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Video-Assisted Thoracic Surgery in the Primary Management of Advanced Ovarian Carcinoma with Moderate to Large Pleural Effusions: A Memorial Sloan Kettering Cancer Center Team Ovary Study

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Abstract

Objectives—We assessed the utility of video-assisted thoracic surgery (VATS) in defining extent of intrathoracic disease in advanced ovarian carcinoma with moderate-to-large pleural effusions.

Methods—Beginning in 2001, VATS was performed on all patients with suspected advanced ovarian carcinoma and moderate-to-large pleural effusions, evaluating for macroscopic intrathoracic disease. The algorithm recommended primary debulking surgery (PDS) for ≤ 1 cm, neoadjuvant chemotherapy (NACT)/interval debulking surgery (IDS) for >1 cm intrathoracic

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disease. We reviewed records of patients undergoing VATS from 10/01–01/19. Differences between treatment groups were tested using standard statistical techniques.

Results—One-hundred patients met eligibility criteria (median age, 60; median CA-125 level, 1158 U/mL; medium serum albumin, 3.8 g/dl). Macroscopic pleural disease was found in 70 (70%). After VATS, 50 (50%) underwent attempted PDS (PDS group), 50 (50%) received NACT (NACT/IDS group). Forty-seven (94%) underwent IDS. Median overall survival (OS) for the entire cohort ($n=100$) was 44.5 months (95% CI:37.8–51.7). The PDS group had significantly longer survival than the NACT/IDS group [45.8 (95% CI:40.5–87.8) vs. 37.4 months (95% CI:33.3–45.2); $p=0.016$]. On multivariable analysis, macroscopic intrathoracic disease (HR 2.18, 95% CI:1.14–4.18; $p=0.019$) and age ≥ 65 (HR 1.98, 95% CI:1.16–3.40; $p=0.013$) were independently associated with elevated death risk. Patients with the best outcome had no macroscopic disease at VATS and underwent PDS (median OS, 87.8 months).

Conclusions—VATS is useful in therapeutic decision-making for PDS vs. NACT/IDS in advanced ovarian cancer with moderate-to-large pleural effusions.

Keywords

Pleural effusion; Pleural disease; Advanced ovarian carcinoma; Primary debulking surgery

INTRODUCTION

Epithelial ovarian cancer (EOC) is the leading cause of death from gynecologic malignancy in the United States. In 2020, an estimated 21,750 women will be diagnosed and 13,940 will die of the disease [1, 2]. Most patients present in advanced stages, which accounts for the high mortality rate [2]. Previous studies have found pleural effusion in 30–48% of those with advanced ovarian cancer at diagnosis [3–6].

The decision to recommend primary debulking surgery (PDS) versus neoadjuvant chemotherapy with interval debulking surgery (NACT/IDS) in patients with pleural effusions is difficult, given the benefits of successful PDS weighed against the theoretical lack of benefit if macroscopic pleural disease (common in women with moderate-to-large effusions) is not removed at PDS [7]. Video-assisted thoracic surgery (VATS) has been safely used in this setting to evaluate for macroscopic pleural disease and, when possible, resect gross tumor [7].

Most patients with pleural effusions have had a chest computed tomography (CT) scan to determine if bulky intrathoracic disease is present, which would preclude an attempt at PDS. However, CT is inaccurate in assessing pleural involvement [8]. Given that the goal of PDS is complete gross resection (CGR), the presence of macroscopic pleural disease—especially if undetected and unresected after PDS—may alter treatment decision-making and markedly affect survival; even in stage IV disease, gross residual tumor is strongly associated with worse survival [5,9]. The objective of this study was to evaluate the frequency with which VATS identifies gross intrathoracic disease in advanced ovarian cancer patients with moderate-to-large pleural effusions, its impact on management, and the survival outcomes

associated with treatment approaches based on the findings at VATS [5, 10, 11]. The study builds on our prior reported experiences [7, 12, 13].

METHODS

This study was approved by our Institutional Review Board. We retrospectively reviewed data from a prospective database of patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) Stage III/IV) ovarian, tubal, or primary peritoneal carcinoma who underwent VATS for initial evaluation of moderate-to-large pleural effusions between 10/2001 and 01/2019. All were considered candidates for attempted PDS depending on VATS findings. Patients undergoing VATS for previously treated disease, or those with bulky pleural or isolated supradiaphragmatic nodal disease on preoperative imaging, or with a malignancy other than ovarian, tubal, or peritoneal carcinoma, were excluded from this analysis. Cases of pleural disease discovered after full-thickness diaphragm resection at time of abdominal PDS were not included if they had not undergone a VATS procedure prior to the laparotomy.

