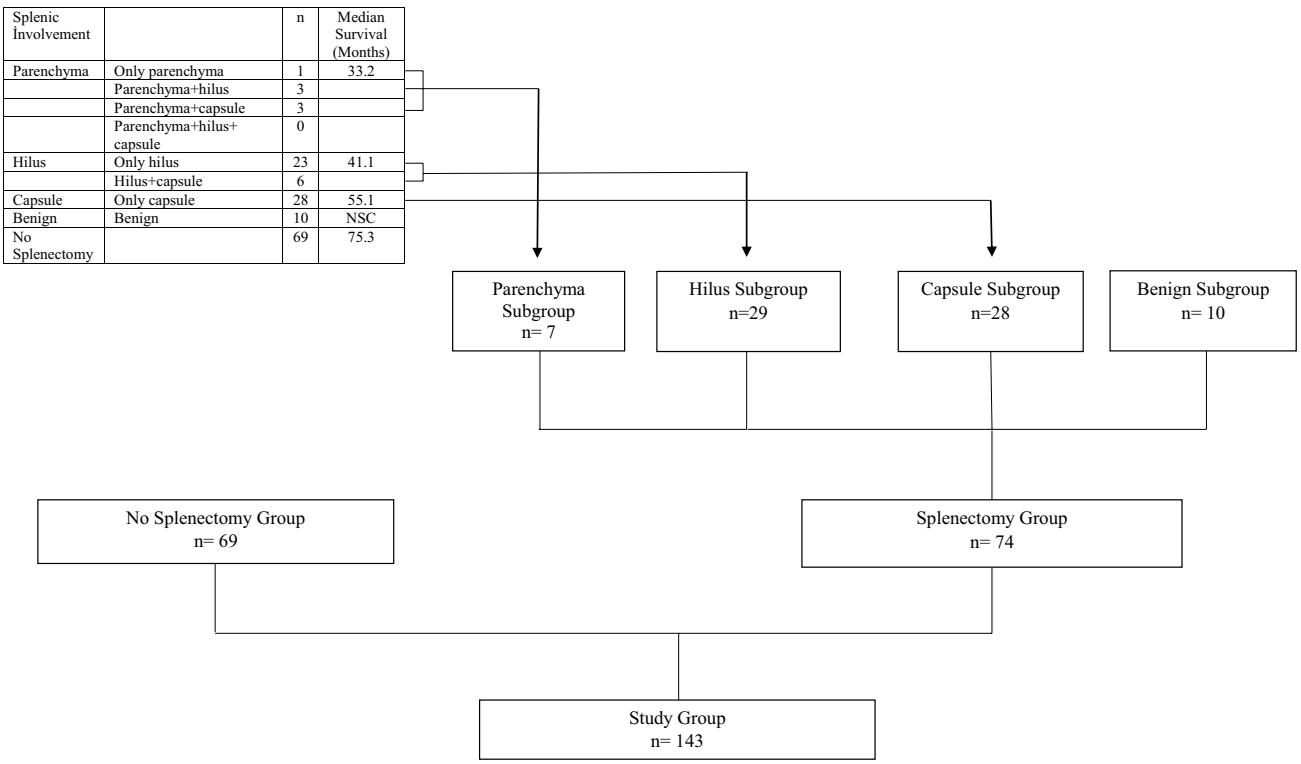

Fig. 1 Study group. *NSC* no statistics calculated

Data were analyzed using the chi-square test and Fisher's exact test for categorical variables, and the independent sample *t* test for continuous variables. Overall survival (OS) was defined as the time from the date of surgery to the date of death or last follow-up. The Kaplan–Meier method was used to estimate survival curves, and differences in survival were analyzed using the log-rank test. Factors found to be significantly associated with survival in previous studies and factors identified by univariate analyses in this study were entered into a Cox regression analysis to determine independent predictors of survival. Differences were considered statistically significant at a p value < 0.05. The statistical software SPSS (version 17.0, SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

