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Diaphragmatic Surgery in Advanced Ovarian, Tubal and Peritoneal Cancer. A 7-Year Retrospective Analysis of the Tumor Bank Ovarian Cancer Network

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Abstract. *Aim: This study aimed to analyze diaphragmatic interventions and their complications in primary cytoreductive surgery (PCS) and to study their impact on attaining complete tumor resection (CTR) in advanced ovarian cancer (AOC), which is purportedly reflected in better disease-free and overall survival. Patients and Methods: The study's collective consisted of 536 consecutive patients presenting a first diagnosis of AOC who underwent PCS between 2007 and 2013 at the Charité Medical University, Berlin. A total of 268 patients underwent diaphragmatic interventions, while 268 did not undergo any kind of diaphragmatic surgery. Results: Diaphragmatic interventions were indicated in 50% of cases with AOC. The surgical interventions varied between diaphragmatic partial resection (44.8%), stripping (53%) and only infrared coagulation (2.2%). The postoperative complication rate was higher in the diaphragm-intervention group in comparison to the group without any diaphragmatic intervention (49.6% vs. 38.8%), but most postoperative complications were not directly related to the diaphragmatic intervention itself but to the statically significant increase of other radical surgical procedures in this group. Pleura effusion was the only increased complication with a direct correlation with diaphragmatic surgery (25.4% vs. 14.2%). Preoperatively apparent stage IV (pleura effusion) disease, very high cancer antigen-125 value, serous papillary tumors and the presence of massive ascites (>500 ml) were statistically significant predictors of the need for diaphragmatic surgery in order to achieve CTR. Conclusion: Our current findings consider diaphragmatic surgery as being acceptable, feasible and in many cases as an essential intervention to achieve CTR or suboptimal debulking with an acceptable complication rate.*

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In advanced ovarian cancer (AOC), most patients present with substantial tumor spread in the upper abdomen (1) and involvement of the diaphragm is one of the most common (18-71%) sites of metastasis (2-4).

Based on accumulated evidence indicating that complete tumor resection (CTR) at primary cytoreductive surgery (PCS) for AOC results in significantly improved prognosis (5-7), there is currently no doubt that surgical attempts should be made to resect all visible tumors (8, 9). This means a greater need to train for and perform radical surgical diaphragmatic procedures.

The aim of our study was to show the outcomes of radical surgical procedures to treat diaphragmatic disease in AOC at our Institute, to analyze their complications and to study their impact on attaining CTR in PCS, which is purportedly reflected in better progression-free (PFS) and overall (OS) survival.

Patients and Methods

In order to identify patients with AOC, we checked our database from the Tumor Bank Ovarian Cancer (www.toc-network.de). This database is a prospective documentation tool which includes clinical data, disease history, tumor spread, presence of ascites, and presence and location of residual tumor mass intra-operatively. These parameters are obtained through an interview with the surgeon immediately after the surgical procedure. All patients undergoing surgery at our Institution due to suspected ovarian malignancy between 2007 and 2013 were reviewed. After the exclusion of patients with non-epithelial ovarian cancer or borderline tumors, patients who underwent only a second-look operation or diagnostic procedure, and those with early stages of epithelial ovarian cancer, we included 268 patients with and 268 patients without

Table I. *Characteristics of 536 patients with advanced ovarian cancer who underwent primary cytoreductive surgery with and without diaphragmatic intervention.*