Since 2001, our institutional practice has been to consider VATS for any patient with a pleural effusion occupying one-third or more of the pleural cavity on upright chest radiograph. VATS was exclusively performed by thoracic surgeons at Memorial Sloan Kettering Cancer Center, as previously described [7]. In cases of visible tumor burden, macroscopic disease was histologically proven via biopsy. Patients with residual intrathoracic disease measuring ≥ 1 cm at the end of the VATS procedure were deemed eligible for PDS on the same day or within 4 weeks, at the discretion of the attending thoracic and gynecologic oncology surgeons. Patients with >1 cm intrathoracic residual disease at the end of VATS were deemed ineligible for PDS, and received NACT with the aim of undergoing IDS after 3–4 cycles of chemotherapy. In cases of bilateral moderate-to-large effusions, we performed VATS bilaterally. All patients had at least 12 months of follow-up. Electronic medical records were reviewed to abstract patient demographics, clinicopathological characteristics, and survival data. Complete gross resection (CGR) was defined as no visible disease at completion of surgery; optimal and suboptimal surgical debulking was defined as residual disease of 0.1–1 cm and >1 cm in maximal tumor diameter, respectively. All patients were included in the survival analysis.

Descriptive statistics were provided. The differences between two treatment groups (PDS vs. NACT/IDS) were tested using Fisher's Exact test for categorical variables and the Wilcoxon Rank-Sum test for continuous variables. Overall survival (OS) was defined as the time from the date of VATS to time of death or last follow-up. Median OS, and OS at 3 years, were estimated using the Kaplan-Meier method. The Log-rank test was applied to identify the association between prognostic clinical variables and OS in univariable analyses. Due to the time-dependent nature of treatment groups and variables after time zero (i.e. abdominal surgery residual), landmark analysis was applied. Appropriate landmark times were used when dealing with different time-dependent variables. A multivariable Cox Proportional Hazards model for OS was built based on the findings of univariable analyses, and considering the correlation of treatment group (PDS and NACT/IDS) and macroscopic pleural disease. Stastical analyses were performed using SAS 9.4.

RESULTS

One hundred consecutive patients met the study criteria during the study period. Demographics and clinicopathological findings are presented in Table 1. In the entire cohort ($n=100$), VATS identified no macroscopic disease in 30 patients (30%) (Figure 1). Of the 70 patients with macroscopic disease at VATS, tumor lesions of 0.1–1cm were identified in 24/70 (34%); tumors >1cm were found in 46/70 (66%). Pleural cytology was performed preoperatively or at the time of VATS in 96 patients (96%), was positive in 75/96 (78%) and negative in 21/96 (22%). Six of the 21 patients (29%) with negative pleural cytology had macroscopic disease at VATS and were upstaged to stage IV disease, based solely on the findings at VATS. Outcomes of VATS are shown in Supplementary Table S1. The median time for VATS was 39 min (range: 8–96). No major complications or delays in planned therapy occurred in the entire cohort ($n=100$). At the end of VATS 34 patients (34%) received at the discretion of the attending thoracic surgeon additional talc pleurodesis to prevent recurrent pleural effusions; in (21%) a pleur-x® catheter was placed, and in 45 (45%) a regular chest tube.

Management after the VATS procedure for all 100 patients is shown in Figure 1. Twenty-four of the 30 patients (80%) without macroscopic intrathoracic disease, 20 of the 24 (83%) with gross intrathoracic disease of 0.1–1cm, and 6 of the 46 (13%) with initial gross intrathoracic disease >1cm underwent PDS. Thirteen of the 70 patients (19%) with gross intrathoracic disease identified at VATS underwent intrathoracic cytoreduction at the time of VATS; complete resection of all visible intrathoracic disease was achieved in 8 (62%). Of the 60 patients who were found to have no gross or gross intrathoracic disease of 0.1–1 cm, 10 (no gross $n=6$; gross 0.1–1.0 $n=4$) underwent NACT/IDS due to individualized decision by the gynecologic oncologist ($n=7$), or unresectable disease noted at abdominal laparoscopy after VATS ($n=3$).

