The surgical outcomes and perioperative complications of bowel resection as part of debulking surgery of advanced ovarian cancer patients.

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Research

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Abstract

Background: To review the utilization and perioperative outcomes of bowel resection during cytoreduction of ovarian cancer patients in our institution.

Methods: All the patients who received bowel resection including anastomosis and ostomy formation between 2006/01 and 2018/12 were identified. Clinicopathological information was abstracted from the medical records. Postoperative morbidities were assessed according to Clavien-Dindo classification (CDC).

Results: There were 182 patients in the anastomosis group and 100 patients in the ostomy group, leading to a total of 282 patients. The median age was 57 years and most patients had high-grade serous histology (88.7%). 49 (17.3%) patients received neoadjuvant chemotherapy. During operation, 78.7% patients had ascites and the median volume was 800 mL. Extensive bowel resection (at least two-segment) and upper abdominal operation was performed in 29 (10.2%) and 69 (24.4%) patients, respectively. Rectosigmoid colon was the most commonly resected (83.8%), followed by right hemicolectomy (5.9%) and small bowel resection (2.8%). No macroscopic residual disease was observed in 42.9% of the patients, while 87.9% of had residual disease ≤1 cm. For the entire cohort, 19.9% (56/282) experienced different complications, not including anastomotic leak (AL). Severe complications (CDC 3-5) accounted for 7.8%, mostly pleural effusion requiring drainage (3.5%), and followed by wound dehiscence requiring delayed repair in operation room (1.8%). Nine patients experienced AL: one in the ostomy group with extensive bowel resection and eight in the anastomosis group. The overall AL rate was 4.2% (9/212) per anastomosis. The AL rate per anastomosis was quite comparable in different populations: 4.4% (patients in the anastomosis group), 4.3% (patients with one-segment bowel resection and anastomosis), 4.0% (patients with extensive bowel resection and anastomosis) and 5.0% (patients with isolated rectosigmoid resection and anastomosis).

Conclusions: Execution of bowel resection as part of debulking surgery of patients with newly diagnosed ovarian cancer resulted in an acceptable morbidity rate.

Background

Ovarian carcinoma is the most lethal gynecologic malignancy (1). Most patients present with advanced stage tumor, and optimal cytoreduction is well accepted to be the cornerstone of effective treatment (2, 3). Debulking surgery for advanced ovarian cancer patients is complicated, which requires removal of several organs and extensive amounts of peritoneum (4). According to a recent publication from Japan, gynecologic oncologists rarely perform bowel resection and upper abdominal operation (4). It is quite the same situation in China. Only a few gynecologic oncologists are willing to perform extensive radical surgery, possibly due to either a lack of the relevant surgical skills or the intense patient-physician relationship (5).

As one of the leading cancer centers with high-volume cases, the gynecologic oncologists in our department have adopted the concept of radical surgery including upper abdominal surgery (5, 6) and modified posterior pelvic exenteration (7, 8). Back in 2004, we first reported low colorectal staple anastomosis after rectosigmoid resection in primary surgery in eight ovarian cancer patients in a Chinese journal (7). Then a series of 50 cases between January 2006 and December 2010 was updated in 2018 (8). The two publications were both in Chinese and only focused patients undergoing rectosigmoid resection and anastomosis. Not only large bowels but also small bowels are involved in ovarian cancer patients with bulky tumor.

Therefore, we conducted the current study to comprehensively review the utilization of bowel resection as part of debuking surgery in ovarian cancer patients. The specific details of bowel surgery and surgical-related outcomes were evaluated. A standardized scoring system was applied in assessing perioperative complications.

Methods

The study was approved by the institutional review board and the requirement for written informed consent was waived considering its retrospective design. We searched the electronic medical record database and included all the patients with advanced ovarian cancer who underwent bowel surgery in primary or interval cytoreduction between January 2006 and December 2018 in our department.

