Cytoreductive surgery for late recurrence after surgically treated stage IV ovarian cancer. A case report

Nicolae Bacalbasa[1], Irina Balescu[2], Dan Navolan[3]

1. "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
2. "Ponderas" Hospital, Bucharest, Romania
3. Department of Obstetrics-Gynecology and Neonatology, "Victor Babes" University of Medicine and Pharmacy Timisoara, City Emergency Clinical Hospital Timisoara, Romania

Correspondence:
Dr. Nicolae Bacalbasa
e-mail: nicolae_bacalbasa @yahoo.ro

Abstract

Recurrence is a common finding after surgically treated ovarian cancer even in cases submitted to initially R0 resection. However, it is well known that an aggressive surgical approach is perfectly justified at the moment of relapse, being the only solution in order to increase the survival rates. We present the case of a 62 year old patient who was previously submitted to surgery for stage IV ovarian cancer followed by 6 cycles of adjuvant chemotherapy. At 4 years follow up she was diagnosed with disseminated abdominal recurrences and she was submitted to secondary cytoreduction. Postoperatively, adjuvant chemotherapy with platinum based regimens was instituted.
Keywords: *stage IV ovarian cancer, chemotherapy, secondary cytoreduction*

Introduction

Large studies have demonstrated the benefits of complete cytoreduction at the moment of primary surgical approach in advanced stage ovarian cancer[1-3]. However the presence of upper abdominal disseminations at the moment of initial diagnosis was usually associated with a biologically aggressive tumor with low chances of long term survival[4-7]. Once the surgical technique improved and surgical procedures such as hepatic resection have been included in the ovarian cancer therapeutic armamentarium increased rates of disease free survival and overall survival were obtained, enabling the surgeon to consider that an aggressive surgical approach is perfectly justified in stage IV ovarian cancer too. However, although an R0 resection is achieved, most patients will recur at a certain moment.

Case report

A 62 year old patient was previously submitted to surgery for stage IV ovarian cancer in Poderas Hospital from Bucharest, Romania. At that moment we performed a total hysterectomy, bilateral adnexectomy, omentectomy, pelvic and parietal bilateral peritonectomy and two atypical hepatic resections for two isolated liver metastases. The histopathological examination revealed the presence of a moderately differentiated serous ovarian adenocarcinoma. Pathological examination of the specimens of hepatectomy confirmed the presence of two parenchimatous lesions measuring 3/4/4 cm and 2/3/1 cm respectively, entirely surrounded by normal hepatic parenchima measuring at least 2 cm in depth. In this case, the final diagnosis was stage IV serous ovarian adenocarcinoma and the patient was submitted to 6 cycles of adjuvant chemotherapy. Four years after ending the adjuvant oncologic therapy the patient re-addressed for diffuse abdominal pain and sub-occlusive syndrome. The computed tomography revealed the presence of disseminated abdominal tumors involving the small bowel mesentery, bilateral diaphragmatic peritoneum, glissonian surface of the liver and the spleen. We decided to re-operate the patient. Therefore, at the moment of secondary cytoreduction diaphragmatic peritonectomy with partial diaphragmatic resection, segmentary enterectomy, splenectomy and Glissonian nodules resection were performed (Figures 1-7). The patient was discharged in the 10th postoperative day and she was re-submitted to adjuvant chemotherapy.

Discussion

Ovarian cancer is one of the most aggressive gynaecologic malignancies, with a high capacity of producing disseminated recurrences[8,9]. Most patients are diagnosed in an advanced stage of the disease when distant metastases have already appeared. In these cases, the most efficient treatment remains an aggressive surgical approach in order to remove the entire tumor burden[6,7]. Since Meigs exposed for the first time the principles of cytoreductive surgery and Griffiths demonstrated their efficiency by an inverse proportionality between residual disease and survival, these principles became the cornerstone in treating advanced ovarian cancer[10,11]. Advances in surgical technique and formation of multidisciplinary teams including oncologic surgeons, gynecologic oncologist and hepato-bilio-pancreatic surgeons increased the rates of complete cytoreduction even in patients diagnosed in advanced stages with upper abdomen tumor burden and improved the outcomes[12,13].