Characteristic		All patients, n=536 (%)	Diaphragmatic surgery, n=268 (%)	Without diaphragmatic surgery, n=268 (%)	*p*-Value
Median age at first diagnosis (range), years		59 (18-89)	60 (18-89)	58 (20-86)	0.372[a]
Cancer antigen-125, U/ml		446,85	753	198	<0.001
Tumour type	Ovarian	490 (91.4%)	248 (92.5%)	242 (90.3%)	
	Tubal	15 (2.8%)	4 (1.5%)	11 (4.1%)	
	Peritoneal	31 (5.8%)	16 (6%)	15 (5.6%)	
FIGO classification	III	383 (71.5%)	175 (65.3%)	208 (77.6%)	<0.001
	IV	130 (24.3%)	89 (33.2%)	41 (15.3%)	
	Not defined	23 (4.3%)	4 (1.5%)	19 (7%)	
Grading	1-2	139 (25.9%)	74 (27.6%)	65 (24.3%)	
	3	362 (67.5%)	182 (67.9%)	180 (67%)	
	Not defined	35 (6.5%)	12 (4.5%)	23 (8.6%)	
Histology	Serous papillary	459 (85.6%)	249 (92.9%)	210 (78.4%)	<0.001
	Mucinous	6 (1%)	2 (0.7%)	4 (1.5%)	
	Endometrioid	8 (1.5%)	2 (0.7%)	6 (2.2%)	
	Clear cell	6 (1%)	1 (0.37%)	5 (1.9%)	
	Mixed	3 (0.6%)	1 (0.37%)	2 (0.7%)	
	Undifferentiated	4 (0.7%)	0 (0%)	4 (1.5%)	
	Other/unknown	50 (9.3%)	13 (4.9%)	37 (13.8%)	
Ascites	None	198 (36.9%)	69 (25.7%)	129 (48%)	<0.001[b]
	<500 ml	160 (29.9%)	81 (30.2%)	79 (29.5%)	
	>500 ml	175 (32.6%)	117 (43.6%)	58 (21.6%)	<0.001
	Unknown	3 (5.6%)	1 (0.37%)	2 (0.7%)	

FIGO: International Federation of Gynecology and Obstetrics. [a]Mann–Whitney *U*-test; [b]Kendal's tau b.

diaphragmatic surgery who underwent debulking procedures in the sense of primary treatment of ovarian cancer. A total of 536 consecutive patients presenting at first diagnosis of AOC were enrolled. Patients who underwent interval debulking were excluded from this study.

All operations were performed by one of the experienced Gynecological Oncology surgeons.

All patients provided their written informed consent before clinical data were collected. Approval from Charité local Ethics Committee was provided for this study (EK207/2003). The International Federation of Gynecology and Obstetrics (FIGO) classification stages mentioned in this study depended on the old classification before the modification from 2014 (10). All patients included in the study had FIGO stage III or IV.

Perioperative morbidity and mortality were defined as any adverse event occurring within 30 days of surgery. The majority of postoperative complications at our Institution were graded according to Chassagne's glossary for complications of treatment in gynecological cancers (11) and the National Cancer Institute Common Toxicity Criteria version 2.0 (NCI-CTC v2) classification system (12).

The statistical analysis was performed at the Charite Medical University Berlin. All analyses were performed by IBM SPSS Statistics 21.0 (SPSS, Chicago, IL, USA). Data were analyzed by descriptive statistics. Frequency counts and percentages were used to describe categorical variables, and continuous variables were summarized by the median and range. Groups were compared using Chi-square test, Fisher's exact test, Kendall's tau b, and Mann–Whitney *U*-test where appropriate. Medians, and 95% confidence intervals (CI) of PFS and OS were estimated according to the Kaplan–Meier method. PFS was defined as the length of time between the end of the last chemotherapy cycle to the occurrence of the relapse. OS was determined as the length of time between the date of first diagnosis and the date of death or end of follow-up. Log-rank test statistics for analysis of the equality of survival distribution were performed. Statistical significance was defined by $p<0.05$ and two-sided tests were applied.