Patient-, disease- and surgery-related information was abstracted from the medical records. The data collection included age at diagnosis, body mass index (BMI, calculated as weight (kg)/[height (m)]^2), histology, and administration of neoadjuvant chemotherapy. Preoperative laboratory values, including hemoglobin, albumin, and cancer antigen 125 (CA-125), were also recorded. The surgery-related variables were listed as follows: the presence and volume of ascites, upper abdominal surgery, type of bowel resection, estimated blood loss (EBL), intra-operative transfusion, extent of cytoreduction, postoperative complications, postoperative hospital stay and time interval from surgery to chemotherapy. A protective stoma was not routine and was performed at the surgeon’s discretion.

The bowel resections were dichotomized into one-segment and extensive bowel resection (at least two-segment) (9). The postoperative complications were graded according to Clavien-Dindo classification (CDC) (10) and further categorized into mild (CDC 0–2) and severe (CDC 3–5) subgroup (11). All the complications and CDC scores were recorded in patients who experienced more than one complication. We specially focused on anastomotic leak (AL) after bowel resection and anastomosis which was defined as follows: 1) feculent fluid from drainage tube, wound or vagina; 2) extravasation/leakage from anastomotic site verified by imaging and/or intraoperative findings (12). The AL rate is calculated as both per patient and per anastomosis considering one patient might have at least two anastomoses after extensive bowel resection. Concerning extent of debulking, R0 resection is defined as no visible gross tumor after cytoreduction, while R1 resection refers to residual disease ≤ 1 cm.

Statistical Package for Social Science (SPSS) (Version 17.0, SPSS, Inc., Chicago, IL, USA) was used for the analyses and GraphPad Prism (Version 5.0, GraphPad Software, Inc., La Jolla, CA, USA) was used for figure illustration. Continuous data were presented as median (range) and categorical data as proportions. Parametric Student's *t*-tests were employed in evaluating continuous variables, while chi-square tests were used for the categorical variables. All of the *P* values reported were two-sided, and a value of $P < 0.05$ was considered statistically significant.

Results

A total of 282 ovarian cancer patients with advanced tumor received bowel resection as part of debulking surgery. Among them, 182 and 100 patients underwent anastomosis and ostomy formation, resepectively. Figure 1 illustrates the number of bowel resection at our institution over the past 13 years. Table 1 presents the patient information and the surgery-related variables. For the entire cohort, the median age was 57 years (range, 23–92 years). The majority of the patients had high-grade serous histology (88.7%). Neoadjuvant chemotherapy was administered in 49 (17.3%) patients. Ascites was present in 78.7% of the patients, and the median volume was 800 mL (range, 50-8000 mL). Extensive bowel resection and upper abdominal operation was performed in 29 (10.2%) and 69 (24.4%) patients, respectively. Three patients had protective stoma. The debulking results were 121 (42.9%) patients with no gross residual disease, 248 (87.9%) with residual disease ≤ 1 cm. The median operation time was 197 minutes (range, 60–371 minutes), while the median blood loss was 1000 mL (range, 100–3500 mL). During operation, 87.9% of the patients received a transfusion, and the median volume transfused was three units (range, 1-11units). For the whole population, the median time from surgery to discharge and chemotherapy was 13 days (range, 5–53 days) and 19 days (range, 7–50), respectively.

Table 1

Patient information and surgery-related outcomes.

