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Bowel Resection during Surgery for Advanced Ovarian Carcinoma Oncological Outcomes

*Maria Cuadra[1], Jose Domingo Sardon[2], Baltasar Cermeno[2], Julene Argaluza[3] and Inaki Lete[1]**

[1]Department of Obstetrics and Gynecology, Araba University Hospital, Spain

[2]Department of General Surgery, Araba University Hospital, Spain

[3]Department of Epidemiology and Public Health, Bioaraba Health Research Institute, Spain

Abstract

Objective: To evaluate the short-term (morbidity associated with surgery) and long-term oncological outcomes results: Disease Free Survival (DFS) and Overall Survival (OS) of patients who underwent intestinal resection compared with those who did not undergo this technique during a surgery for advanced ovarian cancer.

Methods: Retrospective study of patients undergoing surgery for stage IIB to IV ovarian cancer at our centre in the period from January 1st, 2010 to December 31st, 2019.

Results: During the time period analyzed, we have treated 105 patients with stage IIB to IV ovarian cancer. In 71 patients (67.6%) the surgery did not include a bowel resection; while in 34 (32.4%) a resection was performed. Patients who underwent intestinal resection underwent longer surgeries, required more blood transfusions, more admissions to the Intensive Care Unit (ICU) and were admitted to the hospital for more days. The disease-free survival time was similar between both groups (41.8 months versus 32.2 months [p=0.91]) and the overall survival too (82.1 months *vs.* 50.4 months [p=0.66]).

Conclusion: In the case of advanced stage ovarian carcinomas, bowel resection is associated with higher rates of morbidity and hospital stay but is not associated with lower DSF or OS.

Keywords: Advanced ovarian neoplasms; Bowel resection; Disease free survival; Overall survival; Morbidity

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Correspondence:
Inaki Lete, Department of Obstetrics and Gynecology, Araba University Hospital, 01009 Vitoria, Spain, Tel: +34 945007204;
E-mail: luisignacio.letelasa@osakidetza.net

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Introduction

Ovarian cancer is one of the most common gynecologic cancers that has the highest mortality rate. In 2018, 4.4% of entire cancer-related mortality among women was attributed to ovarian cancer [1]. Treatment of ovarian cancer is based on surgery and chemotherapy and surgery remains a key determinant of survival outcome in advanced ovarian cancer [2].

The goal of ovarian cancer surgery is to achieve complete resection of the disease defined as the absence of visible disease [3]. To achieve complete debulking, it is sometimes necessary to perform procedures on the intestine and/or upper abdomen. Resection of the rectosigma represents the most frequent extra-gynecological procedure during debulking surgery and is usually necessary in 60% of the occasions [4].

Resection of the rectosigma can be associated with immediate complications such as leakage or fistula, low anterior resection syndrome, and others [5]. On the other hand, the maximum surgical effort that includes bowel resections is associated with a greater survival of the patients [6].

Our objective in this study was to evaluate the short-term (morbidity associated with surgery) and long-term (oncological outcomes) results of patients who underwent intestinal resection compared with those who did not undergo this technique during a surgery for advanced ovarian cancer.

Material and Methods

Design

Retrospective study of patients undergoing surgery for stage IIB to IV ovarian cancer at our centre in the period from January 1st, 2010 to December 31st, 2019.

Objectives

The main objective of our study was to evaluate the oncological results in patients with advanced stage ovarian cancer who underwent bowel resection compared with those in patients who did not undergo this surgical technique. As secondary objectives, we have analyzed intra and postoperative morbidity in both groups of patients, as well as the specific complications associated with intestinal resection.

Population

The study included all consecutive patients operated on in that time who met the following inclusion criteria: (i) Being diagnosed with a high-grade serous, low-grade serous, mucinous, endometrioid or clear cell primary ovarian carcinoma; (ii) Be classified as stage IIB to IV during the preoperative study according to the 2014 FIGO classification [7]; and (iii), not having contraindications for surgery.

Patients were divided into two groups: Group A composed of those who underwent surgery without bowel resection and Group B in which the patients who underwent intestinal resection were included. Patients with non-primary ovarian tumors, those with stage less than IIB and histological types not included in the inclusion criteria were excluded: borderline tumour, germ cell tumors and metastatic tumors, as well as recurrences of carcinomas operated previously of the start date of the study.

