EJGO European Journal of Gynaecological Oncology

Original Research

The impact of secondary cytoreductive surgery on survival in first recurrence of platinum sensitive epithelial ovarian cancer

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Summary

Objective: Analyze the effect on survival of secondary cytoreduction surgery (SCS) in treatment of first recurrence platinum-sensitive epithelial ovarian cancer (REOC). *Methods:* Retrospective analysis of patients with first REOC who had platinum time-free interval (TFIp) $>$ 6 months and were treated either with SCS followed by chemotherapy or chemotherapy only (CT). Clinical data such as patient's performance status and number of sites with metastases were specifically assessed. The primary endpoint was overall survival (OS). *Results:* Seventy-one patients were treated either by SCS (n = 37) or CT (n = 34). Complete resection after SCS was achieved in 89% of patients. After a median follow-up of 51.2 months, median OS, and progression-free survival (PFS) were 68.2 and 21.6 months, respectively, for the whole series of the SCS patients had better survival and disease progression survival than the CT only patients (HR: 0.33, 95%CI: 0.17-0.6; p= 0.001) and (HR: 0.28, 95%CI: 0.15-0.5; p= 0.001), respectively. TFIp $<$ 12 months and multiple metastases were most important prognostic factors for risk of death (HR: 7.7 and 6.2, respectively) and recurrence (HR: 5.8 and 3.8, respectively). Probability to undergo successful SCS is related to oligometastatic disease and no residual disease after first surgery (OR: 30.0 and 5.9, respectively). *Conclusions:* In women with REOC oligometastatic disease and no residual disease at first surgery are associated with successful SCS. In these patients oligometastatic disease and long platinum TFI are associated with improved probability of survival.

Key words: Ovarian cancer; Recurrence; Secondary cytoreductive surgery; Survival; Morbidity.

Introduction

Current standard treatment for recurrent epithelial ovarian cancer (REOC) is principally chemotherapy (CT); based on a combination of platinum-containing drugs for those considered platinum-sensitive [1, 2]. Secondary cytoreductive surgery (SCS) has also been considered in patients with progression free interval (PFI) $\geq$ 6 months and limited disease volume, with a survival benefit associated with complete cytoreduction and optimal post-operative chemotherapy.

As with all elective procedures, the benefits of SCS need to be weighed against the risks of morbidity and mortality, so there is need for the identification of factors that will allow us to select the best candidates for SCS [3-7]. Various predictive scores have been developed to accomplish this goal. The AGO score has been the most used worldwide so far [4]. Nevertheless, a high false negative rate of some scores is of concern and additional prognostic factors have been included in the models to try to overcome this limitation [8-14].

Few studies have directly compared the outcomes of REOC patients who underwent SCS to those treated with CT alone. They found a clear benefit of SCS over CT alone, but there are concerns that this benefit may reflect selection bias rather than superiority of SCS [15-18].

Currently, two prospective multicenter randomized surgical trials in platinum-sensitive REOC have been accomplished, the DESKTOP III [19] and GOG 213 [20], with overall survival as the primary end point. The final results of GOG 213 showed that, despite a 67% rate of complete resection in the surgery arm, SCS did not result in longer overall survival than chemotherapy alone [21]. The DESKTOP study results presented at the 2020 American Society of Clinical Oncology meeting showed a clear advantage of overall survival for surgically treated patients. In 74.2% of them a macroscopic complete resection was achieved and overall survival in this subgroup was significantly better compared with patients in the no surgery arm [19].

Objectives

The aim of this study is to identify factors associated with successful SCS. We also aim to compare the outcome of patients who are selected to undergo SCS to those who are treated with chemotherapy only.