Results

Seventy four patients eligible with the inclusion criteria who underwent splenectomy and 69 patients who did not undergo splenectomy were included. The mean age was 53.5 ± 9.1, and the median follow-up time was 39.1 ± 42.9 months. Four patients who had undergone cytoreductive surgery for stage 3C OTP epithelial cancer died within 30 days following surgery and thus were not included in the analyses. Two of the patients had undergone splenectomy, and two had not. For a more accurate evaluation, only patients whose surgery resulted in optimal cytoreduction were included. Cytoreductive surgery resulted in no macroscopic residue for 112 patients (78.3%). For the remaining 31 patients (21.7%), cytoreductive surgery resulted in ≤ 1 cm residual tumor. The median number of resected lymph nodes was 56.0 ± 23.9. The median OS of the study group was 61.4 months.

The study focused on evaluating metastatic patterns of the spleen and their association with survival outcomes in abdomen-confined disease. The splenectomy and the no splenectomy groups showed no statistical differences with regard to age, preoperative serum Ca-125 level, organ of origin, histological subtype, histological grade, presence of ascites, and residual disease. The rate of patients who underwent diaphragm surgery was significantly higher in the no splenectomy group. On the other hand, the rates of patients who underwent distal pancreatectomy, tumor resection from the porta hepatis, and tumor resection from the lesser sac were significantly higher in the splenectomy group (Table 1).

According to pathology reports, one patient had splenic parenchymal involvement only, 23 patients had splenic hilar involvement only, and 28 patients had splenic capsular involvement only. Twelve patients had metastases in more than one site of the spleen. The median OS of patients who had only parenchymal, only hilar, and only capsular involvement were 33.2 months, 41.1 months, and 55.1 months, respectively. Patient who had isolated splenic parenchymal metastasis had shorter survival compared with patients who had isolated hilar and isolated capsular involvement. Patients who had splenic parenchymal involvement had already been upstaged to stage 4B in FIGO's 2014 OTP cancer staging modification. Thus, patients who had splenic parenchymal involvement were included in the parenchyma subgroup even if they had hilar or capsular metastases simultaneously. The median survival of patients with splenic hilar involvement only was shorter than that of patients with capsular involvement only. Thus, patients who had both hilus and capsule involvement were categorized in the hilus subgroup. Patients who had splenic capsular involvement only formed the capsule subgroup. There were 7 patients in the parenchyma subgroup, 29 patients in the hilus subgroup and 28 patients in the capsule subgroup. Pathology reports of ten splenectomy specimens indicated the absence of any malignant tissue; thus, those patients were categorized in the benign subgroup (Fig. 1).

The median OS of patients in the hilus subgroup was 41.1 months. The median OS of patients who were not in the hilus subgroup was 65.5 months. Patients in the hilus subgroup showed significantly shorter survival compared with the other patients in the study group ($p = 0.035$) (Fig. 2). Clinicopathological and surgical features of the patients in the hilus subgroup and patients who were not in the hilus subgroup are compared in Table S2. All the clinicopathological and surgical features were similar and there were no statistically significant differences (Table S2).

Survival analyses were performed with regard to FIGO stage, histological subtype, grade, ascites, residual tumor, splenectomy, splenic involvement, splenic parenchymal involvement, splenic capsular involvement and none indicated a statistically significant difference. Patients in the splenectomy group tended to have shorter survival compared with patients in the no splenectomy group; however, there was no statistically significant difference ($p = 0.064$). Similarly, patients who had splenic tumor involvement showed shorter survival compared with those who did not, but analyses did not show a statistically significant difference ($p = 0.088$). The median OS of patients in the capsule subgroup was 55.1 months, versus 66.1 months for patients who were not in the capsule subgroup—the difference was not statistically significant ($p = 0.976$). Seven patients had splenic parenchymal involvement. Patients in the parenchyma subgroup showed the shortest median survival in the study group—33.9 months—compared with 62.1 months for those who were not in the parenchyma subgroup. However, statistical analyses did not show a statistically significant difference ($p = 0.643$) (Table 2).