Methods

In our centre, the standard of treatment for ovarian cancer includes the performance of total hysterectomy, double adnexectomy, infra and supracolic omentectomy, bilateral pelvic lymphadenectomy and para-aortic lymphadenectomy up to the level of the left renal vein. Since the publication of the results of the Lion study [8] we omit lymphadenectomy in advanced stages (>IIB) when there are no suspicious lymphatic nodes.

All patients with a suspected diagnosis of ovarian cancer are referred to the Gynecology Oncology Unit of our hospital. The basic diagnostic procedure includes: medical history, physical examination, transvaginal and abdominal ultrasound, thoraco-abdominal-pelvic Computed Tomography (CT) and measurement of tumour markers (Ca 125, Ca 19, and HE4). With the results of these tests, the patients are presented to the Gynecological Tumors Committee of the centre where the imaging tests are reviewed, the disease staged and a treatment proposal is made. The Tumor Committee is a multidisciplinary board in which the following participate on a stable basis: Gynecologist oncologists, radiotherapists, medical oncologists, radiologists, specialist in Nuclear Medicine, pathologists and in an unstable way: Colorectal surgeons, specialists in the digestive system, urologists and vascular surgeons.

When surgery is suspected to include intestinal resection, the patient is treated preoperatively with enemas, thromboembolism prophylaxis, and antibiotic prophylaxis with cefoxitin and metronidazole.

Typically, patients receive an epidural catheter, for pain control, and a central venous access line. The surgery is performed through a midline infra- and supra-umbilical laparotomy and we use the Thompson retractor.

The surgery begins with an inspection of the entire abdominal cavity and calculation of the Peritoneal Carcinomatosis Index [9] and then the planned surgery is performed.

To perform bowel resection, we use a linear cutter stapler for section and a 29 mm circular cutter endostapler for end-to-end mechanical anastomosis. Always, after performing the anastomosis, the tightness of the suture is checked using a pneumatic test.

Study variables

For this study we have collected the following variables: Age; histological type; diagnostic method (intraoperative biopsy, finding in delayed biopsy, core needle biopsy or diagnostic laparoscopy); stage; primary debulking surgery or interval surgery after Neoadjuvant Chemotherapy (NACT); duration of surgery; pre and postoperative Hemoglobin (Hb); blood transfusion and number of units transfused; intraoperative complications and type; degree of debulking (R0, R1 or R2); admission to ICU; days of hospital stay; complications in the 30 days after surgery according to the Clavien-Dindo classification [10]; recurrence and/or persistence of the disease; months to which recurrence occurred; surgeries performed to treat recurrences; disease-free survival, overall survival, and mortality rate.

Statistical analysis

Data were collected using a CRF specifically designed for the study. The database included ranges and internal consistency rules to guarantee quality control of the data.

Categorical variables were described as absolute and relative frequencies. For continuous variables, the mean, SD, median, IQR, minimum and maximum and total number of valid values were calculated. Parametric tests (Student's t-test or ANOVA) were used to compare subgroups of patients. The χ^2 test was performed for qualitative variables. For the survival analysis we have used the Kaplan-Meier method. The difference was considered statistically significant when the p value was <0.05. The normality of the variables was analyzed; if they did not follow a normal distribution, the corresponding nonparametric statistical tests were applied. SPSS version 23.0 was used to carry out the statistical analyses.

Ethics

The Spanish health authorities allow that since it is a retrospective study, in which the patients are anonymized, it is not necessary for each patient to sign a specific informed consent for the study.

Results

During the time period analyzed, we have treated 105 patients with stage IIB to IV ovarian cancer. In 71 patients (67.6%) the surgery did not include a bowel resection; while in 34 (32.4%) a resection was performed.

