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Extended Pelvic Resections as Part of Secondary Cytoreduction for Relapsed Ovarian Adenocarcinoma

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Abstract. *Background/Aim: Ovarian cancer presents an aggressive tumor biology, a significant number of patients experiencing recurrent disease. The aim of this study was to examine the feasibility and effectiveness of secondary debulking surgery for relapsed ovarian cancer. Patients and Methods: Between 2014 and 2018, debulking surgery for relapsed ovarian cancer was performed in 40 cases. Results: Debulking surgery to no residual disease was achieved in 31 cases; among the remaining cases, an R1 resection was feasible in six cases, while in the remaining three cases an R2 resection was performed. The most commonly performed visceral resections were represented by rectosigmoidian resection, right colon resection, total or partial cystectomy and unilateral or bilateral ureteral resection. The early postoperative morbidity rate was 32.5% while the postoperative mortality rate was 2.5%. Conclusion: Extended pelvic resections are feasible in patients with relapsed ovarian cancer and might be performed with acceptable rates of postoperative complications.*

Ovarian cancer remains the most lethal gynecologic malignancy and a common cancer affecting women worldwide (1). Due to the fact that there is no available screening test for early detection of this pathology, up to two thirds of patients are still diagnosed in advanced stages of the disease. Unfortunately, in such cases, although a therapeutic strategy with curative intent is applied, the majority of patients will develop recurrent disease and a significant proportion of these cases will finally die due to this disease. Therefore, attention was focused on determining which is the most effective therapeutic strategy when relapse occurs. Once the benefits of maximal debulking surgery followed by adjuvant chemotherapy were clearly demonstrated, study groups worldwide investigated whether this strategy might be feasible and beneficial for patients diagnosed with ovarian cancer relapse (2-7).

As for the sites of relapse, it has been widely demonstrated that recurrence might occur in any abdominal quadrant as isolated recurrence or, most often, as multiple tumoral lesions. In consequence, in such cases, multiple visceral abdominal and pelvic resections should be performed if cytoreductive surgery with radical intent is proposed. When it comes to the feasibility and efficacy of extended pelvic resections for recurrent disease, the fact that these patients have already been submitted to certain gestures of pelvic surgery at the time of primary cytoreduction has to be considered. Therefore, the anatomy of the pelvic area probably suffered certain modifications, which might induce an increase in the difficulty of performing extended pelvic resections for ovarian cancer relapse (8-10).

Patients and Methods

After obtaining the Ethical Committee's approval, data of patients in which secondary cytoreduction for relapsed ovarian cancer was attempted were retrospectively reviewed. Between 2014 and 2018, 54 patients diagnosed with ovarian cancer pelvic relapse were submitted to surgery with radical intent. However, among these cases, debulking surgery was feasible in only 40 cases; among the remaining 14 cases surgery consisted only of biopsy in five cases and respectively of palliation surgery in the remaining nine cases. In the remaining 40 cases debulking surgery was feasible: the cytoreductive procedure was defined as maximal if no residual disease was achieved, as optimal if the residual tumor was lower than 1 cm and suboptimal if the maximal residual tumor was higher

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than 1 cm. Postoperative complications were defined according to the Dindo-Clavien classification (11).

Results

The median age at the time when secondary cytoreduction was attempted was 67 years (range=43-78 years), while the median disease-free survival between the end of adjuvant chemotherapy and the diagnosis of the pelvic recurrence was 16 months (range=12-54 months). Among these cases, the initial stage at diagnosis was FIGO (International Federation of Gynecology and Obstetrics) III in 31 cases, FIGO IV in seven cases and FIGO II in the remaining two cases. Details of the clinic-pathological characteristics and of the surgical procedures at the time of the initial diagnosis are shown in Table I.