Results

Patient characteristics of the entire cohort are summarized in Table I. Using the old FIGO staging system, 71.5% of patients had stage III and 24.3% had stage IV disease at first diagnosis. The rate of stage IV disease was doubled (33.2%) in the group of patients with diaphragmatic surgery *versus* those without (15.3%) ($p<0.001$). Most patients had primary ovarian cancer (91.4%). Using the old FIGO staging system, 71.5% of patients had stage III and 24.3% had stage IV disease at first diagnosis. The rate of stage IV disease was double (33.2%) in the group, which underwent diaphragmatic surgery *versus* that without (15.3%) ($p<0.001$). Most patients (85.6%) had serous papillary tumors; the rate was significantly higher in the diaphragmatic surgery group in comparison to the group without

Table II. *Surgical characteristics in all advanced ovarian cancer cases.*

Characteristic		All patients, n=536 (%)	Diaphragmatic surgery, n=268 (%)	Without diaphragmatic surgery, n=268 (%)	*p*-Value
Residual tumor	No residual	354 (66%)	176 (65.7%)	178 (66.4%)	
	<10 mm	122 (22.8%)	73 (27.2%)	49 (18.3%)	
	≥10 mm	52 (9.7%)	17 (6.3%)	35 (13%)	
	Unknown	8 (1.5%)	2 (0.7%)	6 (2.2%)	
Median operation duration (range), min		265 (30-592)	282.5 (30-592)	244 (30-540)	<0.001[a]
Bowel resection		318 (59.3%)	191 (71.3%)	127 (47.4%)	<0.001[a]
Atypical liver resection		12 (2.2%)	8 (3%)	4 (1.5%)	
Partial resection of liver capsule		63 (11.8%)	49 (18.4%)	14 (5.2%)	<0.001
Cholecystectomy		40 (7.5%)	27 (10.1%)	13 (4.9%)	0.03
Splenectomy		86 (16%)	65 (24.3%)	21 (7.8%)	<0.001
Stomach partial resection		8 (1.5%)	7 (2.6%)	1 (0.4%)	0.068
Lung partial resection		1 (0.2%)	1 (0.4%)	0	
Anus praetor		71 (13.2%)	36 (13.4%)	35 (13.1%)	
Postoperative complications		237 (44.2%)	133 (49.6%)	104 (38.8%)	0.04
Thrombo-embolic events		27 (5%)	18 (6.7%)	9 (3.35%)	
Postoperative infection		55 (10.3%)	36 (13.4%)	19 (7%)	0.02
Postoperative sepsis		13 (2.4%)	4 (1.5%)	9 (3.3%)	
Postoperative pneumonia		21 (3.9%)	12 (4.5%)	9 (3.3%)	
Postoperative pleura effusion		106 (19.8%)	68 (25.4%)	38 (14.2%)	0.002
Postoperative lung edema		2 (0.3%)	0	2 (0.6%)	
Postoperative pneumothorax		10 (1.9%)	5 (1.9%)	5 (1.9%)	
Postoperative ileus		18 (3.35%)	10 (3.7%)	8 (3%)	
Bowel perforation		7 (1.3%)	5 (1.9%)	2 (0.75%)	
Anastomosis insufficiency		17 (3.2%)	12 (4.5%)	5 (1.9%)	
Wound dehiscence		21 (3.9%)	10 (3.7%)	11 (4.1%)	
Postoperative cardiac arrhythmia		29 (5.4%)	16 (6%)	13 (4.9%)	
Postoperative bleeding		16 (3%)	5 (1.9%)	11 (4.1%)	
Neurologic complications		24 (4.5%)	16 (6%)	8 (3%)	
Postoperative organ failure		18 (3.35%)	8 (3%)	10 (3.7%)	
Postoperative fistula		6 (1.1%)	4 (1.5%)	2 (0.75%)	
30 Day mortality		16 (2.99%)	5 (1.9%)	11 (4.1%)	

[a]Mann–Whitney *U*-test.

diaphragmatic surgery ($p<0.001$). Cancer antigen (CA)-125 was preoperatively measured in 510 patients (95.1%). The median preoperative CA-125 was more than 3-fold higher in the diaphragmatic surgery group compared to the non-diaphragmatic surgery group ($p<0.001$).

The rate of massive ascites (>500 ml) was clearly higher in the diaphragmatic surgery group (43.6%) *versus* the no-diaphragmatic surgery group (21.6%) ($p<0.001$).