After VATS, 50 patients (50%) underwent PDS (PDS group), and 50 (50%) had NACT with intention to perform IDS after 3–4 chemotherapy cycles (NACT/IDS group). In the PDS group, 21 patients (42%) had abdominal debulking at the time of VATS, and 29 (58%) within 4 weeks. In the NACT/IDS group, 47 patients (94%) went on to IDS, and 3 patients (6%) did not. Two patients progressed while on NACT and 1 patient declined IDS after having a complete clinical response to chemotherapy. There was no difference with respect to demographics and clinicopathological characteristics between the two treatment groups, except for residual disease status after abdominal cytoreduction. The PDS group had a CGR rate of 38% (19/50), compared to 64% (30/47) for the NACT/IDS group ($p=0.03$).

Median OS for the entire cohort ($n=100$) was 44.5 months (95%CI: 37.8–51.7). Median follow-up for all survivors was 45.8 months (95%CI 12.2–181.9), with a median follow-up of 61.9 months (95%CI 12.2–181.9) and 35.8 months (95%CI 14.3–89.2) for patients treated with PDS and NACT/IDS, respectively. Patients in the PDS group had significantly longer survival compared with the NACT/IDS group [45.8 months (95%CI 40.5–87.8) vs. 37.4 months (95%CI 33.3–45.2) $p=0.016$] (Table 2). Other factors significantly associated with shorter OS on univariable analysis were macroscopic versus no macroscopic pleural disease at VATS [38.6 months (95%CI: 34.6–44.5) vs. 83.7 months (95%CI: 46.3–106.6); $p=0.007$]

and age ≥ 65 yrs. vs. <65 yrs. [35.5 months (95%CI: 32.5–52.6) vs. 46.3 months (95%CI: 42.6–63.1); $p=0.03$] (Table 2). Notably, in patients with intrathoracic disease, OS was similar between the PDS and NACT/IDS groups [40.5 months (95%CI 29.5–45.5) vs. 37.4 months (95%CI 31.4–45.1); $p=0.717$, subset analysis] (Supplementary Figure S1), whereas PDS was associated with improved survival in patients without macroscopic pleural disease, compared with NACT/IDS [87.8 months (45.8–159.5) vs. 45.2 months (5.7–77.5); $p=0.047$, subset analysis].

On multivariable analysis, both macroscopic pleural disease found at VATS (HR 2.182, 95%CI 1.139–4.182; $p=0.019$) and age ≥ 65 yrs. (HR 1.982, 95%CI 1.157–3.396; $p=0.013$) were independent prognostic factors of decreased survival (model that did not take interaction into account, not shown). However, as further treatment (PDS or NACT/IDS) was strongly correlated with findings of macroscopic intrathoracic disease, we accounted for this interaction in the multivariable model reported in Table 3. In the PDS group we observed a highly elevated risk of death among patients with macroscopic pleural disease [HR: 2.68, 95%CI 1.28–5.62]; in patients treated with NACT no difference between treatment groups was observed [HR: 1.26, 95%CI 0.44–3.63].

To better understand the impact on survival of abdominal residual disease after cytoreduction in relation to the findings at VATS, we analyzed the outcomes of patients in relation to findings at VATS and abdominal residual disease status after debulking (Supplementary Figure S1). No macroscopic disease at VATS, and CGR at abdominal debulking ($n=11$) were associated with the best oncologic outcome, with median OS of 80.9 months (38.9–NE) and 3-year OS rate of 100%. Patients with no evidence of macroscopic disease at VATS who had gross residual disease after PDS or IDS ($n=17$) had a median OS of 50.5 months (95%CI 11.8–98.5) and 3-yr. OS rate of 77% (95%CI 49–90). Evidence of both macroscopic pleural disease at VATS and gross disease after PDS or IDS ($n=30$) was associated with the worst outcome, with median OS of 26.5 months (95%CI 21–34.6) and 3-yr. OS rate of only 29% (95%CI 14–46).

To evaluate the benefits of intrathoracic cytoreduction, we compared the OS of patients in the PDS cohort showing no evidence of macroscopic disease at VATS ($n=24$) versus those undergoing complete intrathoracic debulking with no visible intrathoracic residual disease ($n=9$) versus those with gross intrathoracic residual disease ≥ 1 cm ($n=17$). Although the numbers are small, median OS was very favorable for patients without intrathoracic disease: 87.8 months (95%CI 45.8–159.5). Patients with or without complete intrathoracic debulking showed similar OS: 40.5 (95%CI 29.5–NE) and 41.5 months (95%CI 25.6–45.5), respectively. However, of the 9 patients with complete resection of intrathoracic metastasis, 6 (67%) also had a CGR of abdominal disease at PDS, leading to an improved median OS of 54 months, with 2 patients still alive at >5 years of follow-up.