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
41, n. 4, 2020
doi: 10.31083/j.ejgo.2020.04.8051

Table 1. — *General characteristics of the patients*

	All (n = 71)	S+CT (n = 37)	CT (n = 34)	*p*
Age in years, mean (range)	59 (24-80)	55.4 (24-80)	62.8 (24-79)	0.01
BMI, mean (range)	26 (18-38)	26.4 (18-37)	25.9 (19-38)	0.6
PFI, mean (range)	33 (6-141)	37.2 (6-141)	26.0 (8-93)	0.1
TFIp, mean (range)	27 (6-129)	33.0 (6-129)	21.3 (7-87)	0.09
No RD 1^{st} surgery, N (%)	49 (100)	31 (63.3)	18 (36.7)	0.009
FIGO stage				
I-II	16 (22.5)	16 (100)	0	0.001
III-IV	55 (77.5)	21 (38.2)	34 (61.8)	0.001
ASA (%)				0.98
1-2	63 (88.7)	33 (89.2)	30 (88.2)	
>3	8 (11.3)	4 (10.8)	4 (11.8)	
ECOG				0.7
0-1	64 (90)	34 (91.9)	30 (88.2)	
≥ 2	7 (10)	3 (8.1)	4 (11.8)	
Histology (of recurrence) n (%)				0.06
Serous	57 (80.3)	25 (43.9)	32 (56.1)	
High grade	41 (73.2)	15 (60.0)	26(83.9)	
Low grade	15 (26.8)	10 (40.0)	5 (16.1)	
Endometrioid	3 (4.2)	2	1	NA
Mucinous	3 (4.2)	2	1	NA
Clear Cell	6 (8.5)	6	0	NA
Mixed/Other	2 (2.8)	2	0	NA
Grade n (%)				0.08
1	10 (14.3)	8 (21.6)	2 (6.1)	
2	13 (18.6)	8 (21.6)	5 (15.2)	
3	47 (67.1)	21 (56.8)	26 (78.8)	
Diagnostic Tool				0.77
CT-scan $\pm$ Ca-125	45 (63.3)	23 (62.2)	2 (5.4)	
PET-CT scan $\pm$ Ca-125	24 (33.8)	12 (34.4)	12 (35.3)	
Biopsy	2 (2.8)	2 (5.4)	0	
Ascites (at diagnosis)				0.2
Yes	5 (7.2)	1 (2.7)	4 (12.5)	
No	66 (92.8)	36 (97.3)	30 (87.5)	
CA-125(log) mean(range)	1.8-(0.6-3.5)	1.6 (0.6-2.7)	1.9 (0.6-3.6)	0.008
CT at recurrence, n (%)				0.1
Carboplatin/paclitaxel	42 (59.2)	26 (70.3)	16 (47.1)	
Carboplatin/paclitaxel	11 (15.5)	6 (16.2)	5 (14.7)	
pegylated doxorubicin	12 (16.9)	3 (8.1)	9 (26.4)	
gemcitabine	6 (8.5)	2 (5.4)	4 (11.8)	
Others***	29 (40.8)	11 (37.9)	18 (62.1)	0.05
Bevacizumab Number of Cycles, median(range)	5.9 (2-12)	6.0 (2-12)	5.9 (3-8)	0.66

S: surgery. CT: chemotherapy. PFI: Progression-free interval. TFIp: Platinum treatment-free interval.

Methods

From January 2000 to December 2014, 180 recurrent ovarian cancer patients came to our institution seeking treatment. After Institutional Review Board approval was obtained (UNAV2018.007), seventy-one (39%) patients who were platinum sensitive (> 6 months from the last cycle of CT to progression) and had good performance status (ASA $\leq$ 3/ECOG < 2) and who underwent SCS or CT alone were considered as eligible for this study.

According to our institution's criteria derived from studies published during the late nineteen-nineties [5], candidates for surgery had to be oligometastatic (< 4 metastatic lesions), either within the abdomen (intra- or retroperitoneally) or out of the abdomen (inguinal recurrence, cardiophrenic, supraclavicular, pulmonary or hepatic, among others) if risk/benefit was considered proportionate. Whereas candidates for CT alone were those who had > 4 metastatic sites or the risk for surgery was consid-

Table 2. — *Characteristics of the recurrences*

	All (n = 71)	S+CT (n = 37)	CT (n = 34)	*p*
Site of Recurrence*	n (%)	n (%)	n (%)	
Peritoneal				0.014
Abdomen	17 (23.9)	7 (41.2)	10 (58.8)	
Pelvis	19 (26.7)	16 (84.2)	3 (15.8)	
Lymph nodes				NA
Abdomen	9 (12.7)	4 (44.4)	5 (55.6)	
Parenchymal**	8 (11.3)	6 (75.0)	2 (25.0)	0.73
Mixed	16 (22.5)	4 (25.0)	12 (75.0)	0.01
Number of metastases				0.0001
Single	22 (31.0)	21 (56.8)	1 (2.9)	
Isolated ($\leq$ 4)	14 (19.7)	10 (27.0)	4 (11.8)	
Multiple	35 (49.3)	6 (16.2)	29 (85.3)	