We performed multivariate analyses for further evaluation of the findings determined in the univariate analyses. Factors identified in the univariate analyses of the current study

Table 1 Clinical, pathological and surgical characteristics of the study group

	Total $n=143$ (%)	No splenectomy group $n=69$ (%)	Splenectomy group $n=74$ (%)	p value
Mean age at diagnosis ± SD	53.5 ± 9.1	54.2 ± 10.1	52.9 ± 8.0	0.410
Mean preoperative Ca-125 (IU/ml) ± SD	1434.9 ± 1453.7	1299.3 ± 1439.3	1568.4 ± 1466.3	0.288
Organ of origin				
Ovary	130 (90.9)	63 (91.3)	67 (90.5)	0.971
Tube	4 (2.8)	2 (2.9)	2 (2.7)	
Peritoneum	9 (6.3)	4 (5.8)	5 (6.8)	
FİGO stage				
3C	136 (95.1)	69 (100)	67 (90.5)	0.014
4B	7 (4.9%)	0 (0)	7 (9.5)	
Histology				
Serous	130 (90.9)	63 (91.3)	67 (90.5)	0.928
Mixt epithelial	5 (3.5)	2 (2.9)	3 (4.1)	
Non-serous	8 (5.6)	4 (5.8)	4 (5.4)	
Grade				
1	16 (11.2)	11 (15.9)	5 (6.8)	0.211
2	41 (28.7)	18 (26.1)	23 (31.1)	
3	86 (60.1)	40 (58.0)	46 (62.2)	
Ascites				
No	45 (31.5)	27 (39.1)	18 (24.3)	0.057
Yes	98 (68.5)	42 (60.9)	56 (75.7)	
Residual disease (cm)				
0	112 (78.3)	58 (84.1)	54 (73.0)	0.108
$>0, \leq 1$	31 (21.7)	11 (15.9)	20 (27.0)	
Procedures performed				
Hysterectomy	140 (97.9)	67 (97.1)	73 (98.6)	0.609
Salpingooopherectomy	142 (99.3)	68 (98.6)	74 (100)	0.483
Omentectomy	143 (100)	69 (100)	74 (100)	NSC
Pelvic lymphadenectomy	140 (97.9)	68 (98.6)	72 (97.3)	0.601
Paraaortic lymphadenectomy	140 (97.9)	68 (98.6)	72 (97.3)	0.601
Appendectomy	121 (84.6)	57 (82.6)	64 (86.5)	0.521
Small bowel resection	14 (9.8)	5 (7.2)	9 (12.2)	0.323
Colon resection	72 (50.3)	33 (47.8)	39 (52.7)	0.560
Diaphragm peritonectomy/resection	130 (90.9)	69 (100)	61 (82.4)	<0.001
Tumor resection from liver capsule	67 (46.9)	27 (39.1)	40 (54.1)	0.074
Distal pancreatectomy	8 (5.6)	0 (0)	8 (10.8)	0.007
Tumor resection from bowel mesenterium	50 (35.0)	25 (36.2)	25 (33.8)	0.759
Tumor resection from morrison's pouch	44 (30.8)	19 (27.5)	25 (33.8)	0.419
Tumor resection from lesser sac	26 (18.2)	6 (8.7)	20 (27.0)	0.005
Tumor resection from omentum minus	58 (40.6)	23 (33.3)	35 (47.3)	0.089
Tumor resection from gastric serosa	17 (11.9)	5 (7.2)	12 (16.2)	0.098
Tumor resection from porta hepatis	27 (18.9)	6 (8.7)	21 (28.4)	0.003

SD standard deviation, *FIGO* International Federation of Gynecology and Obstetrics, *NSC* no statistics calculated

and factors which were reported as predictors of survival in previous studies were entered into a Cox regression analysis. Only the hilus subgroup was associated with a statistically significant increase in mortality risk (hazard ratio 1.971, 95% confidence interval 1.1–3.531) (Table 3).

