

Original Article



Rectosigmoid resection during Visceral-Peritoneal Debulking (VPD) in patients with stage IIIC-IV ovarian cancer: morbidity of gynecologic oncology vs. colorectal team

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ABSTRACT

Objective: This study investigates the specific morbidity of rectosigmoid resection (RSR) during Visceral-Peritoneal Debulking (VPD) in a consecutive series of patients with stage IIIC-IV ovarian cancer and compares the results of the colo-rectal vs. the gynaecologic oncology team.

Methods: All patients with the International Federation of Gynecology and Obstetrics (FIGO) stage IIIC-IV ovarian cancer who had VPD and RSR were included in the study. Between 2009 and 2013 all operations were performed by the gynecologic oncology team alone (group 1). Since 2013 the RSR was performed by the colorectal team together with the gynecologic oncologist (group 2). All pre-operative information and surgical details were compared to exclude significant bias. Intra- and post-operative morbidity events were recorded and compared between groups.

Results: One hundred and sixty-two patients had a RSR during VPD, 93 in group 1 and 69 in group 2. Groups were comparable for all pre-operative features other than: albumin ($1 < 2$) hemoglobin ($2 < 1$) and up-front surgery ($1 > 2$). Overall morbidity was 33% vs. 40% ($p=0.53$), bowel specific morbidity 11.8% vs. 11.5% ($p=0.81$), anastomotic leak 4.1% vs. 6.1% ($p=0.43$) and re-operation rate 9.6% vs. 6.1% ($p=0.71$) in groups 1 and 2, respectively. None of them were significantly different. The rate of bowel diversion was 36.5% in group 1 vs. 46.3% in group 2 ($p=0.26$).

Conclusions: Our study failed to demonstrate any significant difference in the morbidity rate of RSR based on the team performing the surgery. These data warrant further investigation as they are interesting with regards to education, finance, and medico-legal aspects.

Keywords: Ovarian Cancer; Surgery; Morbidity

INTRODUCTION

Over 75% of the patients with ovarian cancer are diagnosed at stage IIIC-IV. The standard of care is surgery followed by chemotherapy or vice versa with neo-adjuvant chemotherapy given to reduce the tumor burden. Irrespective of the timing, the ideal surgery must aim at

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Conceptualization: T.R., V.G.; Data curation: T.R., V.G., V.D., C.R.G., F.F.; Formal analysis: T.R., V.G., F.F.; Investigation: T.R., V.G., F.F.; Methodology: T.R., V.G., V.D., F.F.; Project administration: T.R., V.G.; Resources: T.R., V.G.; Software: T.R., V.D.; Supervision: T.R.; Validation: T.R., C.M., F.F.; Visualization: T.R., V.G., F.F.; Writing - original draft: T.R., V.G., F.F.; Writing - review & editing: T.R., V.D., C.R.G., C.M., F.F.

removing all visible disease. A complete resection (CR) of all visible disease is associated with the best prognostic outcome [1-4]. Several studies reported that in 20-80% of the patients a bowel resection is needed to achieve a CR [5,6]. Gastrointestinal complications are the most common adverse events, accounting for 9%–26% of the overall morbidity associated to surgery [7-10]. A controversial matter is who should undertake bowel surgery in patients with ovarian cancer. Colo-rectal surgeons have the most exposure to bowel surgery, but they rarely perform bowel resection in the presence of widespread peritoneal disease. Traditionally gynecologists do not have the expertise to undertake bowel surgery. The same does not apply to gynecologic oncologists, who have specific modules of their training dedicated to bowel surgery. Nonetheless clear guidelines are lacking, vary in different countries and depend a lot on inter-personal relationships. That leaves room for unclarity and at times medico-legal disputes. In this study we tried to provide data on the matter. In Oxford, 2 teams, one of gynecologic oncologists and the other of colorectal surgeons, undertook rectosigmoid resection (RSR) surgery in the same university hospital and in the same patient setting (stage IIIC–IV ovarian cancer; OC) during consecutive periods. We compare the surgical outcomes and the morbidity of the 2 different teams.