As it can be seen from the above presented data, in this cohort, extended pelvic resections were associated in certain cases with upper abdominal resections in order to achieve a complete cytoreductive procedure. Therefore, the most commonly involved upper abdominal viscera were represented by liver and spleen, being followed by pancreas and stomach. As for the pattern of involvement, the peritoneal route (through peritoneal carcinomatosis) was most frequently encountered (in 33 cases) and was followed by the hematogenous route (in 11 cases) and the lymphatic route (in three cases); synchronous – peritoneal and hematogenous route was encountered in seven cases.

When it comes to the influence of the number of recurrences on the completeness of cytoreduction, no significant correlation was observed between this number and the feasibility of a complete cytoreduction. Contrarily, the volume of ascites significantly influenced the feasibility of a complete cytoreduction; therefore, 26 of the 28 cases presenting low ascites volume benefited from complete cytoreduction, while only five cases presenting higher amounts of ascites were submitted to a radical surgical approach.

The median estimated blood loss on the entire study group was 550 ml (range=200-980 ml), while the median length of surgery was 330 min (range=280-360 min). During the perioperative interval, transfusion was needed in 11 of the 40 cases, the median number of transfused units being 2 (range=0-3). When it comes to the early postoperative evolution, complications were encountered in 13 cases and were classified as grade 2 in four cases, grade 3 in five cases and grade 4 in the remaining four cases. The most commonly encountered complications were respiratory dysfunctions in three cases, pleural effusion necessitating pleural drainage in three cases, wound infection in four cases, postoperative digestive or urinary leaks in five cases, abdominal abscesses in four cases and postoperative bleeding in four cases. All patients who experienced postoperative bleeding were classified as Dindo-Clavien grade 4 complications and needed reoperation. Patients diagnosed with abdominal abscesses were treated in a conservative manner (by percutaneous drainage in two cases) and by reoperation in the other two cases, and patients who experienced digestive or urinary leaks were treated in a conservative manner in two cases and by re-operation in the remaining three cases. In one case where a ureteral leak at the site of reimplantation (after partial cystectomy and distal ureteral resection) was encountered, the patient finally died due to septic shock in the 34th postoperative day. The median length of hospital stay was 18 days (range=7-34 days).

Table I. *Clinic-pathological and surgical details at the time of the initial diagnosis.*

Parameter	No. of cases
Stage at the initial diagnostic	
II	2
III	31
IV	7
Histopathological subtype	
Serous	29
Mucinous	5
Endometroid	4
Clear cell	2
Degree of differentiation	
Well differentiated	13
Moderately differentiated	21
Poorly differentiated	6
Number of recurrences	
Single	8
Multiple	32
Ascites	
Low volume (<500 ml)	28
High volume (>500 ml)	12
Association of visceral resections	
Rectosigmoidian resection	11
Right colon resection	9
Small bowel resection	7
Cystectomy (total/partial)	6 (4/2)
Ureteral resection (unilateral/bilateral)	5 (1/4)
Atypical hepatectomy	5
Splenectomy	3
Distal pancreatectomy	1
Parcelar gastrectomy	1
Completeness of cytoreduction	
R0	31
R1	6
R2	3

Discussion

It has been widely demonstrated that despite achieving a maximal surgical cytoreduction and an adequate adjuvant chemotherapeutic regimen, most patients diagnosed with

advanced stage ovarian adenocarcinoma will develop recurrent disease at a certain moment of their evolution. Therefore, in such cases different therapeutic strategies have been proposed; however, it seems that a maximum benefit in terms of survival is achieved if secondary debulking surgery to no residual disease is feasible. These findings are best supported by the studies which compared the outcomes of patients diagnosed with recurrent ovarian cancer and treated solely by chemotherapy to those of patients treated by secondary debulking surgery followed by chemotherapy (12).