To evaluate any probable influence of splenectomy and loss of immune function on OS, we compared patients in the benign subgroup with patients in the no splenectomy group. The mean OS of patients in the benign subgroup was 49.3 months. Their median survival was not

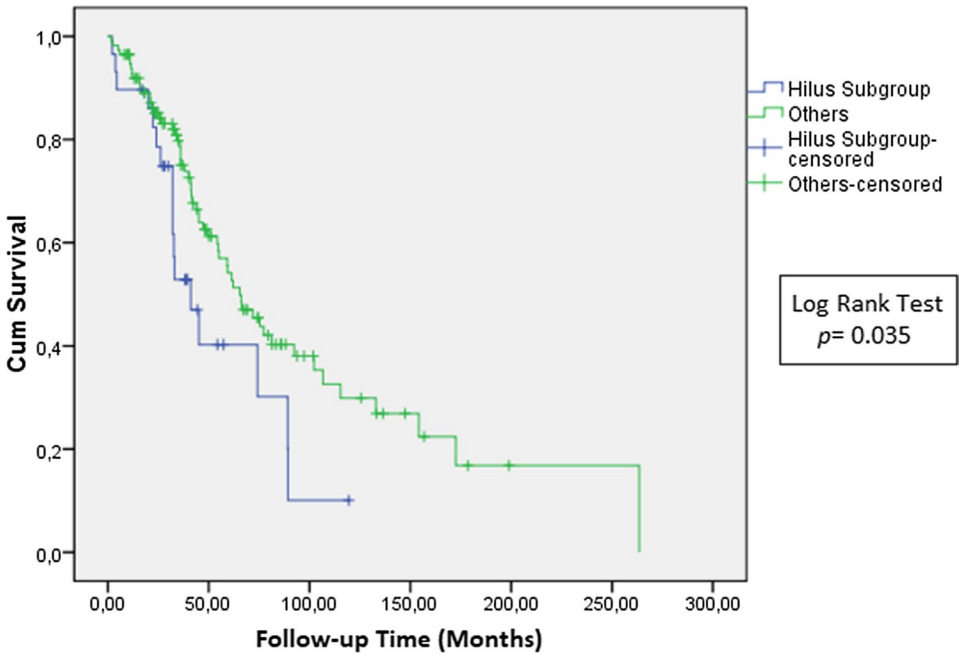

Fig. 2 Comparison of patients in the hilus subgroup with the patients who were not in the hilus subgroup

calculated by SPSS. The median and mean survival periods of patients in the no splenectomy group were 75.3 months and 102.3 months, respectively. There was no statistically significant difference in survival between the two groups ($p=0.374$) (Figure S1).

We displayed surgical outcomes and postoperative complications in Table 4. In the splenectomy group, 41 of the 74 patients (55.4%) developed a postoperative complication. In the no splenectomy group, 29 of the 69 patients (42.0%) developed a postoperative complication ($p=0.110$). The mean hospital stay of patients in the splenectomy group was significantly longer than that of patients in the no splenectomy group ($p=0.015$). The rate of patients who developed pneumothorax was significantly higher in the no splenectomy group than in the splenectomy group ($p=0.011$). Complications attributed to splenectomy were portal vein thrombosis and pancreatic leak/fistula [18–20]. In the splenectomy group, one patient (1.4%) developed a portal vein thrombosis, and three (4.1%) developed pancreatic fistulas (Table 4). The patient with portal vein thrombosis was successfully treated with heparinization. All three patients who developed a pancreatic leak/fistula were successfully managed in a conservative manner.

Discussion

Our results revealed the significance of splenic involvement patterns and their association with survival among patients who had advanced OTP epithelial cancer and expansion to the upper abdomen. In the current study, splenic hilar metastasis was a significant prognostic factor, associated with shorter survival. Splenic capsule metastasis did not affect survival outcomes.