**Total number of each site with metastasis, **Liver, Spleen, Pleural, Lung, C+CT = chemotherapy and surgery, CT = chemotherapy.*

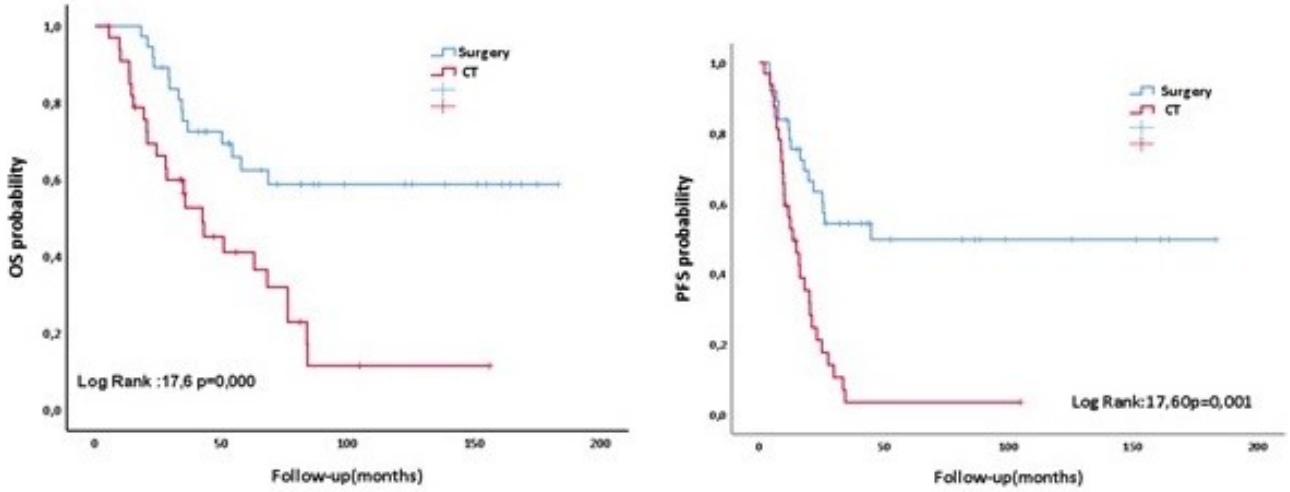

Figure 1. — Overall survival (A) and progression free survival (B) according to treatment (Secondary cytoreduction surgery and chemotherapy versus chemotherapy only).

ered as disproportionate.

Age, degree of tumor cytoreduction at the time of primary surgery or the presence of ascites on computerized tomography (CT-scan) were not exclusion criteria for being considered as a surgical candidate. In addition, a laparoscopic evaluation of intraperitoneal disease was recommended to assess the feasibility of complete resection when suspicion of multiple metastases or the appropriateness of any extraordinary surgical approach.

Patients who were not fit for surgical resection underwent CT alone, while those who completed surgery were treated with adjuvant CT after surgery. Adjuvant or CT alone consisted of a combination of platinum derivatives and taxanes, doxorubicin, gemcitabine, etoposide, and topotecan. Poly (ADP-ribose) polymerase (PARP) inhibitors were rarely given. Bevacizumab (BV) was administered according to a case-by-case decision. No information was recorded about the number of patients who refused any treatment.

Follow-up of at least two years since the end of either treatment was requested. Follow-up evaluation consisted of history and physical examination, routine biochemical and hematologic laboratory assessment including CA-125, CT-scan or positron emission tomography (PET-CT scan). Diagnosis of recurrence was considered as true when both images and CA-125 were compatible with disease, and very rarely a confirmation biopsy was required.