CTR was achieved in 66% of all patients. This rate did not differ significantly between the two surgical groups. Sub-optimal debulking was performed in 27.2% of diaphragmatic surgery group and in only 18.3% of the group without diaphragmatic surgery but this difference was not statistically significant. Adding diaphragmatic surgery resulted in a significantly ($p<0.001$) longer surgical time: the median operating time was 282.5 minutes *versus* 244 minutes in the diaphragmatic and non-diaphragmatic surgery group, respectively. The patients in the diaphragmatic surgery group also underwent statistically significantly more resections compared with the non-diaphragmatic surgery group (Table II).

The postoperative complication rate was 49.6% in the diaphragmatic surgery group, all kinds of complications were included, and the rate dropped to 38.8% when no diaphragmatic surgery was performed ($p=0.04$). Postoperative infections were diagnosed in 13.4% of patients in the diaphragmatic surgery group and in only 7% in the non-diaphragmatic surgery group ($p=0.02$). The incidence of postoperative pleura effusion increased statistically significantly in the diaphragmatic surgery group, with 68 patients affected (25.4%) compared to the group of patients who did not undergo any diaphragmatic intervention (38 patients, 14.2%). All perioperative complications are summarized in Table II.

There were only five (1.9%) postoperative deaths in the first 30-day postoperative observation period for the group of with diaphragmatic interventions *versus* 11 (4.1%) deaths in the group of without ($p=0.2$).

Table III. *Characteristics of 268 patients with advanced ovarian cancer who underwent primary cytoreductive surgery with diaphragmatic surgery.*

Characteristic		Diaphragmatic resection, n=120 (44.8%)	Diaphragmatic stripping, n=142 (53%)	Infrared coagulation, n=6 (2.2%)
Median age at first diagnosis (range), years		60 (27-80)	60.5 (18-89)	71 (49-79)
Tumour type	Ovarian	113 (94.2%)	131 (92.3%)	4 (66.7%)
	Tubal	1 (0.8%)	3 (2.1%)	0
	Peritoneal	6 (5%)	8 (5.6%)	2 (33.3%)
FIGO classification	III	75 (62.5%)	98 (69%)	2 (33.3%)
	IV	43 (35.8%)	43 (30.3%)	3 (50%)
	Not defined	2 (1.7%)	1 (0.7%)	1 (16.7%)
Grading	1-2	37 (30.8%)	35 (24.6%)	2 (33.3%)
	3	79 (65.8%)	99 (69.7%)	4 (66.7%)
	Not defined	4 (3.3%)	8 (5.6%)	0
Histology	Serous papillary	112 (93.3%)	132 (93%)	5 (83.3%)
	Mucinous	0	1 (0.7%)	1 (16.7%)
	Endometrioid	0	2 (1.4%)	0
	Clear cell	1 (0.8%)	0	0
	Mixed	1 (0.8%)	0	0
	Undifferentiated	0	0	0
	Other/unknown	6 (5%)	7 (4.9%)	0
Ascites	None	27 (22.5%)	41 (28.9%)	1 (16.7%)
	<500 ml	42 (35%)	37 (26%)	2 (33.3%)
	>500 ml	51 (42.5%)	63 (44.4%)	3 (50%)
	Unknown	0	1 (0. 7%)	0
Residual tumour	No residual	88 (73.3%)	87 (61.3%)	1 (16.7%)
	<10 mm	29 (24.2%)	40 (28.2%)	4 (66.7%)
	≥10 mm	3 (2.5%)	13 (9.2%)	1 (16.7%)
	Unknown	0	2 (1.4%)	0
Median operation duration (range), min		295 (42-592)	282 (30-559)	200 (175-215)
Postoperative complications		58 (48.3%)	71 (50%)	4 (66.7%)
30-Day mortality		1 (0.8%)	2 (1.4%)	2 (33.3%)

FIGO: International Federation of Gynecology and Obstetrics.