DISCUSSION

For patients with EOC, FIGO stage is considered to be one of the main prognostic factors [2, 14]. Other prognostic factors include age, presence of ascites, low serum albumin, and the amount of residual disease after surgery [15]. Approximately 10% of patients presenting

with advanced EOC will have stage IV disease. The benefit of cytoreductive surgery in patients with malignant pleural effusions compared with other stage IV disease criteria has been explored previously [14, 16–21]. In a large retrospective Gynecologic Oncology Group (GOG) study of 360 patients with stage IV EOC undergoing PDS followed by six cycles of platinum/paclitaxel, Winter et al. demonstrated that residual tumor was highly associated with recurrence-free survival and OS [5]. Nearly half of the patients (47.8%) in this study had evidence of pleural effusions. Interestingly, patients with pleural effusions experienced decreased survival relative to patients with other distant metastatic sites of disease such as supraclavicular/axillary lymphadenopathy, parenchymal lung metastases or mediastinal lymphadenopathy (HR=1.73; 95% CI: 1.17–2.54; $p=0.006$). As was subsequently hypothesized by Eitan et al., the poor prognosis of patients with pleural effusions who underwent PDS in the study by Winter et al. may be related to undiagnosed and unresected pleural-based disease in those who were thought to have undergone “optimal” cytoreduction [3]. The benefit of diagnosing and resecting intrathoracic metastatic disease was demonstrated by Cowan et al., who reported on clinical outcomes of 54 patients with advanced EOC undergoing resection of enlarged cardiophrenic lymph nodes (CLPN) at the time of PDS [22]. In 51 of the 54 patients (94%) there was positive metastatic nodal involvement, with a median OS of 72 months for patients with CGR and 69 months for patients cytoreduced to ≤ 1 cm residual disease.

In our study, macroscopic intrathoracic disease was identified in 70% of patients, and its presence was an independent predictor of worse survival. In an age of personalized medicine, this knowledge seems crucial in making the decision to assign patients to PDS versus NACT/IDS. If one assumes that all patients with moderate-to-large pleural effusions have macroscopic disease and should be treated with NACT/IDS, 30% will be deprived of the benefits of PDS and the associated median OS of 87.8 months, as seen in our subset of patients with no intrathoracic disease who underwent PDS. Alternatively, if one assumes that all patients with moderate-to-large pleural effusions do not have macroscopic intrathoracic disease or that the macroscopic intrathoracic disease is clinically insignificant and they should be treated with PDS, many will undergo extensive abdominal surgical procedures to attain CGR or “optimal” abdominal cytoreduction, but their OS will not be improved (it appears to be no different than if they were triaged to NACT/IDS) (Supplementary Figure S1). This is consistent with the findings of Eitan et al. and Winter et al. [3, 5].

An alternative to VATS would be to perform thoracentesis and triage patient management based on the cytology. However, in our study, 16% of patients (12/75) with positive pleural cytology did not have macroscopic intrathoracic disease; more importantly, 29% of cases (6/21) with negative pleural cytology were found to have macroscopic intrathoracic disease at VATS. Therefore, pleural cytology is not an accurate or reliable tool in primary decision management.

Although complete resection of all visible disease in the abdominal cavity has been proven to be a major independent prognostic factor for improved survival in advanced ovarian cancer, we cannot make any definitive statements regarding the benefits of intrathoracic cytoreduction in patients with macroscopic disease at VATS. This is due to the fact that only 6 patients in our study were found to have macroscopic intrathoracic disease and had it

completely resected, then went on to CGR of intra-abdominal disease at PDS. While their OS appears improved, compared to all other subsets with macroscopic intrathoracic disease, the small number precludes definitive conclusions. However, the benefits of CGR in both the intrathoracic and intra-abdominal cavities makes sense intuitively, especially considering the excellent survival shown by Cowan et al. following removal of metastatic CPLNs, and the fact that there is probably a significant number of patients during the time of our study who underwent full-thickness diaphragm resection, and had pleural disease resected with the diaphragm as part of a PDS CGR with extended OS, but were not included in our study because they did not have a VATS prior to the PDS [23, 24].

Our study has several limitations, including its small sample size and the biases inherent in a retrospective review. The study covered a long time period of 18 years, spanning the introduction of new therapies such as bevacizumab, PARP-inhibitors, and other targeted treatments [25, 26]. However, these therapies had no effect on the decision regarding primary treatment (PDS vs. NACT), which was based solely on tumor and patient factors at the initial VATS. The triage of patients to PDS who had no macroscopic disease in the chest is consistent with patient management in numerous other institutions and was not affected by the long time period of the study.