MATERIALS AND METHODS

This study is part of a service evaluation project and obtained Trust approval (n=3,265). Between June 2009 and April 2018, 371 consecutive patients with primary International Federation of Gynecology and Obstetrics (FIGO) stage IIIC–IV ovarian cancer underwent to Visceral-Peritoneal Debulking (VPD) at the Oxford University Hospital (OUH, Oxford, UK). We use the Oxford Ovarian Cancer Surgical Database to record, monitor and audit surgical data. We identified all patients who underwent RSR defined as the resection of a segment of sigmoid rectum below the pelvic brim. Additional large or small bowel resections were recorded. Between June 2009 and April 2013, the gynecologic oncology team undertook RSR and anastomosis (group 1). In 2013 the OUH Board introduced multi-specialty teams to do multi-visceral surgery and RSR was undertaken with the colorectal team (group 2). In addition, all patients had up-front VPD until 2012. After that, following the publication of the European Organisation for Research and Treatment of Cancer (EORTC) trial, the department moved to neo-adjuvant chemotherapy. All patients were seen in the Department of Gynaecologic Oncology, underwent computed tomography (CT) scan of chest, abdomen + pelvis and were discussed in the local multi-disciplinary team (MDT) meeting. The VPD technique was previously described [11].

The triage process is reported in **Table 1** and elected patients to VPD if: 1) the performance status (PS) was scored as American Society of Anesthesiologists (ASA) ≤ 3 at pre-operative assessment, 2) CT review showed no lung or multiple parenchymal liver metastases, 3) exploratory laparoscopy (EXL) demonstrated no small bowel serosal disease or porta hepatis

Table 1. Inclusion and exclusion criteria for VPD

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> Pre-operative: Histology proven or suspected stage IIIC–IV ovarian cancer Performance status: ASA score $\leq 3^*$ 	<ul style="list-style-type: none"> Pre-operative: CT scan showing presence of lung metastases, three or more liver segments involvement and/or disease progression on chemotherapy Intra-operative: Exploratory laparoscopy showing diffuse small bowel serosal deposit, porta hepatis encasement
<ul style="list-style-type: none"> Post chemotherapy patients with stabile disease or any response 	

ASA, American Society Anaesthesiology; CT, computed tomography; VPD, Visceral-Peritoneal Debulking.

*Patients with ASA score 3 were eligible to surgery if passed extended pre-operative assessment, including cardiopulmonary exercising test when appropriate.

encasement, 4) following neo-adjuvant chemotherapy, patients displayed any response or stable appearances on CT scan. The goal of the VPD was a CR of all visible disease.

All patients received mechanical bowel preparation with Bisacodyl 20 mg the day prior to the operation. They underwent EXL using a 10 mm port for the camera and one or 2 additional 5 mm trocars (Karl Storz, Tuttlingen, Germany) to manipulate organs or for adhesiolysis. Once the possibility of a CR was confirmed, the patients underwent to a xifo-pubic laparotomy. In group 1 the gynecologic oncology team undertook the entire VPD including RSR, anastomosis and diversion if necessary. In group 2 the gynecologic oncology team performed the VPD and called upon the colorectal team at time of RSR. Standard chemotherapy regimen was platinum and paclitaxel: 6 cycles after surgery or three cycles before interval VPD. Surgery was offered 4-6 weeks after last chemotherapy.

From the electronic patients records (EPRs), we extracted pre-operative characteristics, including tumor stage and grade, patients' age, type of bowel preparation, relevant haematology (hemoglobin) and biochemistry (initial CA-125, albumin) levels, presence of ascites, type of treatment (up-front surgery vs. neo-adjuvant chemotherapy) and type of chemotherapy. From the operation notes we extracted the intra-operative outcomes including the number and type of bowel resection, type of instrument used for and anatomic level of the resection, performance of anastomosis, type of anastomosis, type of stapler used for the anastomosis, performance of bowel diversion. We also pulled out all type of morbidity recorded within the first 30 days from the surgery, divided in overall morbidity and bowel specific morbidity (anastomosis breakdown, ileus >1 week, stoma retraction, pelvic abscess, or enteric fistula). All events of mortality occurred within 90 days of the VPD were recorded.