The patients who underwent diaphragmatic surgery was divided into three subgroups according to the type of diaphragmatic intervention performed: Diaphragmatic resection (120 patients, 44.8%), *i.e.* complete full thickness resection of diaphragm or any kind of partly diaphragmatic resections; diaphragmatic stripping (142 patients, 53%), *i.e.* diaphragmatic peritonectomy without resection of diaphragmatic muscles; and infrared contact coagulation (six patients, 2.2%) of the peritoneal carcinomatosis on the surface of the diaphragm.

Characteristics of patients with AOC who underwent PCS with diaphragmatic surgery are summarized in Table III. There were no statistically significant differences between the two main subgroups of diaphragmatic surgeries (diaphragmatic resection *versus* diaphragmatic stripping) in terms of patient's age, tumor type, FIGO stage, grading, histological type and ascites.

Diaphragmatic resection was associated with an increased rate of CTR (73.3%) compared to only 61.3% in diaphragmatic stripping ($p<0.001$). The rate of postoperative pneumothorax and pleura effusion was identical in both subgroups of patients.

The 30-day mortality rate was obviously higher in the group of those treated with only infrared contact coagulation (two out of six patients), whereas it dropped to 1.4% and to 0.8% in diaphragmatic stripping and resection, respectively ($p<0.001$).

The median follow-up time was 22 months (range=1-98.4 months). The median PFS was 20 months (95% CI=15.8-24.2 months) in PCS-group without diaphragm surgery *versus* 18 months (95%CI= 16.1-19.9) in the diaphragmatic surgery group. This outcome did not show any difference between the main tow types of diaphragmatic surgery. These results are illustrated in Figure 1.

The median overall survival (OS) was 57.6 months (95% CI= 47.3-67.9 months) in non-diaphragmatic intervention *versus* 43.9 months (95% CI=38.9-48.9 months) in diaphragmatic surgery group ($p=0.188$). The median OS in diaphragmatic resection subgroup was 47.1 months (95% CI=36.9-57.3 months) *versus* 43.9 months in the

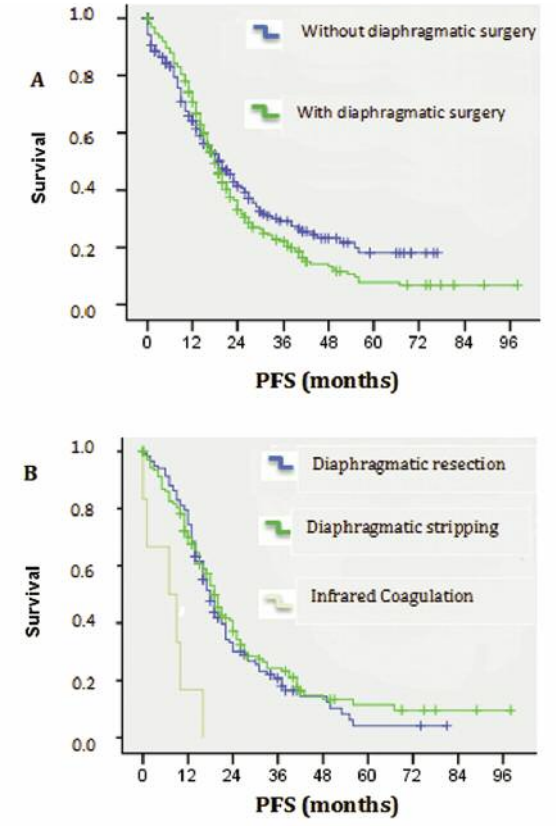

Figure 1. *Progression-free survival (PFS) in patients with advanced ovarian cancer who underwent primary cytoreductive surgery according to performance or not of diaphragmatic intervention (A), and to type of diaphragmatic intervention (B).*