Variables	Total (n = 282)	Anastomosis (n = 182)	Ostomy (n = 100)	P
Age (years)	57(23–83)	55 (25–77)	58.5 (26–83)	0.003
Body mass index (kg/m^2)	22.2 (14.2–37.3)	22.0 (14.2–34.2)	23.2 (16.0-37.3)	0.101
Neo-adjuvant chemotherapy (%)	49 (17.4%)	29 (15.9%)	20 (20.0%)	0.389
Preoperative laboratory values				
CA-125 (U/mL)	1006.5 (3.5-31803.7)	1114.5 (3.5-31803.7)	907.3 (7.4-23156.0)	0.551
Albumin (g/L)	40.0 (24.4–55.3)	40.7 (26.9–55.3)	39.6 (27.6–48.5)	0.638
Hemoglobin (g/L)	119 (62–151)	119 (76–151)	120 (62–147)	0.873
Postoperative day 1 laboratory values				
Albumin (g/L)	31.0 (19.3–48.9)	31.2 (19.9–48.9)	30.2 (19.3–43.5)	0.279
Hemoglobin (g/L)	111 (69–159)	111 (72–159)	111 (69–142)	0.157
High-grade serous carcinoma (%)	250 (88.7%)	157 (86.3%)	93 (93.0%)	0.088
Presence of ascites at surgery (%)	222 (78.7%)	147 (80.8%)	75 (75.0%)	0.257
Ascites volume (mL)	800 (50-8000)	800 (50-8000)	1000 (50-7500)	0.721
Extensive bowel resection (%)	29 (10.2%)	20 (11.0%)	9 (9.0%)	0.599
Upper abdominal surgery (%)	69 (24.4%)	57 (31.3%)	12 (12.0%)	< 0.001
Extent of debulking				
Residual disease = 0 cm (%)	121 (42.9%)	88 (48.4%)	33 (33.0%)	0.013
Residual disease ≤ 1 cm (%)	248 (87.9%)	166 (91.2%)	82 (82.0%)	0.023
Operation time (minutes)	197 (60–371)	203 (97–371)	172 (60–324)	0.002
Estimated blood loss (ml)	1000 (100–3500)	950 (100–3500)	1000 (200–2500)	0.983
Transfusion (%)	248 (87.9%)	156 (85.7%)	92 (92.0%)	0.121

Variables	Total (n = 282)	Anastomosis (n = 182)	Ostomy (n = 100)	P
Red blood cell transfusion (unit)	3 (0–11)	3 (0–11)	3 (0–9)	0.931
Postoperative hospital stay (days)	13 (5–53)	13 (5–53)	10 (5–40)	< 0.001
Time to chemotherapy (days)	19 (7–50)	20 (7–50)	18 (7–41)	0.139
Abbreviations: CA-125 = Cancer Antigen 125				

We further compared the patient information and perioperative outcomes between anastomosis and ostomy group. Patients who received ostomy formation were significantly older than the anastomosis counterparts. The percentage of upper abdominal surgery was higher in the anastomosis group compared to the ostomy group (31.3% Vs. 12.0%, $P < 0.001$). More patients in the anastomosis group achieved complete (R0) or R1 resection. Not surprisingly, patients with anastomosis had both longer operation time (203 Vs. 172 minutes, $P = 0.002$) and postoperative hospital stay (10 Vs. 13 days, $P < 0.001$). However, there was no difference between two groups concerning the time interval from surgery to chemotherapy.

Totally, 29 patients received more than one-segment bowel resection and the specific details are listed in Table 2. Rectosigmoid colon was the most commonly resected (268/320, 83.8%), followed by right hemicolectomy (19/320, 5.9%) and small bowel resection (9/320, 2.8%).

Table 2
Type of bowel resections

One-segment bowel resection (n = 253)	
Rectosigmoid resection	238
Right hemicolectomy	7
Ileocecal resection	2
Transverse colon resection	2
Left colon segmental resection	2
Left colon resection	2
Extensive bowel resection (n = 29)	
Rectosigmoid resection + small bowel resection	5
Rectosigmoid resection + ileocecal resection	3
Rectosigmoid resection + right hemicolectomy	10
Rectosigmoid resection + transverse colon resection	1
Rectosigmoid resection + left colon resection	4
Rectosigmoid resection + right colon segmental resection + small bowel resection	1
Rectosigmoid resection + right hemicolectomy + small bowel resection	1
Rectosigmoid resection + right hemicolectomy + left colon resection	1
Rectosigmoid resection + transverse colon segmental resection + left colon segmental resection	2
Rectosigmoid resection + left colon resection + small bowel resection	1
Rectosigmoid resection + right colon segmental resection + small bowel resection	1
Type of bowel surgery in descending order (n = 320)	
Rectosigmoid resection	268
Right hemicolectomy	19
Small bowel resection	9
Left colon resection	8
Ileocecal resection	5
Left colon segmental resection	4
Transverse colon resection	3