Recurrent disease was classified based on the following anatomic sites: *parenchymal* disease (involvement of liver, spleen, and lung metastases); *peritoneal* (involvement of the peritoneum (abdomen or pelvis) and/or colon-sigmoid); *nodal disease* (involvement of lymph, either abdominal (pelvic, para-aortic) or extra-abdominal (groin, latero-cervical, mediastinum)); and *mixed* (combination

Table 3. — *Surgical procedures performed in the surgical group*

Procedure	Patients (n = 37)
Lymphadenectomy	
Aortic	5 (13.5)
Extra-abdominal*	4 (10.8)
Porta-hepatis	3 (4.2)
Intestinal Resection	
Small inestine	5 (13.5)
Large intestine	4 (10.8)
Sigmoidectomy	13 (18.3)
Partial Gastrectomy	1 (2.7)
Colostomy/Ileostomy	0
Others	
Appendectomy	2 (5.4)
Splenectomy	4 (10.8)
Partial Hepatectomy	4 (10.8)
Cholecystectomy	2 (5.4)
Ureterectomy/cystectomy	4 (10.8)
Omentectomy	5 (13.5)
Abdominal wall	3 (8.1)
Complex Retroperitoneal	2 (5.4)
Partial lobectomy	1 (2.7)
Peritonectomies	
Pelvic	14 (37.8)
Abdomen	4 (10.8)
Diaphragm (peritoneal stripping)	2 (5.4)
Radical	19 (51.4)
Surgery Time in hours [mean (range)]	3.6 (1-9.7)

**Supraclavicular (1), Inguinal (1), Mediastinal (2).*

of different sites). Extent of disease was classified as *oligometastatic* ($\leq$ 4 lesions) and *multiple*.

Overall survival (OS) was measured in months from the date of primary surgery or the beginning of chemotherapy to the time of death or last follow-up visit. Progression-free survival (PFS) was measured from the date of surgery or the beginning of CT to the time of failure or death.

Complications occurring during the first 30 days after surgery were captured and graded according to the Clavien-Dindo scale [22].

All data were extracted by reviewing patients' medical and surgical records.

Statistical analysis was performed with SPSS for Windows 20 software. Continuous data are presented as mean with standard deviation or range or median with interquartile range (IQR). Categorical data are presented as the number of cases and percentages. Categorical data were compared using two-tailed Fisher's exact test where appropriate. Kruskal-Wallis test was used for comparing two or more independent samples of equal or different sample sizes. Continuous data were compared using Mann-Whitney U test when data distribution was not normal and one-way analysis of variance when distribution was normal. Odd ratios with 95% confidence intervals (CIs) for predicting morbidity were calculated for several prognostic factors by using a binary logistic regression analysis, choosing a forward stepping model procedure. Survival analysis was done with the Kaplan-Meier method, compared by the long-rank and Breslow statistical method. Univariate and multivariate Cox proportional hazard ratio (HR) analysis were performed to identify potential prognostic factors choosing a forward stepping model procedure. Cut-off points for some continuous variable were evaluated by the receiver-operating characteristics curve (ROC) as well as for the performance of prediction model.

Once univariate analysis was completed, we performed a multivariate forward stepwise logistic regression analysis (MLR) that included as independent variables only those variables that were found to be statistically significant in the univariate analysis. This analysis allowed us to identify actual independent predictors for optimal surgical candidates and to establish their individual importance by the calculation of their respective odds ratios with 95% CIs. The Hosmer-Lemeshow test was used to assess the goodness-to-fit.

A p value of less than 0.05 was considered statistically significant for all tests. Neither CIs nor p value are shown in the text when results are in tables.

Results

General Characteristics

Out of the 71 patients analyzed, 37 (52%) women were treated with surgery followed by adjuvant CT and 34 (48%) women were treated with CT alone.General characteristics of the patients are shown in Table 1. Overall, most patients had a platinum treatment-free interval (TFIp) $>$ 12 months (73%), most women had high-grade serous tumor, and most were ASA 1-2 and ECOG 0-1. Patients who underwent SCS were younger and had no residual disease at primary surgery more frequently.

Table 2 shows the recurrence characteristics in these series. Most recurrence locations were peritoneal (51%) or mixed (23%). Women who underwent SCS had oligometastatic recurrence and less mixed recurrence compared to CT alone.