Table 1 shows the baseline characteristics of both groups of patients. We found no differences between the groups. Table 2 presents the data related to the surgical outcome and oncological outcomes. Patients who underwent intestinal resection underwent longer surgeries, required more blood transfusions, more admissions to the ICU and were admitted to the hospital for more days. Kaplan-Meier curves for DFS by bowel resection or not are displayed in Figure 1. The disease-free survival time was similar between both groups (41.8 months *vs.* 32.2 months [p=0.91. Kaplan-Meier curves for OS are displayed in Figure 2. The OS was also similar between both groups (82.1 months *vs.* 50.4 months [p=0.66]).

We have not performed diverting ileostomy in any of the intestinal resections. Two anastomotic leaks occurred in the 34 procedures performed (5.9%) (Table 3). In 31 of the 34 bowel resections carried out (91.2%), the pathological analysis showed intestinal infiltration by

Table 1: Basic characteristics of the patients. Data are presented in absolute numbers and percentages unless otherwise specified.

	Group A (N=71)	Group B (N=34)	P value
Age in years (mean ± SD)	59.2 (10.6)	61.5 (14.5)	0.421
Histological type Serous HG Other	60 (84.5) 11 (15.5)	27 (79.4) 7 (20.6)	0.083
Diagnostic method Diagnostic laparoscopy Intraoperative biopsy CNB Delayed biopsy	7 (9.8) 23 (32.5) 34 (47.9) 7 (9.8)	6 (17.6) 8 (23.5) 18 (53.0) 2 (5.9)	0.262
Type of surgery Primary debulking surgery Interval cytoreduction after NACT	32 (45.0) 39 (55.0)	11 (32.3) 23 (67.7)	0.304
Stage IIB III IV	6 (8.4) 53 (74.7) 12 (16.9)	1 (2.9) 27 (79.4) 6 (17.7)	0.364

Table 2: Comparative surgical and oncological outcomes.

	Group A (N=71)	Group B (N=34)	P
Duration of surgery in minutes ($\bar{x}$ ± SD)	230 (62.2) Range: 75-420	313 (72.9) Range: 205-465	<0.001*
Preoperative Hb gr/dl ($\bar{x}$ ± SD)	11.8 (1.47)	12.1 (1.53)	0.344
Postoperative Hb gr/dl ($\bar{x}$ ± SD)	10.4 (1.47)	8.6 (1.77))	<0.001*
Blood transfusion Yes No	10 (14) 61 (86)	23 (67.6) 11 (32.4)	<0.001*
Intraoperative complications Yes No	3 (4.2) 68 (95.8)	2 (5.9) 32 (94.1)	0.658
Admission to ICU Yes No	4 (5.6) 67 (94.4)	16 (47.0) 18 (53.0)	<0.001*
Cytoreduction R0 R1 R2	52 (73.2) 9 (12.7) 10 (14.1)	26 (76.5) 6 (17.6) 2 (5.9)	0.455
Postoperative complications >2 Grade IIIa Grade IIIb Grade IV Grade V	N= 10 (14) 6 4 0 0	N=6 (17.6) 0 5 1 0	0.634
Days of admission ($\bar{x}$ ± SD)	7.3 (5.0)	11.4 (7.9)	0.008*
Recurrence Yes No	52 (73.2) 19 (26.8)	19 (55.8) 15 (44.2)	0.161
Death Yes **No**	26 (36.6) 45 (63.4)	7 (20.6) 27 (79.4)	0.263

$\bar{x}$: Median; SD: Standard Deviation; Hb: Haemoglobin

ovarian cancer, while in 3 cases no intestinal involvement was found.

Discussion

Our data confirm that surgeries in which bowel resection associated with debulking is performed are longer, require more blood transfusions, more scheduled admissions to the ICU, and more days of hospital stay. All of this makes sense because intestinal resection increases the complexity of the surgery.

In our series we have performed bowel resection in 32.4% of the patients. In the study by Chi et al. [11] in which information was collected from 141 patients with stage IIIC-IV ovarian cancer, rectosigmoid resection was performed in 56% of cases. The difference between our resection rate and that of the previous study is probably due to the fact that we have included patients in less advanced

Table 3: Type of bowel resection and anastomotic leakage: 2/34 (5.9%).