In the current investigation, patients with splenic parenchymal metastasis showed shorter survival compared with patients who had hilar or capsular metastasis. Seven patients (4.9%) had splenic parenchymal metastases; because of this low number, statistical analyses did not show any significant difference with regard to survival. Magtibay et al. reported on 112 patients with epithelial ovarian cancers who had undergone splenectomy. Of those patients, 66 had undergone primary cytoreductive surgery, and 46 had undergone secondary cytoreductive surgery. Any patient from stages 1 to 4 was included in both the primary and secondary cytoreductive surgery groups. In the primary cytoreductive surgery group, seven patients had splenic parenchymal metastasis. The authors reported that disease involving splenic parenchyma was not associated with a more unfavorable prognosis [16]. Tanner et al. studied 576 patients with FIGO stage 3B-4 epithelial OTP cancer. Splenectomy was performed in 97 patients, and splenic parenchymal involvement was reported in 20 patients. Of the 20 patients with splenic parenchymal metastases, 6 had other evidence of stage 4 disease. The median OS periods of patients with and without splenic parenchymal metastasis were 28.5 months and 49.9 months, respectively. They reported that splenic parenchymal metastasis was an independent risk factor for poor prognosis in patients with advanced epithelial OTP cancer [13]. The new FIGO staging guideline for OTP cancer was approved by the FIGO Executive Board in 2012 and published in 2014. FIGO upstaged patients with splenic parenchymal metastasis

Table 2 Survival analyses

	Median survival (months) [95% CI]	*p* value
FIGO stage		
3C	62.1 [45.6–78.6]	0.643
4B	33.9 [0–71.0]	
Histology		
Serous	65.5 [47.5–83.4]	0.278
Mixt epithelial with serous component	32.1 [8.5–55.7]	
Non-serous	54.3 [24.8–83.8]	
Grade		
1	66.1 [32.6–99.6]	0.761
2	45.2 [22.5–67.9]	
3	62.1 [51.1–73.1]	
Grade		
Low grade (grade 1)	66.1 [32.6–99.6]	0.978
High grade (grades 2 and 3)	61.4 [45.9–76.9]	
Splenectomy group vs. no splenectomy group		
Splenectomy group	45.2 [27.9–62.5]	0.064
No splenectomy group	75.3 [59.9–90.6]	
Any splenic involvement vs. no splenic involvement		
Any splenic involvement	45.2 [29.6–60.8]	0.088
No splenic involvement	71.8 [54.4–89.2]	
Splenic parencyma subgroup vs. others		
Parenchyma subgroup	33.9 [0–71.0]	0.643
Others	62.1 [45.6–78.6]	
Splenic hilus subgroup vs. others		
Hilus subgroup	41.1 [25.9–56.3]	0.035
Others	65.5 [50.5–80.4]	
Splenic capsule subgroup vs. others		
Capsule subgroup	55.1 [32.8–77.4]	0.976
Others	66.1 [47.9–84.3]	
Ascites		
Yes	66.1 [48.3–83.9]	0.330
No	59.2 [27.7–90.6]	
Residual tumor (cm)		
R = 0	71.8 [56.1–87.5]	0.167
R > 0, R ≤ 1	43.7 [35.9–51.4]	

CI confidence interval, vs. versus, *R* residue

Table 3 Multivariate survival analyses

Factor	HR	95% CI	*p* value
Age	0.983	0.955–1.012	0.245
Grade 1 vs. grade 2–3 (ref.: grade 1)	0.766	0.367–1.597	0.476
Splenic parenchyma subgroup vs. other patients (ref.: other patients)	1.384	0.478–4.002	0.549
Splenic hilus subgroup vs. other patients (ref.: other patients)	1.971	1.1–3.531	0.023
Ascites present vs. absent (ref.: present)	1.556	0.914–2.651	0.104
Residue tumor R = 0 cm vs. R ≤ 1 cm (ref.: R = 0 cm)	1.574	0.898–2.757	0.113