One of the most eloquent studies which demonstrated the efficacy of association of upper abdominal resections at the

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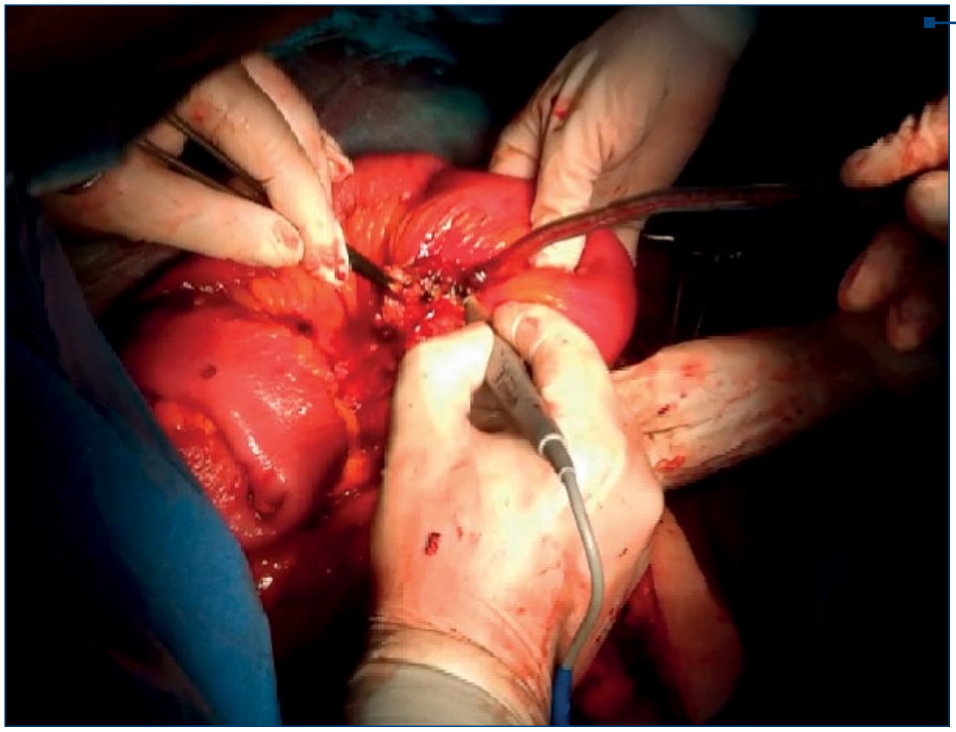