Type of bowel resection	N	Anastomotic leakage
Single resection	30	
Rectosigmoid	21	
Ileal	6*	
Sigmoid	2	
Transverse colon	1	1
Multiple resection	4	
Sigmoid and transverse colon	1*	
Sigmoid and right colon	1	1
Sigmoid and terminal ileum	1	
Rectosigmoid and splenic flexure	1	

* Case in which anastomotic leakage occurred

stages (IIB) in our series than in theirs. If we limit our cases to stages IIIC and IV, we find 33 resections in 82 cases (40.2%), a rate similar to that reported by Tozzi et al. [12] who in their series had an intestinal resection rate of 39.3%. In our experience, anastomotic leakage has occurred in 2 cases (5.9%). A prospective series of 17,518 patients enrolled in the American College of Surgeons database and undergoing colorectal resection reported a 3.9% leakage rate [13]. It is likely that our results are influenced by the relatively low number of cases collected. However, our results are similar to those recently published in Spain. A retrospective study in which information was collected on 695 ovarian cancer patients who received colorectal resection in 8 Spanish centers, found a leakage rate of 6.6% [5].

In the study by Bartl et al. [14] in 192 patients with ovarian cancer who underwent bowel resection, the overall leakage rate was 4.7% (including multiple resections) and 1.9% for single rectosigmoid resections. In this study, anastomotic leakage was associated with lower overall survival.

As seems logical, the aggressiveness of the surgery is associated with better oncological results and higher rates of intraoperative complications [15]. We had 5 intraoperative complications (complications rate of 4.7%): 3 in group A (2 ureteral injuries and 1 bladder injury that were detected intraoperatively and corrected immediately) and 2 in group B (1 severe acute bleeding that required massive blood transfusion and 1 ileum injury that required suturing).

Regarding postoperative complications, we have collected 16 cases >grade 2 of the Clavien-Dindo classification (15.2%); 10 in group A and 6 in group B.

We have not registered any case of thromboembolism in our patients. This may be due to the fact that our protocol includes the administration of enoxaparin (40 mg/day) for 30 days from the day of surgery.

Our low rate of complications could be influenced by the high percentage of patients who receive NACT prior to surgery (59%). The use of NACT has been shown to decrease the rates of multiple bowel resections and, as a consequence, associated complications [16].

The higher the complexity index of the surgery performed, the greater the probability of complications, but also the greater the survival if complete debulking is achieved [17]. In this study, patients undergoing surgeries with a low Surgical Complexity Scoring (SCS) had a lower survival than those undergoing surgeries with intermediate or high SCS (1.89, 3.50 and 4.05 years respectively).

Our complete cytoreduction rate (R0) was 73.2% in group A patients and 76.5% in group B, comparable to that of other published studies. Despite this, the overall survival rate was lower in group B than in group A. We did not find a logical explanation for these findings because, in addition, the stages in both groups were overlapping.