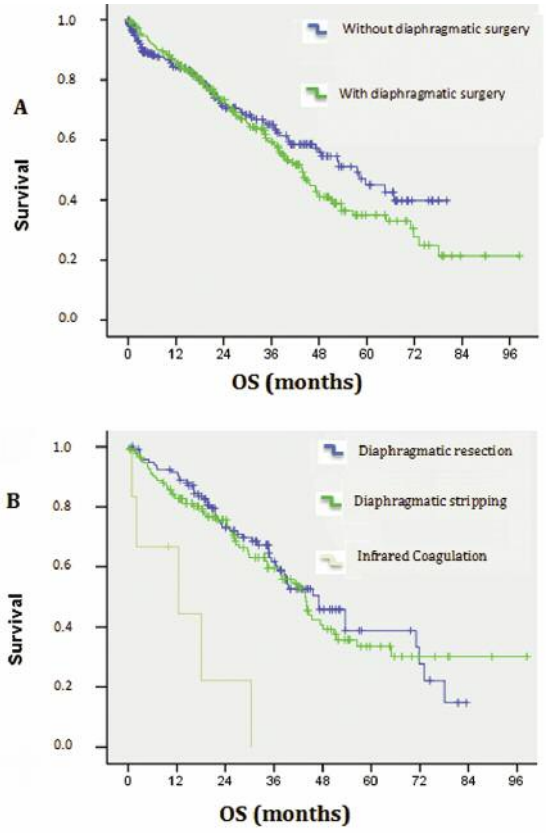

Figure 2. *Overall survival (OS) in patients with advanced ovarian cancer who underwent primary cytoreductive surgery according to performance or not of diaphragmatic intervention (A), and to type of diaphragmatic intervention (B).*

diaphragmatic stripping subgroup (95% CI=38.2-49.6 months) (p=0.63). These results are presented in Figure 2.

The median OS and PFS were 28 and 29 months, and 11 and 15 months in the patients with suboptimally debulked AOC (residual tumor <10 mm) without and with diaphragmatic surgery, respectively (p=0.639 and p=0.296, respectively).

Discussion

In the current study, we analyzed our results for all patients with stage III-IV ovarian cancer who underwent or did not undergo any diaphragmatic surgical intervention at the time of PCS between 2007 and 2013. To the best of our knowledge, this study is largest study of diaphragmatic surgery as a part of PCS for AOC.

In our current series, preoperatively apparent stage IV (pleura effusion) disease, a very high CA-125 value, serous papillary tumors and the presence of massive ascites (>500 ml) were statistically significant predictors of the need for diaphragmatic surgery in order to achieve CTR in the frame of PCS.

Unfortunately, we could not find any other study comparing PCS with and without diaphragmatic surgery, but only series, which studied PCS with different approaches to diaphragmatic surgery as one collective without a control group.

As our debulking operations always aimed to achieve CTR when possible, we found that diaphragmatic surgery was needed in almost half of all patients undergoing PCS. Furthermore, 60% of suboptimally debulked patients (residual tumor <10 mm) needed some kind of diaphragmatic surgery.

Performing a diaphragmatic surgery as a part of PCS correlated in our findings with a statistically significant increase of bowel resection, partial resection of liver capsule, cholecystectomy, splenectomy and partial stomach resection. This did increase the operating time or postoperative complications, but most of these complications were not directly related to the diaphragmatic intervention with only one exception (pleura effusion).

In our study, we noticed longer PFS and OS in the non-diaphragmatic surgery group in comparison to the diaphragmatic surgery group. These results were not

statistically significant and they reflect more the difference between the two groups regarding the distribution of peritoneal carcinosis, which was clearly more massive in the diaphragmatic surgery group.