Most SCS procedures were approached by laparotomy (60 patients, 84%) and half of them were preceded by laparoscopy. In most cases, complete resection was achieved (33 patients, 89%) after SCS. In two cases (5.5%) residual disease $<$ 10mm and in another two cases residual disease $>$ 10 mm was left. Surgical treatment included a wide variety of procedures (Table 3).

Chemotherapy only was more likely delivered in cases of mixed recurrence (OR: 4.5, 95%CI: 0.9-22; p = 0.07) or multiple peritoneal metastases (OR: 21, 95%CI: 7-70; p = 0.001). The regimen most frequently administered was a platinum-based combination (paclitaxel or doxorubicin) followed by doxorubicin combined with gemcitabine (Table 1). Bevacizumab was more frequently delivered to

Table 4. — *Overall survival (OS) and progression free survival (PFS) Cox regression analysis for the whole series (n = 71) (expressed as HR with 95%CI)*

Univariate	OS	p	PFS	*p*
ASA > 3	3.1 (1.1-9.0)	0.03	3.7 (1.7-7.2)	0.003
Age > 65 years	2.3 (1.2-4.5)	0.003	1.9 (1.0-3.0)	0.024
TFIp	3.0 (1.5-5.9)	0.002	2.5 (1.2-5.3)	0.012
Metastasis				
Oligo (≤ 4)	4.7 (1.7-13.0)	0.003	4.1 (1.5-10.0)	0.005
Multiple	7.4 (2.8-16.0)	0.001	6.3 (2.7-14.0)	0.001
Mixed	2.0 (1.0-3.9)	0.023	1.9 (1.0-3.4)	0.032
BV	1.7 (0.9-3.2)	0.106	2.0 (1.1-3.6)	0.021
Multivariate				
TFIp	5.5 (2.7-11.3)	0.001	5.8 (2.5-13.3)	0.001
Multiple Metastases	6.2 (2.8-13.5)	0.001	3.8 (1.9-7.3)	0.001
ASA >3	-	-	7.5 (3.0-16.0)	0.001
Mixed recurrence	-	-	3.1 (1.5-6.5)	0.002

BV: bevacizumab

women who received only CT than to the SCS group, as well as those with multiple metastases (54% *vs*. 27%; $p = 0.03$) (OR: 3.0, 95%CI: 1.2-8.2).

Survival analysis

At a median follow-up of 51.2 months (IQR: 72.0), median OS and PFS for the whole series were 68.2 and 21.6 months, respectively.

The probability of survival was better for patients selected for SCS than those who recived CT only (HR: 0.33, 95%CI: 0.17-0.6; $p = 0.001$). The median OS of the SCS patients has not been reached at the time of this analysis. There was also a benefit of disease progression (HR: 0.28, 95%CI: 0.15-0.5; $p = 0.001$) in surgically treated patients (Figure 1).

In multivariate analysis, for the whole series, TFIp and multiple metastases were the most important independent prognostic factors for survival and recurrence. Performance status and a mixed recurrence pattern were also significant for risk of recurrence (Table 4). Quite similar results were observed in a specific analysis of the SCS+CT group (Table 5). Ascites and CA-125 were not included due to their association with multiple implants.

The use of BV did not significantly impact either OS or PFS in both SCS+CT and CT groups.

In order to evaluate the actual performance of our selection criteria (ECOG < 2 or ASA <3, TFIp > 6 months and number of sites with metastasis) for prediction of whether the patient is an adequate candidate for SCS, a regression analysis was made using these factors. Only the number of sites with metastasis was statistically significant (OR: 30.0).When this analysis was extended by including other factors known to be related with complete cytoreduction and previously mentioned, we observed that patient's age, residual disease at first surgery, CA-125, mixed recurrence, and number of metastasis were statistically significant in univariate analysis. In multivariate, residual disease at first surgery and number of metastasis were associated with adequate selection of patients to undergo SCS (HR: 5.9 and 30.0, respectively) (Table 6).

Morbidity

Intraoperative complications occurred in five patients (13.5%), with six intraoperative injuries [bladder injury (n = 2), liver injury (n = 1), spleen injury (n = 1), colon injury (n = 1), and vascular injury (n = 1)].

Postoperative morbidity according to Clavien-Dindo score was very low. Only 5.4% of the patients developed a severe complication (Clavien-Dindo score ≥ 3). Most frequent complication was paralytic ileus (7.0%) followed by infections (8.1%) and moderate-severe pleural effusion (8.1%). Only one patient required a return to the operating room (relaparotomy) due to abdominal bleeding.