The level of the anastomosis was assessed at time of surgery and confirmed by pre-chemotherapy CT scan. The decision for a bowel diversion was intra-operative taking in account the following: 1) multiple bowel resections; 2) anastomosis ≤5 cm from the anorectal junction; 3) tension on the anastomosis; 4) air spillage at time of air test; and 5) assessment by the surgeon of the bowel tissues before and after the anastomosis based on vascularisation, color (pink vs. pale), bleeding edges of resected margins, pulsation, elasticity and temperature [12,13].

The RSR technique of the gynecologic oncology team has been previously published [14], while the colorectal team used a traditional technique for division and anastomosis [15]. Both teams had significant experience with RSR. The absolute number of resections was higher for the colorectal team, with 7 independent consultants performing averagely 150 RSR a year in patients with both benign and malignant disease. The gynecologic oncology team had more experience of patients with OC undertaking averagely 60 RSR a year during VPD. Primary end point of the study was to compare the rate of 30-day bowel specific morbidity and related complications between the 2 groups.

The Clavien-Dindo classification was used to grade surgery-related complications [16]. Descriptive statistics for continuous and categorical variables have been reported as absolute number, rate and percentage (%). A normality test (D'Agostino-Pearson test) was used to determine whether sample data followed a Gaussian distribution. Comparison between groups was performed using the χ^2 test or Fisher's exact test for categorical variables, and the Student's t-test or Wilcoxon rank-sum tests for continuous variables. All calculated p-values were 2-sided, and p-values less than 0.05 were considered statistically significant were

performed with Graph Pad Prism version 6.0 (Graph Pad Software, San Diego, CA, USA). The time was the only discriminant for the team choice and all consecutive patients were included. However, to rule out the presence of selection bias, the groups were compared for all pre- and intra-operative factors.

RESULTS

In the study period, 371 consecutive patients underwent VPD and 162 out of 371 (43.6%) had RSR. Ninety-three patients had the VPD in the period 2009–2013 and the RSR performed by the gynecologic oncology team (group 1). Sixty-nine patients had the VPD in the period 2013-2018 and the RSR performed by the colorectal team (group 2). In group 1, 72 patients out of 93 (77.4%) had up-front VPD and 21 (22.6%) had interval VPD. In group 2, 67 patients out of 69 (97.2%) had interval VPD and 2 (2.8%) up-front VPD. The difference in the initial treatment modality (up-front vs. interval VPD/ adjuvant vs. neo-adjuvant chemotherapy) between the 2 groups was statistically significant. Overall, 74 patients had a bowel resection during up-front VPD and 88 at interval VPD. As previously reported [12], neo-adjuvant chemotherapy was overall associated to lower rate of bowel resection (26.5% vs. 41.3%).

Table 2 reports tumor and patients' pre-operative characteristics. None of the pre-operative features (age, comorbidity, FIGO stage, grade, histology, CA-125, type of chemotherapy and number of cycles) was significantly different between the groups except for albumin (significantly lower in group 1), hemoglobin and rate of up-front surgery (significantly lower in group 2). As described in **Table 3**, the groups were well matched for surgical complexity (overall number of procedures, number of extra-gynecologic and upper abdominal procedures). In group 1 all patients had RSR with the pelvic en-bloc technique as previously described [14]. The proximal bowel resection was performed over a purse string instrument, the distal rectal resection with a linear GIA and the anastomosis with a trans-rectal circular end to end anastomosis (EEA) device. In group 2, the colorectal team used the purse string device in 45 patients and the linear stapler in 24 patients for the proximal resection. They