One-segment bowel resection (n = 253)	
Right colon segmental resection	2
Transverse colon segmental resection	2

Table 3 shows the details on surgical complications. For the entire cohort, 19.9% (56/282) experienced complications (not include AL) to different extent. Of them, severe complications (CDC 3–5) accounted for 7.8%, mostly pleural effusion requiring drainage (3.5%), and followed by wound dehiscence requiring delayed repair in operation room (1.8%).

Table 3
Surgical complications

Mild complications in entire population (CDC 0–2)	**34**	**12.1%**
Bowel obstruction	15	5.3%
Infection (abdominal/pelvic/bloodstream)	8	2.8%
Wound infection/dehiscence	4	1.4%
Pleural effusion	4	1.4%
Heart arrhythmia	1	0.4%
Pancreatic leak	1	0.4%
Deep venous thrombosis	1	0.4%
Severe complications in entire population (CDC 3–5)	22	7.8%
Pleural effusion requiring drainage	10	3.5%
Wound dehiscence requiring delayed repair in operation room	5	1.8%
Bowel obstruction	2	0.7%
Bleeding requiring return to operating room	2	0.7%
Septic shock	1	0.4%
Acute kidney failure	1	0.4%
Ureterostenosis requiring stent implantation in operation room	1	0.4%
Anastomotic leak		
Anastomotic leak in the entire population with anastomosis	9	4.2% [a]
Anastomotic leak in the anastomosis group	8	4.0% [a]
		4.4% [b]
Anastomotic leak in patients with one-segment bowel resection and anastomosis	7	4.3% [ab]
Anastomotic leak in patients with extensive bowel resection and anastomosis	2	4.0% [a]
		8.0% [b]
Anastomotic leak in patients with rectosigmoid resection only and anastomosis	6	5.0% [ab]

Abbreviations: CDC = Clavien-Dindo Classification
[a] Anastomotic leak rate per anastomosis.
[b] Anastomotic leak rate per patient.

When it comes to anastomotic leak, nine events were reported in total: one in the ostomy group (rectosigmoid resection + right hemicolectomy + left colon resection + ileostomy), and eight in the anastomosis group. The total number of bowel anastomosis in the entire population was 212 and it translated in an overall AL rate of 4.2% (9/212) per anastomosis. In the anastomosis group, the AL per patient was 4.4% (8/182) while the AL per anastomosis 4.0% (8/202). Five patients with AL (four in anastomosis group and one in ostomy group) were successfully managed with conservative treatment. Overall, 187 patients had anastomosis after bowel resection: 162 with one-segment (162 anastomosis) and 25 with multiple bowel resections (50 anastomosis). The AL per patient was higher in patients with extensive bowel resection (8%, 2/25) compared to those with one-segment resection (4.3%, 7/162). However, the AL per anastomosis was quite comparable between two groups (4.3% Vs. 4.0%). We further focused on the patients with isolated rectosigmoid resection and anastomosis (n = 146). Among them, 119 had end-to-end anastomosis while 27 had end-to-side anastomosis. Six patients (5.0%) in the end-to-end anastomosis group experienced AL while no case was reported in the end-to-side group.

Discussion

In the current series, we analyzed the results of patients with advanced ovarian cancer receiving bowel resection in debulking surgery. Different from our previous two publications (7, 8), the current study included all the patients with bowel operation, instead of isolated rectosigmoid resection. To the best of our knowledge, the present study is probably the first study from a Chinese academic center. All the surgical procedures were performed by the gynecologic oncologists in our institution. We demonstrated that the bowel resections as part of debulking were feasible and safe, which resulted in acceptable complication rate.