Mean hospital stay was 8.6 days (range 1-27) and intensive care unit stay was 0.32 days (range 0-2). Mean total units of blood transfused 1.1 (range 0-8). There was no 90-day mortality.

Discussion

This study found that complete resection after SCS was achieved in 89.2% of our patients, most probably due to a highly selected population. Platinum free-time interval, and multiple metastases were prognostic factors for risk of death and recurrence. According to published literature median survival after SCS is of 45-61 months (18) and in our series it has not been reached at the time of this analysis. Median time to progression was more than two years longer for patients selected for SCS compared to those treated with CT only. Since selection to undergo SCS or CT only was not random, we cannot conclude that the better outcome experienced by the patients who underwent SCS is due to the surgery and not due to the factors that made them candidates to undergo surgery.

Few studies have directly compared the outcomes of

Table 5. — *Overall survival (OS) and progression free survival (PFS) Cox regression analysis for the surgery group (n = 37) (expressed as HR with 95%CI)*

Univariate	OS	*p*	PFS	*p*
ASA > 3	3.4 (1.1-10.0)	0.03	1.9 (0.7-5.2)	0.2
Age > 65y	2.0 (0.7-5.4)	0.17	7.7 (2.3-25)	0.001
TFIp < 12 m	3.2 (1.0-9.0)	0.03	1.9 (0.7-5.5)	0.21
Metastasis				
Oligo (≤ 4)	3.9 (1.5-13.0)	0.02	3.4 (1.1-10.0)	0.026
Multiple	9.4 (2.4-433.0)	0.001	9.5 (2.8-31)	0
Mixed	0.8 (0.23-2.8)	0.759	1.2 (0.3-5.7)	0.736
BV	0.3 (0.2-0.9)	0.03	0.3 (0.1-0.8)	0.02
Multivariate				
TFIp < 12 m	9.2 (2.5-26.0)	0.001	6.0 (1.8-17)	0.003
Multiple metastases	10.0 (2.6-30.1)	0.001	5.7 (1.2-26)	0.026
ASA > 3	-	-	4.1 (0.9-20)	0.075

Table 6. — *Factors associated with succesful SCS*

Parameter Univariate	B coefficient	Odds Ratio (OR) (95%CI)	*p* value
RD 1^{st} surgery	0.563	4.6 (1.5-13.8)	0.007
Oligometastatic	3.401	29.0 (8.2-60.0)	0.001
Log CA-125	1.512	4.7 (1.6-14.1)	0.005
Age < 70	0.81	2.3 (1.12-17.5)	0.032
Mixed recurrence	1.52	4.6 (1.5-13.8)	0.007
Multivariate			
Oligometastatic (≤ 4)	3.4	30.0 (8.2-108.0)	0.001
RD 1^{st} surgery	1.743	5.9 (1.2-28.0)	0.025

Hosmer-Lemeshow test, p = 0.150, RD, residual disease

platinum-sensitive REOC patients who underwent SCS to those treated with chemotherapy only [15-18]. Oksefjell *et al*. found that median OS was significantly better for patients who achieved complete resection compared to chemotherapy only (54 *vs.* 13.2 months, respectively), and localized tumor was the only significant predictive factor for complete cytoreduction [15]. Szczesny *et al* reported a similar study but all patients had complete cytoreduction surgery [17]. They found that complete resection plus platinum-based CT improved PFS and OS compared to CT only, and that complete resection was the single factor that explained that outcome. In addition, long treatment-free interval, and isolated lesions (≤ 3) could be useful predictors for complete resection [17]. Gockley *et al*. reported a retrospective analysis of 632 patients who underwent SCS plus CT or CT only [18]. Cases with complete resection at SCS had a significant decreased risk of death (HR: 0.38, 95% CI 0.23-0.64). Although they did not directly,analyzed the outcome according to extent of disease, a better survival after SCS could be explained because of patients who received CT alone more frequently had multifocal recurrences or carcinomatosis.