Table 2. Patients and tumor characteristics group 1 vs. group 2

Characteristics	Group 1 (n=93)	Group 2 (n=69)	p-value
Patients	93/162 (57.4)	69/162 (42.6)	-
Age (yr)	64.1±10.8	63.2±12.0	0.65
CA-125 (U/mL)	1,186.4±638.7	826.9±670.0	0.34
Albumin (g/L)	30.1±9.7	38.5±5.4	<0.003
Hemoglobin (g/dL)	12.3±1.7	11.7±1.4	0.044
VPD			<0.004
Up-front VPD	72 (77.4)	2 (2.9)	
Interval VPD	21 (22.6)	67 (97.1)	
Ascites	62 (66.7)	21 (30.4)	0.06
FIGO stage			0.76
IIIC	83 (89.2)	62 (89.9)	
IV	10 (10.8)	7 (10.1)	
Histology type			
Serous	67 (72.0)	35 (50.7)	0.07
Others	26 (28.0)	34 (49.3)	0.07
Grade			
G3	75 (80.6)	35 (50.7)	0.06
Others	18 (19.4)	34 (49.3)	0.07

Values are presented as number (%) or mean±standard deviation.

FIGO, International Federation of Gynecology and Obstetrics; VPD, Visceral-Peritoneal Debulking.

Table 3. Surgical procedures and outcomes group 1 vs. group 2

Variables	Group 1 (n=93)	Group 2 (n=69)	p-value
Surgical procedures			
En-bloc resection	93 (100.0)	69 (100.0)	-
Rectosigmoid resection	93 (100.0)	69 (100.0)	-
Hysterectomy	79 (84.9)	58 (84.1)	0.08
Bilateral oophorectomy	84 (90.3)	61 (88.4)	0.05
Bladder partial resection	9 (9.7)	11 (15.9)	0.20
Appendectomy	12 (12.9)	7 (10.1)	0.57
Peritonectomy	93 (100.0)	69 (100.0)	-
Upper abdominal surgery			
Supra-colic omentectomy	93 (100.0)	67 (97.1)	0.93
Resection of lymph nodes	21 (22.6)	7 (10.1)	0.38
Diaphragmatic peritonectomy	74 (79.6)	56 (81.2)	0.80
Splenectomy	13 (14.0)	8 (11.6)	0.65
Gastric resection	3 (3.2)	5 (7.2)	0.00
Liver resection	15 (16.1)	10 (14.5)	0.78
Cholecystectomy	4 (4.3)	2 (2.9)	0.08
Pleurectomy	21 (22.6)	14 (20.3)	0.18
Porta hepatis surgery	15 (16.1)	9 (13.0)	0.71
Additional bowel resection			
Small bowel	20 (21.5)	6 (8.7)	0.04
Transverse colon	4 (4.3)	2 (2.9)	
Cecum	3 (3.2)	1 (1.4)	
Total colectomy	-	1 (1.4)	
Colon + small bowel	3 (3.2)	-	
Surgical outcomes			
Mean operative time (min)	341±216.5	416±206.6	0.03
Hospitalization (days)	16.6±14.1	14.2±7.3	0.24
CR rate	93 (100.0)	69 (100.0)	-

Values are presented as number (%) or mean±standard deviation.
CR, complete resection.

used either a transverse anastomosis stapler (49 patients) or a contour device (20 patients) in all 69 patients and the EEA stapler for the trans-rectal anastomosis.