HR hazard ratio, *CI* confidence interval, *Ref.* reference, *vs.* versus

Table 4 Surgical outcomes of the study group

	No splenectomy group $n=69$ (%)	Splenectomy group $n=74$ (%)	p value
Mean hospital stay (days) ± SD	11.5 ± 7.6	16.1 ± 9.8	0.015
Mean time interval from surgery to chemotherapy (days) ± SD	16.5 ± 8.9	19.8 ± 11.1	0.16
Mean intraoperative blood loss (ml) ± SD	668.2 ± 701.6	905.8 ± 869.1	0.309
Mean operation time (mins) ± SD	314.4 ± 40.6	328.1 ± 63.8	0.355
Need for intensive care unit	8 (11.6)	17 (23.0)	0.073
Pleural effusion	14 (20.3)	19 (25.7)	0.445
Pneumonitis	2 (2.9)	3 (4.1)	0.707
Atelectasis	11 (15.9)	6 (8.1)	0.148
Pneumothorax	6 (8.7)	0 (0)	0.011
Pulmonary emboly	0 (0)	1 (1.4)	0.333
Myocard infarctus	0 (0)	1 (1.4)	0.333
Deep vein thrombosis	0 (0)	1 (1.4)	0.333
Portal vein thrombosis	0 (0)	1 (1.4)	0.333
Acute cerebrovascular disease	2 (2.9)	0 (0)	0.231
Chylous ascites	3 (4.3)	3 (4.1)	0.930
Anostomosis leak	4 (5.8)	4 (5.4)	0.919
Sepsis	0 (0)	2 (2.7)	0.497
Subphrenic abscess	0 (0)	2 (2.7)	0.497
Intraabdominal abscess	0 (0)	4 (5.4)	0.121
Wound dehiscence	7 (10.1)	9 (12.2)	0.702
Evisceration	3 (4.3)	8 (10.8)	0.211
GIS fistula	1 (1.4)	4 (5.4)	0.368
Ileus	0 (0)	4 (5.4)	0.121
Gastric perforation	1 (1.4)	1 (1.4)	0.960
Pancreatic leak/fistula	0 (0)	3 (4.1)	0.246
Any complication	29 (42.0)	41 (55.4)	0.110
Perioperative mortality	2 (2.9)	2 (2.7)	0.943

GIS gastrointestinal system, *SD* standard deviation

to stage 4B in the staging modification [21, 22]. Bacalbasa et al. evaluated 66 patients with stage 3C-4 OTP epithelial cancer who had undergone splenectomy. Of these patients, 19 had splenic parenchymal involvement. The median OS periods of patients with splenic parenchymal involvement and peritoneal seeding were 24.5 months and 58.4 months, respectively. Parenchymal metastasis was associated with significantly shorter survival ($p=0.0126$). In that study, 11 patients had non-splenic parenchymatous visceral involvement, such as of the liver or pancreas [15].

Reported rates of splenic parenchymal involvement vary between 0% and 28.8% among patients who underwent splenectomy within the context of primary cytoreductive surgery [15, 23–25]. Of the 64 patients with splenic metastases in our study, 7 had splenic parenchymal metastases. During the study period, three cases who had splenic parenchymal metastases were excluded from the study group, because they met the exclusion criteria (two had thorax metastases, and one had hepatic parenchymal metastasis). We included only stage 3C patients and excluded hepatic parenchymal and extra-abdominal metastases to assess the survival impact of splenic involvement patterns more objectively. In previous studies, significant proportion of patients with splenic parenchymal metastases had additional negative prognostic factors (extra-abdominal metastases and/or other visceral parenchymal metastases), simultaneously [13, 15]. In the study period, three of ten patients with splenic parenchymal metastases treated in our institution were already upstaged, because of thorax or hepatic parenchymal metastases and were excluded from the current study. According to the currently available literature, splenic parenchymal metastasis is associated with poorer survival, but can provide additional prognostic information for a limited number of patients. The survival outcomes of patients who had splenic parenchymal metastases without hepatic parenchymal and/or extra-abdominal metastases should be further evaluated with larger number of patients.