Figure 1. ***Removing a nodule on the mesentery surface***

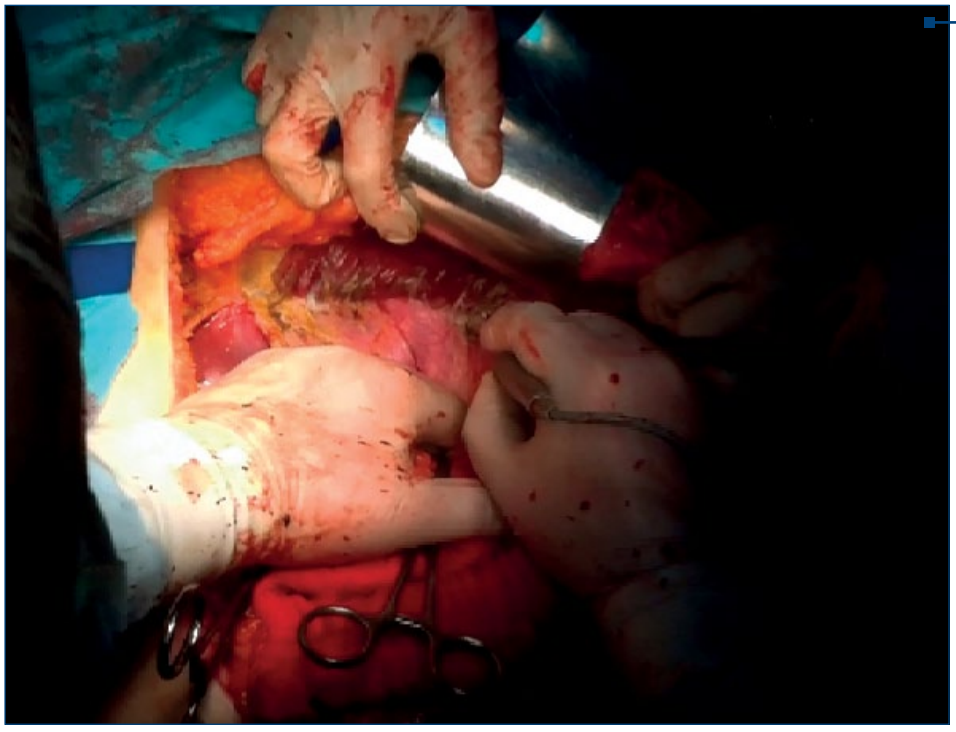

Figure 2. ***Left diaphragmatic peritonectomy***

moment of primary cytoreduction was the one conducted by Chi and contributors[14]. In this study, the contributors included two cohorts of patients with advanced stage ovarian cancer. Upper abdomen surgical procedures were included only in the second subgroup of patients. Group 2 showed an increased rate of optimal cytoreduction (80% vs 46%; p=0.001), while the percentage of patients with no grossly visible disease increased from 11% in Group 1 to 27% in Group 2. Five-year progression free survival and overall survival rates for the second group vs. the first group were