Both teams undertook an air test to prove the integrity of the anastomosis. The anastomosis level was >5 cm from the anorectal junction in 65% and <5 cm in 35% of the patients with no difference between the groups. The only significant differences found in the intra-operative outcomes of group 1 vs. group 2 were the surgical time (341 vs. 416 minutes, $p=0.03$) and the rate of multiple bowel resection (32.2% vs. 14.4%, $p=0.04$). In group 1, 30 patients out of 93 (32.2%) had additional bowel resections as following: 20 patients (66.6%) had small bowel resection, 4 (13.3%) transverse colon resection, 3 (10%) cecum resection and 3 patients (10%) underwent transverse colon and ileum resection. In group 2, 10 patients out of 69 (14.4%) had additional bowel resection as following: 6 patients had small bowel resection, 2 had transverse colon resection, 1 had cecum resection and 1 had pan-colectomy. Despite a higher rate of multiple bowel resections in group 1, a higher rate of bowel diversion was recorded in group 2 although not statistically significant ($p=0.26$): 34 patients out of 93 (36.5%) in group 1 vs. 32 patients out of 69 (46.3%) in group 2. Of note, 4 patients had an end colostomy in group 2 vs. none in group 1.

Table 3 reports the 30-days overall and bowel specific morbidity. No statistically significant difference was found between the 2 groups in terms of overall and bowel specific morbidity (**Table 4**). Likewise, for 90-days mortality. In total 19 patients experienced bowel morbidity: 11 in group 1 and 8 in group 2 (11.8% vs. 11.5%, $p=0.85$). Of note the same number of

Table 4. Overall and bowel specific morbidity group 1 vs. group 2

Variables	Group 1 (n=93)	Group 2 (n=69)	p-value
Overall morbidity	31 (33.3)	28 (40.6)	0.3512
Bowel diversion	34 (36.6)	32 (46.4)	0.2676
Bowel morbidity	11 (11.8)	8 (11.6)	0.851
Ileus >1 week	4 (4.3)	3 (4.3)	
Stoma retraction	1 (1.1)	-	
Pelvic abscess	1 (1.1)	1 (1.4)	
Enteric fistula*	1 (1.1)	-	
Anastomotic leak	4 (4.3)	4 (5.8)	0.684
Return to theater	9 (9.7)	4 (5.8)	0.379

Values are presented as number (%).

*Small bowel fistula, not anastomotic fistula.

anastomosis breakdown (n=4) occurred in either group with no significant difference in rate recorded (4.3% vs. 5.7%, p=0.68). Rate of return to theater was slightly higher in group 1 (9.6% vs. 5.8%, p=0.379). Indications for return to theater were similar in the 2 groups: 50% were related to bowel morbidity, 20% due to bleeding and 15% due to abscess.

DISCUSSION

Bowel resection is reported in 20% to 80% of the patients during surgery for stage IIIC–IV ovarian cancer [5,6]. Despite being a common procedure, no guidelines or data exist on which surgical team is best suited to undertake the resections. Gynecologic oncologist are the surgeons who meet and establish a bond with ovarian cancer patients to provide treatment. Most importantly, they have knowledge and specialized training on the natural history of the disease, the type of spread, the targets of the surgery and the technique to achieve it. During their sub-specialty training they have dedicated modules to learn surgery of non-genital tract including bowel resection. In places like the United States and Australia they are trained and allowed to independently undertake bowel surgery [17,18]. In other places such as the UK, the Royal College of Obstetricians & Gynaecologists training directives are to “independently and competently perform gastrointestinal procedures in collaboration with colorectal surgeons where necessary” [19]. At the same time the NICE guidelines allow a gynecologic oncologist with a specific training to do ultra-radical surgery [20]. Colo-rectal surgeons more often undertake RSR and they clearly have a larger experience including patients with benign and malignant conditions. However, based on the ESMO guidelines [21], they should rarely undertake RSR in patients with disease that exceeds the organ, let alone disease involving the peritoneum and the adjacent organs. The latter is the typical presentation of patients with stage IIIC–IV ovarian cancer in the pelvis [14,22]. In addition, the wide peritoneal involvement towards the pelvic side wall often demands an extensive dissection of the ureters and experience in dissection of the retroperitoneum. That is something the colorectal surgeons are not routinely doing as witnessed by the recent literature [23]. Gynecologic oncologists are used to perform retro-peritoneal surgery as they often undertake pelvic lymphadenectomies. The ideal outcome of any surgery is the highest efficacy with the least morbidity. The efficacy in patients with ovarian cancer is measured by the rate of CR [24,25] which was identical in the groups.