In summary, this study represents the largest analysis of VATS in patients with advanced ovarian cancer. Our results support the use of VATS in the triage of patients with moderate-to-large pleural effusions to PDS versus NACT/IDS. These findings have led us to change our prior management algorithm, last published 10 years ago [12]. In the modified algorithm (**Supplementary Figure S2**), patients who do not have macroscopic intrathoracic disease can be offered PDS. Patients who have intrathoracic macroscopic disease that cannot be resected or ablated should be offered NACT/IDS. The numbers are too small to make any definitive recommendations about intrathoracic cytoreduction; however, if it is being considered, it has benefit only if all macroscopic disease can be eliminated. When intrathoracic cytoreduction was performed, it generally involved limited additional OR time and limited perioperative complications, underscoring its safety and efficacy.

We believe that our findings justify the use of VATS in the management of patients with suspected advanced ovarian carcinoma and moderate-to-large pleural effusions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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HIGHLIGHTS

- Macroscopic intrathoracic disease with moderate-to-large pleural effusions predicts poor survival in advanced ovarian cancer
- Analysis of pleural cytology alone is insufficient to assess macroscopic pleural disease
- Nearly 30% of patients with negative cytology had gross disease at VATS
- In patients with confirmed intrathoracic disease that cannot be debulked, PDS does not improve survival
- Patients with confirmed intrathoracic disease that cannot be completely debulked should be treated with NACT and IDS

Figure 1:
Flow chart of patients with moderate-large pleural effusion stratified findings at VATS and further treatment

Figure 2.
Treatment paradigm for the management of women with suspected advanced ovarian carcinoma and moderate to large pleural effusions

Table 1:

Demographic and clinicopathological findings by treatment groups

Variables	All	PDS	NACT/IDS	<i>p</i> -value*
Whole cohort (<i>n</i>)	100	50	50	
Age at diagnosis (years)				
Median (range)	60 (38–88)	58 (38–78)	61.5 (44–88)	0.078
<65	68 (68%)	35 (70%)	33 (66%)	0.830
65	32 (32%)	15 (30%)	17 (34%)	
ASA status				
2	30 (30%)	17 (34%)	13 (26%)	0.513
3–4	70 (70%)	33 (66%)	37 (74%)	
BMI (kg/m²)				
Median (range)	25.6 (18.8–48.6)	26.4 (18.8–48.6)	24.9 (19–41.3)	0.251
Race				
White	89 (89%)	45 (90%)	44 (88%)	1.000
Black/Asian/Other	11 (11%)	5 (10%)	6 (12%)	
BRCA status, germline				
Negative	46 (46%)	20 (20%)	26 (26%)	0.164
Positive	17 (17%)	11 (11%)	6 (6%)	
Not tested	37 (37%)	19 (19%)	18 (18%)	
Grading				
Well Differentiated	1 (1%)	1 (2%)	0 (0%)	-
Moderately Differentiated	1 (1%)	1 (2%)	0 (0%)	
Poorly Differentiated	95 (97.9%)	48 (96%)	47 (100%)	
Histology				
HGSOC	98 (98%)	49 (98%)	49 (98%)	-
Mucinous adenocarcinoma	1 (1%)	0 (0%)	1 (2%)	
Endometroid	1 (1%)	1 (2%)	0 (0%)	
Preoperative albumin at VATS (g/dl)				
Median (range)	3.8 (2.3–4.7)	3.7 (2.3–4.7)	3.8 (2.9–4.7)	0.123
Alb<4 g/dl	69 (69%)	37 (74%)	32 (64%)	0.387
Alb ≥ 4 g/dl	31 (31%)	13 (26%)	18 (36%)	
Preoperative CA125 at VATS (U/ml)				
Median (range)	1158(39–20889)	1316 (39–20889)	800 (68–8301)	0.064
CA125<500 U/ml	36 (36%)	14 (28%)	22 (44%)	0.144
CA125 ≥ 500 U/ml	64 (64%)	36 (72%)	28 (56%)	
Residual disease after abdominal debulking				
CGR	49 (50.5%)	19 (38%)	30 (63.8%)	0.025
0.1–1cm	39 (40.2%)	24 (48%)	15 (31.9%)	
>1cm	9 (9.3%)	7 (14%)	2 (4.3%)	

Variables	All	PDS	NACT/IDS	<i>p</i> -value*
Time period				
2001–2010	48 (48%)	29 (58%)	19 (38%)	0.071
2011–2019	52 (52%)	21 (42%)	31 (62%)	

* *p*-values obtained by using Fisher-Exact test for categorical variables and Wilcoxon-rank sum test for continuous variables *p*-values not provided for variables which had certain level less than 5 counts.