Most previous studies did not assess survival outcomes with regard to site of involvement (capsule, hilus, parenchyma). Studies reported rate of patients with hilar involvement between 15.9 and 65% [13, 15–17, 23, 25]. Bacalbasa et al. evaluated 66 patients with stage 3C-4 epithelial OTP cancer who had undergone splenectomy within the context of primary cytoreductive surgery. Twelve of them had tumors involving the splenic hilus. The median OS for cases with peritoneal seeding was 58.4 months, while that for those with parenchymatous involvement was 24.5 months. Patients diagnosed with hilar involvement had a median OS of 40.6 months. Patients with hilar involvement had shorter survival, but statistical analyses did not indicate a significant difference ($p=0.457$) [15]. In our study, we included 29 patients in the hilus subgroup, and their median survival was 41.1 months. The median OS of patients who were not in the hilus subgroup was 65.5 months. Patients in the hilus subgroup showed significantly shorter survival compared with patients who were not in the hilus subgroup ($p=0.035$). Both univariate and multivariate analyses showed that hilar involvement predicts worse survival outcomes among patients with advanced epithelial OTP cancer whose disease was limited to abdomen. According to the current study and many published studies, hilar involvement had a higher incidence than parenchymal involvement [13, 16, 23, 25]. Thus, hilar involvement would be a beneficial clinical predictor of survival for larger number of patients compared with parenchymal involvement.

McCann et al. reported on 44 patients with stage 3–4 ovarian epithelial cancer who had undergone a splenectomy and 171 patients who had not. The median OS in the group not requiring a splenectomy was 41 months, compared with 30 months in the splenectomy group, among patients who were optimally debulked ($p=0.045$). However, the rate of stage 4 patients was higher in the splenectomy group compared with the no splenectomy group (34% vs. 19%, $p=0.03$). The authors commented that the addition of splenectomy to up-front cytoreductive surgery was related to a worse prognosis, which may be related not only to innate tumor biology, but also to immunologic properties that are affected once the spleen is removed. To analyze the effect of splenectomy-related immunity loss with regard to survival, we compared patients in the benign subgroup with patients in the no splenectomy group. Our results showed no significant difference in terms of survival ($p=0.374$).

The major limitations of the current study are its retrospective design and low number of patients with splenic parenchymal metastases. The median OS was shortest in the parenchyma subgroup, but analyses did not indicate statistical significance, because of the low number of patients with parenchymal involvement. The inclusion of patients with disease expansion to the upper abdomen, but not to the spleen in the no splenectomy group was an advantage of the current study and supported the comparison of patients who underwent splenectomy with patients who did not. The number of patients with splenic hilar involvement was adequate to show poorer survival outcomes when the splenic hilus was involved with the disease. The exclusion of patients with hepatic parenchymal involvement and/or distant metastases prevented any doubt with the results.

In conclusion, splenic hilus involvement was associated with poorer survival outcomes among patients with advanced OTP epithelial cancer whose disease was limited to the abdomen. Splenic capsular metastases did not affect prognosis when optimal cytoreduction was achieved. Splenectomy was a safe surgical procedure with low complication rate and it was an acceptable option to facilitate optimal cytoreduction when the spleen was involved.

Author contributions YD: project development, data collection and management, data analysis, manuscript writing/editing. EİB: data collection and management, manuscript writing. ASDÇ: data collection, manuscript writing. FK: data analysis, manuscript writing/editing. NB: data analysis, manuscript writing/editing.

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Compliance with ethical standards

Conflict of interest The authors declare that none of them has any potential conflict of interest with respect to the subject of this manuscript.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Institutional Review Board approval was received for this study. Approval date and number: 22.03.2019/90057706–799-E.213.

Informed consent Signed informed consent for anonymous publication of disease-related information was obtained from each patient.

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