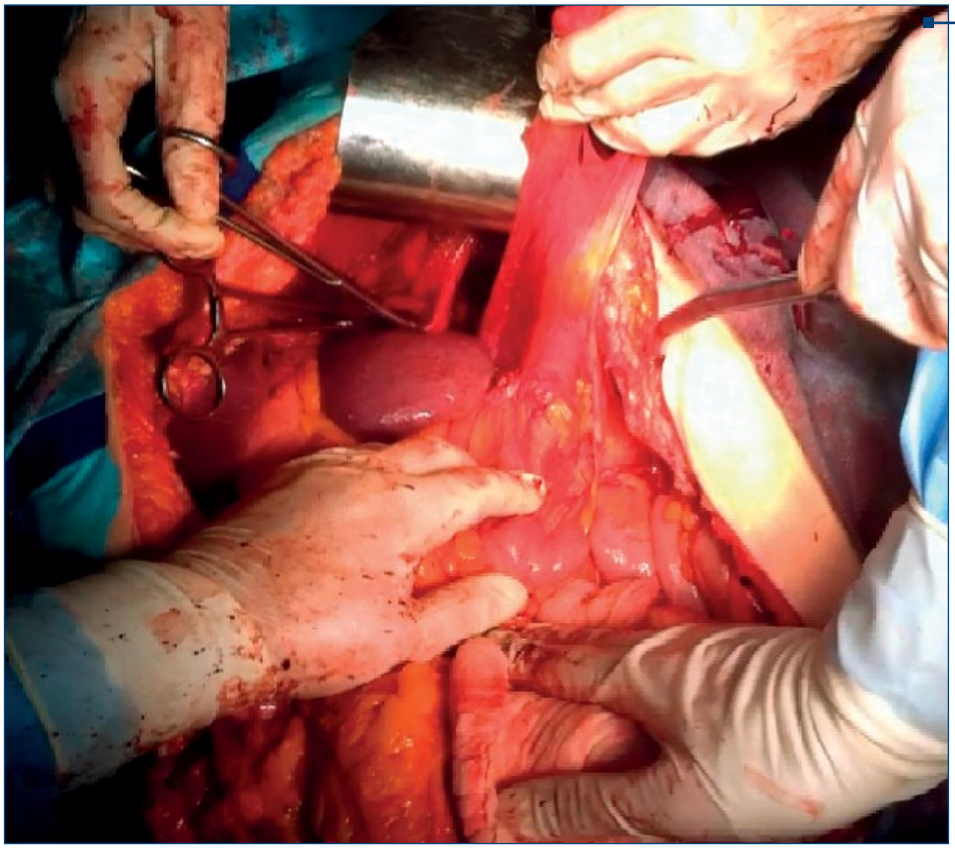

Figure 3. ***The aspect of the left parietal and diaphragmatic peritonectomy***

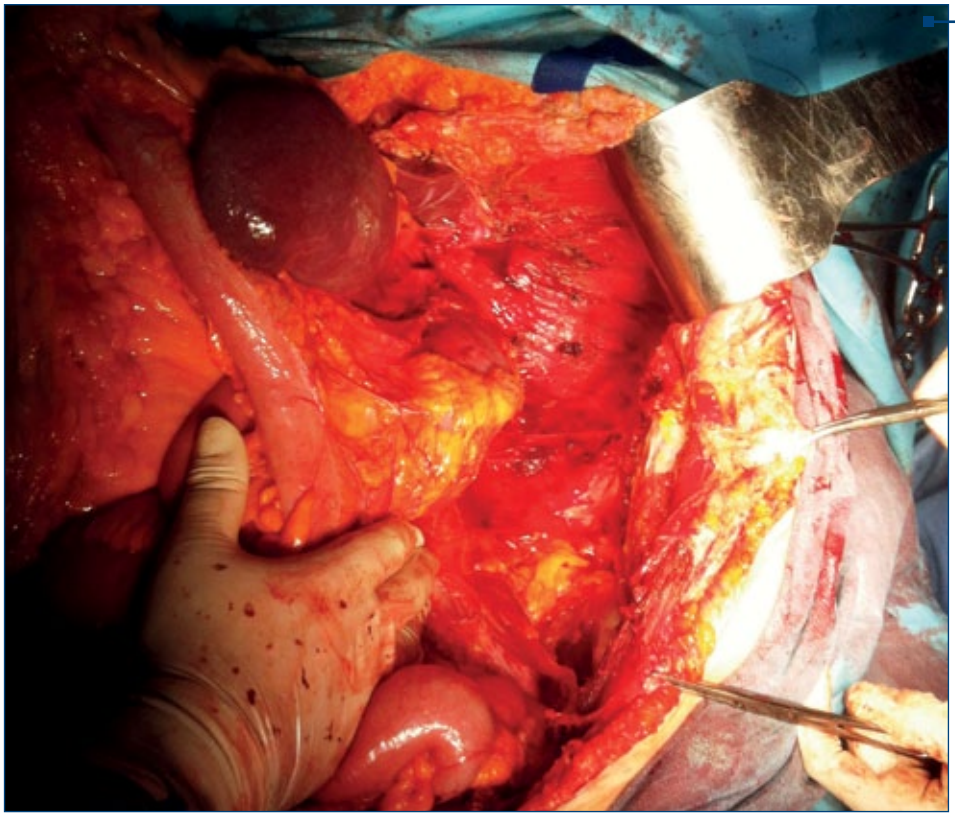

Figure 4. ***The final aspect after left peritonectomy and complete mobilization of the spleen***