DESKTOP III compared SCS plus adjuvant CT versus CT alone with platinum-based regimens in platinum sensitive REOC with AGO-positive score. A significant benefit of more than 12 months on OS in complete resection patients over CT alone was observed [19]. In GOG 213 study, treatment consisted of carboplatin and paclitaxel alone or in combination with bevacizumab (BV) followed by BV maintenance therapy. Patients who were considered appropriate for SCS were randomized to surgery followed by CT versus CT alone [20]. Despite complete resection in 67% of patients, neither OS nor PFS were improved by SCS.

Our findings, although from a retrospective and small series of patients, agree with other retrospective studies that have compared the same treatment modalities and that support a better outcome in localized recurrence when complete SCS is achieved [15-18, 23, 24]. However, there is a concern about selection bias. This fact might explain the superiority of SCS and results must be interpreted with caution. DESKTOP III results emphasize that complete cytoreduction is the key to significantly improve survival [19]. Assuming the fact that the more lesions the higher the risk of an incomplete resection, the number of lesions should have an impact on the complete resection rate.

Ovarian Cancer Consensus Conference current recommendations to consider a patient as a candidate for SCS are as follows: TFIp of > 6 months, positive AGO score, absence of probably unresectable lesions on imaging and absence of contraindications to surgery [25]. Many retro-

spective studies have been published that support the significance of these factors and, therefore, several models for predicting complete cytoreduction in SCS and/or survival have been developed [8-14]. Variables included did not differ much among studies. They were performance status, ascites, residual disease after primary surgery, extent of disease, progression-free interval, CA-125, FIGO stage [8-14]. Roughly, these models showed high positive predictive values (74-89%) for complete resection, but also a high rate of false negatives (42-71%) [13-14]. According to our findings, most patients who underwent SCS had a complete resection and prolonged survival. Therefore, we analyzed the value of our selection criteria for SCS and tried to identify the optimal patient profile that will allow us to select the best candidates for SCS. No residual disease at first surgery and oligometastatic disease had good performance, with oligometastatic disease, being the most significant factor. As mentioned by other authors cited above, factors like TFIp or PFI and good PS are also considered in the decision making process for whether or not to perform SCS.

The chemotherapy regimens administered to our patients are similar to the ones used in several other studies [1, 2] and consisted of platinum-based combination in 74% and doxorubicin based combination in 25 % of patients. No specific CT regimen influenced survival. Bevacizumab was administered to 40% of patients, more frequently to patients who did not undergo SCS (CT alone) and in patients with multiple metastases.Several randomized clinical trials have tested the efficacy of BV in combination with either gemcitabine plus carboplatin [26] or carboplatin plus paclitaxel [20] in platinum-sensitive REOC. The OCEANS study found that PFS for the BV arm was superior to that of the placebo arm, but no such benefit was found for OS (26). GOG 213 study found that PFS was also significantly longer with the addition of bevacizumab to CT compared to CT alone and in patients with complete resection versus those who underwent no surgery [20], but found a negative effect of SCS despite a 67% rate of complete resection [21]. Since all patients in GOG 213 were eligible to receive chemotherapy with or without BV, and more than 80% received BV, it is difficult to prove if the effect of BV may have reduced a potential survival benefit associated with SCS. According to our results, the addition of BV to surgery seems not to significantly influence either survival or PFS.

Severe post-operative morbidity was low, with a similar rate to that reported in the published literature. This fact supports that SCS in REOC does not seem to be more challenging than primary surgery, when performed by a specialized and multi -disciplinary team [7, 15-17, 27].

Our study has several limitations such as retrospective design and a small and highly selected series. Its strength lies in a highly specialized team and experienced center, and that results of a survival benefit in adequately selected patients for SCS and agree with the published retrospective series and the prospective DESKTOP III study.

Conclusion

In conclusion, patients with first REOC and a platinum-free interval $>$ 6 months managed in a specialized and experienced center should be evaluated for their eligibility to undergo SCS. No residual disease after first surgery and oligometastatic disease at recurrence can be considered as good predictors for successful SCS with a high expectancy of complete resection.

Acknowledgments

Thanks to the Editor in Chief for his kind invitation as well as for his opinions and suggestions.

Conflict of Interest

The authors declare no conflict of interest.

Submitted: July 22, 2020
Accepted: August 06, 2020
Published: August 15, 2020

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