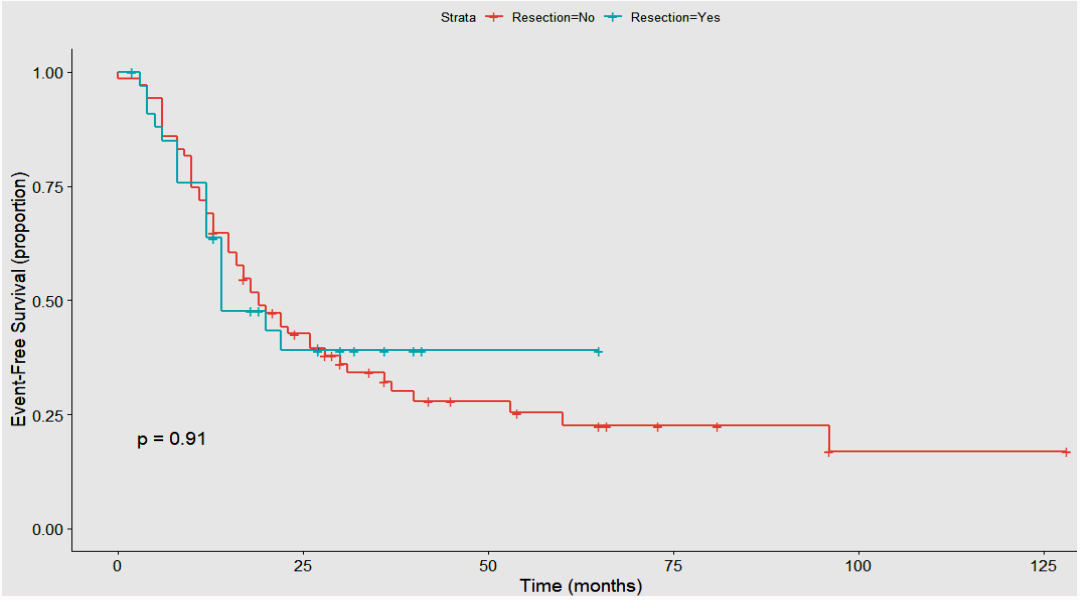

Figure 1: Disease free survival according the need or not of bowel resection.

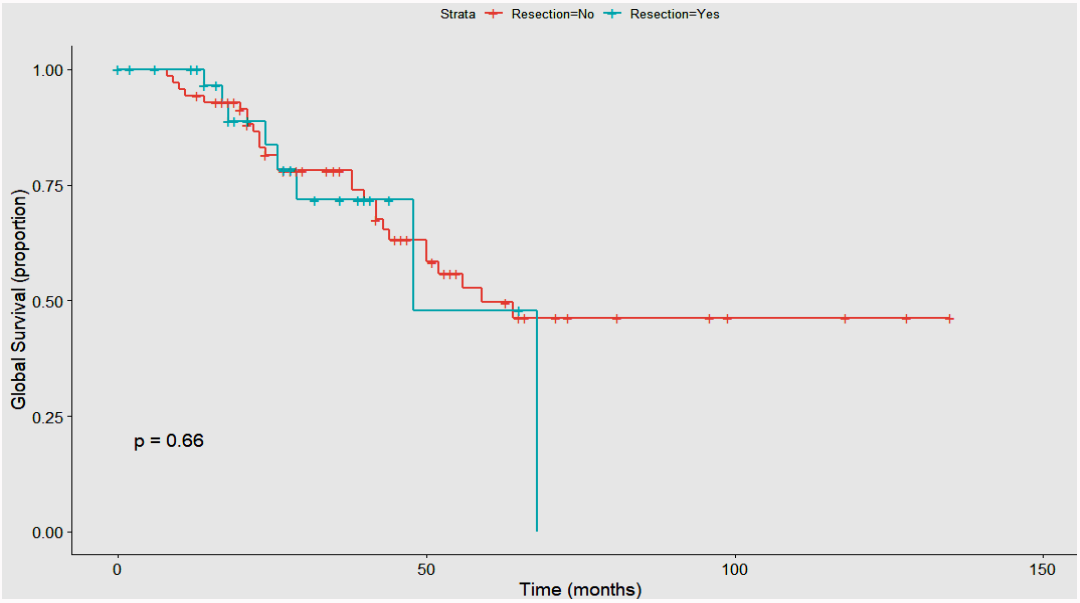

Figure 2: Overall survival according the need or not of bowel resection.

In a study with 146 patients included, 55 patients were treated with Primary Debulking Surgery (PDS) followed by adjuvant chemotherapy and 91 patients received Neoadjuvant Chemotherapy (NACT) followed by Interval Debulking Surgery (IDS). Complete or optimal debulking (0 mm to 10 mm of residual disease) was achieved in 76.4% (n=42) of the PDS group and in 79.1% (n=72) of the IDS group [18]. We know the overall survival is correlated with residual disease >1 cm and stage IV as demonstrated in a retrospective study that included 576 patients with stage IIIC or IV ovarian carcinoma [19].

Disease-free survival and overall survival are similar in patients with advanced ovarian cancer treated with primary surgery or with NACT and subsequent interval surgery according to data from a recent systematic review and meta-analysis [20]. In the meta-analysis, the mean DFS was 12 months (range 11 to 16.4) and the overall survival was 30 months (range: 23 to 49). In our study, we did not find significant differences in DSF or OS in patients who underwent a bowel resection.

Conclusion

In the case of advanced stage ovarian carcinomas, bowel resection is associated with higher rates of morbidity and hospital stay but is not associated with lower DSF or OS.

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