PDS, primary debulking surgery; NACT, neoadjuvant chemotherapy; IDS, interval debulking surgery; BMI, body mass index; VATS, video-assisted thoracic surgery; CGR, complete gross resection; HGSOC, high grade serous ovarian cancer; Alb, albumin

Table 2Univariable OS analysis ($n = 100$, events = 69).

Variables	<i>n</i>	events	Median OS (in months; 95%CI)	3-yr OS rate (95%CI)	HR (95%CI)	<i>p</i> -value
All pts	100	69	44.5 (37.8–51.7)	62.8% (52–71.9%)		
Treatment						
NACT/IDS	50	38	37.4 (33.3–45.2)	54.3% (38.7–67.4%)	1	0.016
PDS	50	31	45.5.8 (40.5–87.8)	71.6% (56.1–82.5%)	0.55 (0.33–0.9)	
Age at diagnosis (years)						
>65	68	46	46.3 (38.6–60.8)	68.4% (55.3–78.4%)	1	0.031
65	32	23	35.5 (32–46.3)	49.8% (30–66.9%)	1.75 (1.05–2.93)	
ASA						
2	30	24	46.7 (32.4–65.4)	64.8% (44.4–79.3%)	1	0.518
3–4	70	45	44.5 (35.6–47)	62% (48.7–72.8%)	1.18 (0.71–1.96)	
BRCA status, germline						
Negative	46	25	46.7 (38.6–83.7)	71.6% (54.4–83.2%)	1	0.680
Positive	17	9	47 (37.2–NE)	80.4% (50.6–93.2%)	0.85 (0.4–1.83)	
Preoperative albumin at VATS						
<4 g/dL	69	42	41.7 (34.6–54.3)	59.5% (46–70.7%)	1	0.703
4 g/dL	31	27	46 (38.6–60.8)	70.1% (50.4–83.2%)	1.1 (0.68–1.79)	
Preoperative CA-125 at VATS						
CA125 < 500 U/mL	36	25	39.4 (32.4–51.8)	58.1% (38.7–73.3%)	1	0.097
CA125 ≥ 500 U/mL	64	44	44.6 (37.5–60.8)	65.2% (51.7–75.8%)	0.65 (0.39–1.08)	
Time period						
2001–2010	48	43	37.5 (30.7–51.8)	52.1% (37.2–65%)	1	0.180
2011–2019	52	26	46.3 (39.4–63.8)	74.1% (57.9–84.8%)	0.71 (0.43–1.17)	
Macroscopic pleural disease						
No	30	17	83.7 (46.3–106.6)	79.7% (60.3–90.4%)	1	0.007
Yes	70	52	38.6 (34.6–44.5)	55.8% (42.7–67.1%)	2.15 (1.22–3.79)	
Residual disease after abdominal debulking*						
CCR	47	26	38.9 (31.3–70.6)	57.4% (39.9–71.5%)	1	0.131
Non-CCR	47	37	34.6 (23.9–43.7)	45.3% (30.1–59.3%)	1.47 (0.89–2.44)	

OS, overall survival; PDS, primary debulking surgery; NACT, neoadjuvant chemotherapy; IDS, interval debulking surgery; VATS, video-assisted thoracic surgery; CCR, complete grossresection; pts., patients; BMI, body mass index; HR, hazard ratio; CL confidence interval

* includes all patients (PDS or NACT/IDS) who underwent abdominal debulking.

The bold values are statistically significant.

Table 3

Multivariable analysis (n = 100, events = 69).

Variables	HR	95% CI lower Bound	95% CI Upper Bound	p-value
Age at diagnosis (years): 65 vs. <65	1.961	1.140	3.373	0.015
Interaction of macroscopic pleural disease and treatment group				0.016
Among PDS:				
Macroscopic pleural disease: Yes vs. No	2.684	1–281	5.623	
Among NACT/IDS:				
Macroscopic pleural disease: Yes vs. No	1.256	0.435	3.629	

PDS, primary debulking surgery; NACT, neoadjuvant chemotherapy; IDS, interval debulking surgery; HR, hazard ratio; CI confidence interval