In our current series, we performed diaphragmatic stripping in 53%, diaphragmatic resection in 44.8% and infrared coagulation in only 2.2% of the patients. Zapardiel *et al*. reported diaphragmatic stripping in 70.5% and full-thickness resection in 29.5% of cases (13). In the study of Tsolakidis *et al*., diaphragmatic disease was coagulated in 22% of patients, stripped in 35%, in 35%, a combination of these techniques was applied, and in 8%, the disease was resected with the adjacent infiltrated part of the diaphragm muscle and the pleura above it (14). We achieved CTR in 73.3% and 61.3% in diaphragmatic resection and stripping groups, respectively. These rates were 63.6% and only 36.7% in the same groups in the study of Zapardiel *et al*. Fanfani *et al*. reported that in their whole study population, optimal residual disease at the end of surgery, defined as residual nodule less than 1 cm, for PCS was achieved (15).

The median OS and PFS in our current study were 47.1 and 43.9 months and 18 and 19 months for diaphragmatic resection and stripping, respectively. Median PFS in the study by Tsolakidis *et al*. was 15, 15, 17 months and median OS was 40, 42, and 50 months for groups of patients treated with coagulation, stripping, and combination stripping with coagulation, respectively (14).

PFS and OS rates were 27.8% and 58.2%, respectively, in the stripping group, and 39.4% and 78.8%, respectively, in the resection group of the study of Zapardiel *et al*. (13). Aletti *et al*. reported a survival advantage for treatment of diaphragmatic disease when considering either all patients with diaphragm disease (53% *vs*. 15%) or only the subset with diaphragmatic disease who were optimally cytoreduced – defined as less than 1 cm of residual tumor (55% *vs*. 28%) (16). For this subgroup of patients, we did not notice this benefit of diaphragmatic surgery in our patients.

Postoperative pleural effusion was the most frequent associated complication (16.9%), followed by pneumothorax (6.6%), and pneumonia (2.2%) in the study by Tsolakidis *et al*. (14). Focusing on complications directly related to diaphragmatic surgery, Chereau *et al*. reported 37% of pleural effusion, 5% of pulmonary embolism, 4% of pneumothorax, and 2% of pulmonary infection (17). Devolder *et al*. reported 59% pleural effusion rate in a group of 69 diaphragmatic surgeries, although none involved full-thickness resection of the diaphragm (18). Postoperative pleura effusion was the most commonly diagnosed complication in the diaphragmatic surgery group of our cohort (25.4%). The incidence of pneumonia and pneumothorax was 4.5% and 1.9%, respectively in the diaphragmatic surgery group, but it did not differ from the incidence rate in the control group. We did not find any statistically significant differences in terms of postoperative complications between the two major types of diaphragmatic surgery. In our series, the infrared contact coagulation group presented a worse complication rate, mortality and survival. This group was too small in our study to reveal any significant results. On the other hand, we tend to perform infrared coagulation only when we believe that achieving a CTR will be impossible or very risky in already morbid patients.

In conclusion, even within the limits of a retrospective study but taking into account the large cohort of patients we had, diaphragmatic surgery at the time of PCS for AOC may be needed in 50% of patients in order to be able to achieve a higher CTR rate. Our current findings support the results of other similar studies considering diaphragmatic surgery as acceptable, feasible and often as an essential intervention in order to achieve CTR or suboptimal debulking.

Conflicts of Interest

The Authors declare no financial or personal conflict of interest.

References

1 Rodriguez N, Miller A, Richard SD, Rungruang B, Hamilton CA, Bookman MA, Maxwell GL, Horowitz NS and Krivak TC: Upper abdominal procedures in advanced stage ovarian or primary peritoneal carcinoma patients with minimal or no gross residual disease: an analysis of Gynecologic Oncology Group (GOG) 182. Gynecol Oncol *130(3)*: 487-492, 2013.

2 Cliby W, Dowdy S, Feitoza S, Gostout B and Podratz K. Diaphragm resection for ovarian cancer: technique and short-term complications. Gynecol Oncol *94(3)*: 655-660, 2004.

3 Griffiths C and Finkler N: Surgery for carcinoma of ovary: extrapelvic cytoreduction. *In*: Gynecologic Oncology. Coppleson M (ed.) London: Churchill Livingstone: pp. 1325-1333, 1992.