Ovarian cancer often spreads along the peritoneal surface and invades the bowel serosa and mesentery (9). According to a previous study, 72% of the advanced ovarian cancer patients had visible tumor in the small and large bowels (13). The bowel resection rate during cytoreductive surgery ranged from 40–80% in institutions adopting radical surgery (12, 14–16). Two recent publications evaluated multiple bowel resections in ovarian cancer, one from Germany (12) and one from Korea (9).

In terms of perioperative adverse events especially anastomotic leak, we presented that the overall AL rate was 4.2% per anastomosis. In our previous work including 50 cases receiving isolated rectosigmoid resection and anastomosis, the AL rate was 4.0% per patient. The AL rate was higher in patients with multiple bowel resections if the rate was calculated by patient (8.0%). However there was no difference concerning AL rate per anastomosis. Our reported AL rate is quite in line with previous findings, as other series reported AL rates of 6.0% (Memorial Sloan-Kettering Cancer Center, USA) (14), 6.6% (eight hospitals in Spain) (17), 2.89% (Hopital Europeen Georges Pompidou, France) (18), and 6.9% (Comprehensive Cancer Center Vienna, Austria) (12).

Given the small number of patients with anastomotic leak, we did not assess the underlying risk factors. A recent multi-center study from Spain, including 457 patients, investigated the risk factors for

anastomotic leak after colorectal resection in ovarian cancer patients (17). They concluded that the following variables were independent risk factors for AL: age at surgery, preoperative serum albumin level, one or more additional small bowel resections, manual anastomosis and distance of the anastomosis form the anal verge (17). Another study from Mayo Clinic evaluated 42 AL cases in comparison to 84 controls with matched factors (19). They found that multiple large bowel resection (rectosigmoid resection coupled with additional large bowel resection) was related with AL and protective diverting stomas decreased the risk (19). In our study, only three patients had protective stomas while the AL rate was acceptable. Therefore, we do not routinely perform protective stomas in our center. We did pay attention to blood transfusion to ensure adequate blood supply and albumin supplementation as reflected by the pre- and post- laboratory parameters (Table 1). Out of curiosity, we compared the different kinds of anastomosis in patients with only rectosigmoid resection and anastomosis (n = 146). Interestingly, six patients (5.0%) in the end-to-end anastomosis group experienced AL while no case was reported in the end-to-side group. However, due to the small size, we could not arrive at a conclusion.

The study has some limitations. Firstly, it has inherent bias pertaining to its retrospective design. Secondly, as mentioned before, we didn't evaluate the risk factors for AL given the small outcome events. Thirdly, we only assessed the perioperative outcomes and survival information was not available. Lastly, given that the study patients were collected from a tertiary referral center, the results might not be generalizable to all of the patients in China.

Conclusions

Performance of bowel surgery in cytoreduction by experienced gynecologic oncologists in a high-volume center were feasible and resulted in an acceptable morbidity rate. Referrals should be considered at institutions where the necessary treatments are unavailable.

Abbreviations

BMI: Body Mass Index; CA-125: Cancer Antigen 125; Estimated Blood Loss (EBL); CDC: Clavien-Dindo classification; AL: anastomotic leak.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board at Fudan University Shanghai Cancer Center. The written informed consent was waived due to retrospective design.

Consent for publication

Not applicable.

Availability of data and material

The dataset supporting the conclusions of this article is available upon request. Please contact Prof. Libing Xiang (xianglibing_123@sina.com) and Prof. Huijuan Yang (huijuanyang@hotmail.com).

Competing interests

All the authors have nothing to declare.

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Author's contributions

All the authors contributed to the contraception and design of the study. SY, YW and LC collected and analyzed patients' clinicopathological data. SY, LX and HY were responsible for statistic analysis. SY, YW and LC were major contributors in writing the manuscript. All authors read and approved the final manuscript.