Due to the fact that in such cases it seems that the key factor which influences long-term outcomes is related to the feasibility of complete cytoreduction, certain authors focused their attention on determining which are the prognostic factors which are associated with a higher chance of obtaining a maximal debulking surgery for recurrent disease. Therefore, the DESKTOP II trial demonstrated that patients with a good performance status, with lower than 500 ml of ascites and with complete debulking surgery at the time of the initial diagnosis are most likely to achieve a complete debulking surgery at the time of relapse (13). These data were also demonstrated by the study conducted by Felsinger *et al*. (14), where the authors introduced 62 patients diagnosed with relapsed ovarian cancer: 30 cases were submitted to secondary cytoreduction and adjuvant chemotherapy and the remaining 32 cases were submitted solely to chemotherapy. Inclusion criteria for debulking surgery were a good performance status, a single site of recurrence, absence of peritoneal carcinomatosis, platinum-free interval higher than 12 months and small volume of ascites. The authors demonstrated a significantly better outcome for surgically treated patients (disease-free survival being of 49.8 months and overall survival being of 54 months within the first group and only of 16.6 months and 26.2 months respectively in the chemotherapy treated group). Among patients submitted to secondary cytoreduction, the long-term outcomes seemed also to be influenced by an age younger than 60 years at secondary surgery and the absence of residual disease after secondary cytoreductive surgery (14).

Another important factor which should be taken in consideration whenever secondary cytoreduction is attempted is the one related to the risk of perioperative complications. This factor is considered by certain authors as a real cornerstone of decision making as well as of patient counseling. An interesting study, which was conducted on this issue was published in 2010 in the European Journal of Surgical Oncology (15). The study included 222 patients submitted to surgery – 48 cases diagnosed with relapsed ovarian cancer and 174 patients diagnosed with advanced stage ovarian cancer. The median time between primary and secondary debulking surgery among the 48 cases submitted to surgery for recurrent disease was 15 months. The outcomes of these cases were compared to the ones reported for patients submitted to surgery for advanced stage ovarian cancer. The authors underlined the fact that the necessity of performing extended surgical procedures was similar between the two groups. However, the median operating time was significantly shorter and the necessity of blood transfusion was lower at the secondary cytoreduction. However, the hospital stay was three days longer among patients submitted to secondary debulking surgery. In terms of postoperative complications, the rates of morbidity were similar between the two groups. However, the rates of intestinal complications such as the number of intestinal injuries and the length of the postoperative ileus were higher among patients submitted to secondary cytoreductive surgery, although the univariate analysis failed to show any significant correlation between the association of specific procedures (such as bowel resection or diaphragmatic procedures) and the risk of postoperative complications. Furthermore, this parameter (the type of surgical procedure) did not influence the overall survival. Therefore, the authors concluded that secondary debulking surgery can be safely performed without increasing the risks of postoperative complications (15).

In order to maximize the completeness of cytoreduction, cases associating upper abdominal lesions might be submitted to upper abdominal resections with acceptable rates of postoperative complications due to improvement of the surgical technique (16-18).

Moreover, in the last decade, attention has been focused on the feasibility of secondary cytoreductive surgery in a minimally invasive manner. Therefore, laparoscopy and robotics proved to be more effective in cases presenting isolated recurrences, while the open approach remained the preferred option in cases presenting peritoneal lesions, multiple recurrences and extensive adhesions. However, the minimally invasive approach was associated with a shorter hospital stay and with reduced blood loss; therefore, the authors concluded that, at the moment the minimally invasive approach should be reserved only for selected cases, diagnosed with isolated recurrences (19).

Conclusion

Extended pelvic resections seem to be feasible and effective in patients diagnosed with recurrent ovarian cancer, an important number of patients benefiting from a complete cytoreductive process. Moreover, in order to maximize the completeness of cytoreduction, upper abdominal resections might be associated without a significant increase in postoperative morbidity and mortality rates.

Conflicts of Interest

There are no conflicts of interest to declare regarding this study.

Authors' Contributions

NB – Performed surgical procedures; IB, MV – prepared the manuscript; IB, MV, SD – data analysis, prepared the table; MV, IB – part of the surgical team; IB – advised about the surgical oncology procedure, revised the final draft of the manuscript.

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