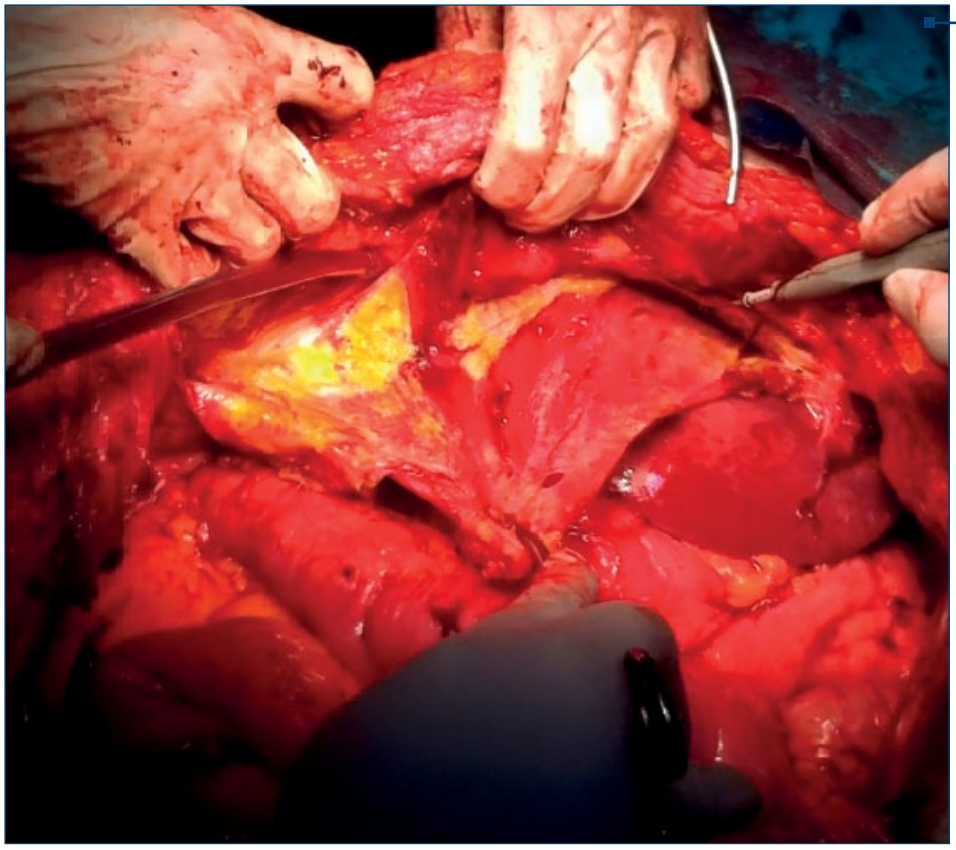

Figure 5. ***Performing right diaphragmatic peritonectomy***

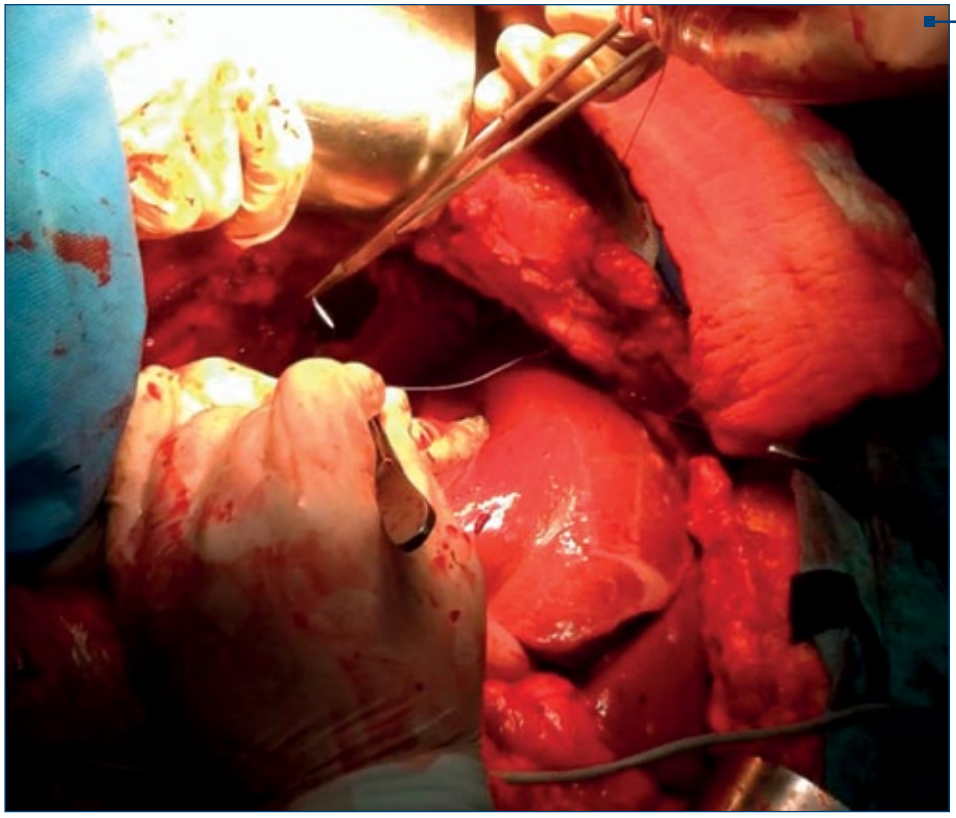

Figure 6. ***Suturing the right hemi-diaphragm after full thickness right diaphragmatic resection***