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Figures

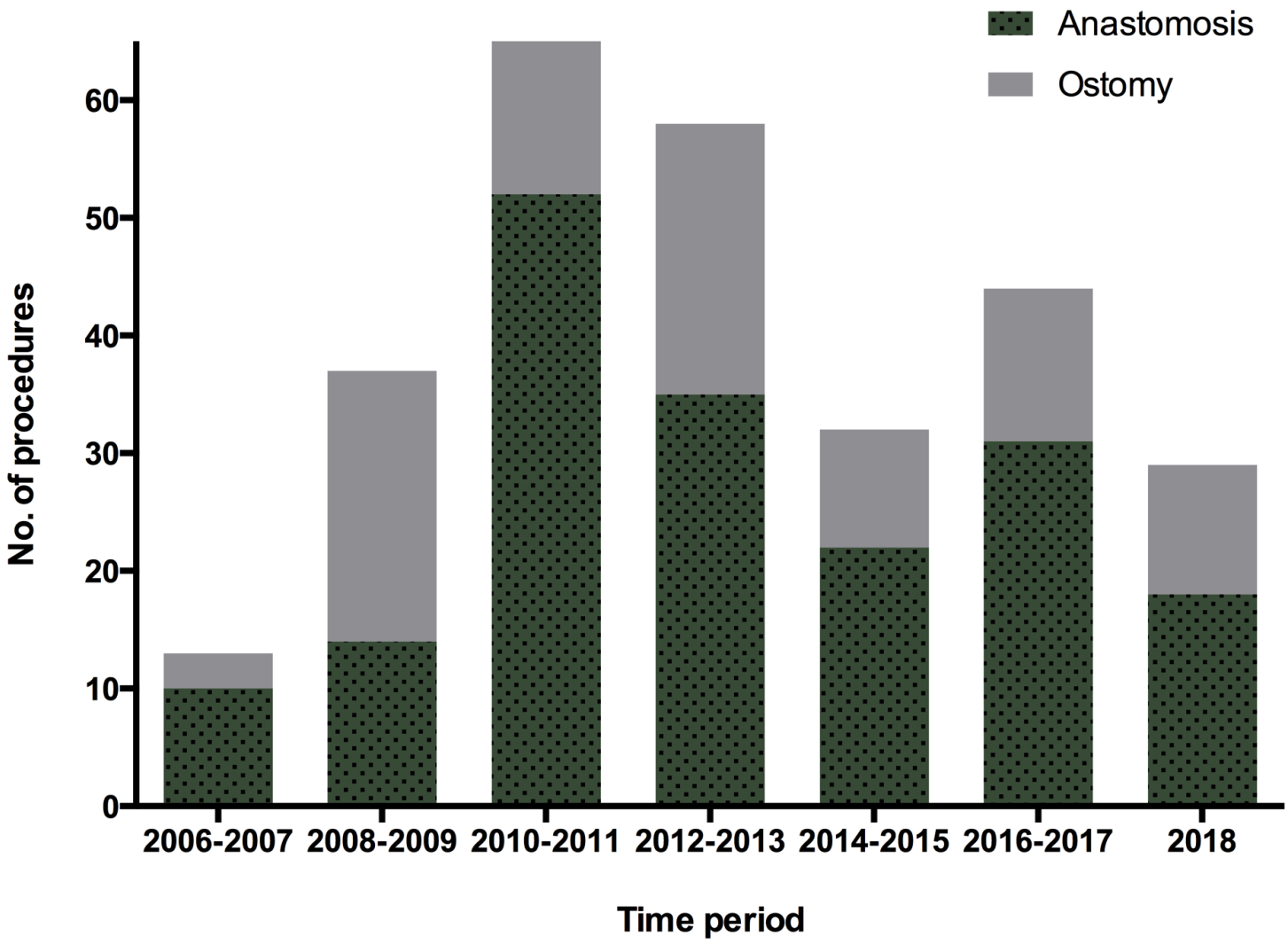

Figure 2

The number of bowel resection during debulking surgery in ovarian cancer patients at the Fudan University Shanghai Cancer Center over the past 13 years.