However, in our study, the efficacy was not the main outcome of interest as the surgery was conducted by gynecologic oncologist anyway. The main finding of this study is the lack of difference in bowel related morbidity between the groups. Another interesting result pertains to the operative time. Group 2 had significantly longer operative time despite a similar

complexity of surgery and number of procedures. We checked if it was secondary to the EXL but we failed to find any difference in the time between the groups: 18' vs. 16'. It is speculative to say that the longer overall operative time is due to the colorectal surgeons and we did not conduct an ad-hoc analysis. However, it is a common scenario, at least in our experience, that colorectal surgeons are not readily available to take over the surgery causing therefore some delay. Likewise, the absence of familiarity with an en-bloc resection of the pelvis, which is now considered the standard of care for the pelvic surgery of ovarian cancer [26] could make the surgery longer. The implications are serious in terms of care to the patients: longer the procedure, higher the morbidity [27]. Another important matter, in times of financial constraints for healthcare, is the costs of having 2 teams as opposed to one team and of longer operations. We did not run a cost analysis, but, in our experience, the colorectal team charged our Department for the time they spent with us. After extensive research of the literature, we could not find any publication on the subject.

The strength of this study is that time was the only determinant of the operating surgical team. This, together with the consecutiveness of patients, the homogeneity of the groups and the consistency of the surgical teams minimized the risk of a selection bias. The lack of randomization was the most obvious limit of the study. Second limit was the rarity of the morbidity events, intended as bowel morbidity, which probably requires a larger study group to reach statistical significance. However, the rate of morbidity we report is consistent with the current literature, for example on the anastomosis breakdown. Another element of potential unbalance is that most patients had up-front surgery in group 1 and had interval surgery in group 2. How that can truly impact on the morbidity of bowel resection is not clear.

It is often postulated that neo-adjuvant chemotherapy should reduce the disease load and simplify the surgery [28,29]. Based on our data, we have previously disagreed to this general perception [11,16] and the data in this study confirm our earlier finding. However, since the tumor burden should be higher in the up-front surgery group, we would expect lower overall and bowel morbidity in group 2. That was clearly not the case in our study as no significant differences were found. With regards to some known risk factors for anastomosis breakdown such as low hemoglobin and low albumin [30-32], as expectable, albumin was lower in group 1 (worse nutritional status) and hemoglobin lower in group 2 (following chemotherapy). Overall, the equal distribution of the 2 factors in the groups should balance the risk of bowel specific morbidity.

One aspect that needed reflection is the higher rate of bowel diversion in group 2 even though it did not reach statistical significance. We questioned whether it could be due to the higher occurrence of interval surgery in group 2 assuming chemotherapy could be perceived as a risk factor for dehiscence. We failed to find literature supporting the latter. In addition, thanks to the data from a previous study [10], we reviewed the diversion rate in the small population of group 1 who had interval VPD. It was only 21 patients so not meaningful for comparison. Nonetheless, only 9.5% (2 patients out of 21) had a bowel diversion in this small sub-group which is clearly lower than 46.3% in group 2. We also broke down the data by individual surgeons, but we found a consistent rate of bowel diversion between the 2 teams. In the absence of significant data to justify for the higher rate of bowel diversion in group 2, we suppose that it has to do with personal preference of the teams.

As this study is the first report on the subject, we recognize that inevitably some of the troubles experienced in group 2 such as longer operations and cancellation of surgery are

possibly due to poor organization and can be improved. Our study failed to demonstrate differences in the morbidity rate of bowel resection experienced by patients with stage IIIC–IV ovarian cancer whose surgery was undertaken by gynecologic oncologist vs. colorectal surgeons, meaning that either team is suitable. The finding of higher rate of bowel diversion and longer operations in group 2 require more data. This study is a first step to draw attention on the matter, to support colleagues, save costs and give some guidance to medico-legal events in the best interest of patients and surgeons.

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