4 Rosenoff S, Young R, Chabner B, Hubbard S, De Vita VT Jr. and Schein PS: Use of peritoneoscopy for initial staging and post therapy evaluation of patients with ovarian cancer. Natl Canc Inst Monogr *42*: 81-86, 1975.

5 Eisenhauer EL and Chi DS: Liver mobilization and diaphragm peritonectomy/resection. Gynecol Oncol *104(2)*: 25-28, 2007.

6 Du Bois A, Reuss A, Pujade-Lauraine E, Harter P, Ray-Coquard I, Pfisterer J. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of three prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). Cancer *115(6)*: 1234-1244, 2009.

7 Chang SJ, Hodeib M, Chang J and Bristow RE: Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. Gynecol Oncol *130(3)*: 493-498, 2013.

8 Stuart GC, Kitchener H, Bacon M, du Bois A, Friedlander M, Ledermann J, Marth C, Thigpen T, Trimble E and participants of Fourth Ovarian Cancer Consensus Conference (OCCC); Gynecologic Cancer Intergroup: 2010 Gynecologic Cancer InterGroup (GCIG) consensus statement on clinical trials in ovarian cancer: report from the Fourth Ovarian Cancer Consensus Conference. Int J Gynecol Cancer *21(4)*: 750-755, 2011.

9 Elattar A, Bryant A, Winter-Roach BA, Hatem M and Naik R: Optimal primary surgical treatment for advanced epithelial ovarian cancer. Cochrane Database Syst Rev DOI: 10.1002/14651858.CD007565 [Online August 10, 2011].

10 Staging Announcement: FIGO Cancer Committee. Gynecol Oncol. 25: 383. 1986.

11 Chassagne D, Sismondi P, Horiot JC, Sinistrero G, Bey P, Zola P, Pernot M, Gerbaulet A, Kunkler I and Michel G: A glossary for reporting complications of treatment in gynecological cancers. Radiother Oncol *26(3)*: 195-202, 1993.

12 Arbuck SG, Ivy SP and Setser A: The Revised Common Toxicity Criteria: Version 2.0. CTEP Website. http://ctep.info.nih.gov, 1999.

13 Zapardiel I, Peiretti M, Zanagnolo V, Biffi R, Bocciolone L, Landoni F, Aletti G, Colombo N and Maggioni A: Diaphragmatic surgery during primary cytoreduction for advanced ovarian cancer: peritoneal stripping *versus* diaphragmatic resection. Int J Gynecol Cancer *21(9)*: 1698-1703, 2011.

14 Tsolakidis D, Amant F, Van Gorp T, Leunen K, Neven P, Vergote I: Diaphragmatic surgery during primary debulking in 89 patients with stage IIIB-IV epithelial ovarian cancer. Gynecol Oncol *116(3)*: 489-496, 2010.

15 Fanfani F, Fagotti A, Gallotta V, Ercoli A, Pacelli F, Costantini B, Vizzielli G, Margariti PA, Garganese G and Scambia G: Upper abdominal surgery in advanced and recurrent ovarian cancer: role of diaphragmatic surgery. Gynecol Oncol *116(3)*: 497-501, 2010.

16 Aletti G, Dowdy S, Podratz K and Cliby W: Surgical treatment of diaphragm disease correlates with improved survival in optimally debulked advanced stage ovarian cancer. Gynecol Oncol *100(2)*: 283-287, 2006.

17 Chéreau E, Rouzier R, Gouy S, Ferron G, Narducci F, Bergzoll C, Huchon C, Lécuru F, Pomel C, Daraï E, Leblanc E, Querleu D and Morice P: Morbidity of diaphragmatic surgery for advanced ovarian cancer: retrospective study of 148 cases. Eur J Surg Oncol *37(2)*: 175-180, 2011.

18 Devolder K, Amant F, Neven P, van Gorp T, Leunen K and Vergote I: Role of diaphragmatic surgery in 69 patients with ovarian carcinoma. Int J Gynecol Cancer *18(2)*: 363-368, 2008.

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