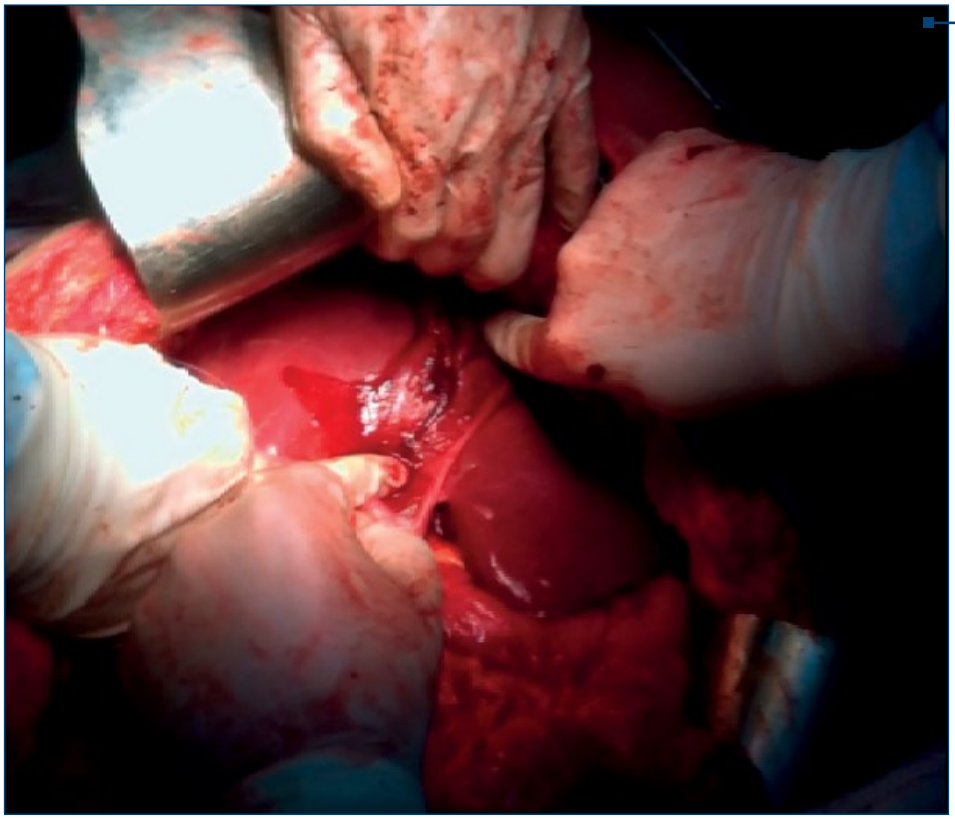

Figure 7. ***The final aspect after removing the glissonian nodules***

31% vs. 14% and 47% vs. 35%, respectively[14]. These results enabled surgeons worldwide to re-consider the therapeutic options especially when treating patients diagnosed in classical classification of stage IV ovarian cancer and to try to obtain a complete cytoreduction in these cases too.

Regarding our case, a disease free survival of 3.5 years (i.e. between ending the adjuvant chemotherapy and diagnosis of disseminated recurrence) for a patient initially diagnosed in stage IV ovarian cancer which was previously submitted to an R0 resection come to sustain the efficacy of an aggressive surgical approach even in cases presenting hematogenous liver metastases.

However, although at that moment complete resection was performed the malignancy relapsed. This is not a rare condition especially when it comes to ovarian cancer, most patients being diagnosed with tumor recurrence at a certain moment. Once the positive diagnosis of recurrent tumor is achieved, there are more therapeutic approaches. There are studies which sustain the benefits of neo-adjuvant chemotherapy in order to diminish the tumor burden before submitting the patient to a novel surgical approach. In certain cases at that moment neo-adjuvant chemotherapy is not very efficient due to the presence of high amounts of old tumor cells with a low mitotic activity and a low susceptibility to the cytotoxic activity of neo-adjuvant chemotherapy[15-17]. Due to these facts, the secondary cytoreductive surgery might be needed in some cases. In order to obtain a complete resection at the moment of secondary cytoreduction multiple visceral excisions might be needed. However, due to the improvements of surgical techniques and postoperative management, nowadays these resections seem to be feasible without increasing the postoperative morbidity but with an improved rate of long term survival.

When discussing about the incidence of metastatic disease in spleen for persistent or recurrent ovarian cancer, it ranges between 0.3 to 4.8%[18,19]. Traditionally, the spleen was considerate a pharmacologic sanctuary in which cytotoxic agents cannot action, allowing in this way to tumor cells to create isolated metastases at this level[20,21].

In order to determine the benefits of splenectomy as part of primary and secondary cytoreductive surgery, Magtibay and contributors[22] included in their study 112 patients: in 66 of them splenectomy was performed at the moment of primary cytoreduction while in the other 46 cases the spleen was removed at the moment of secondary cytoreduction. However no case of sepsis was directly related to splenectomy. The postoperative mortality rate was 5%. Two deaths were associated to thromboembolic events, while the cause of death for 1 patient remained unknown. Patients who underwent splenectomy at the moment of secondary cytoreduction reported a median overall survival rate of 20.3 months, with an estimated 2-year survival of 42.3%[22].

When it comes to bowel obstruction at the moment of diagnosis of recurrent disease, this is a common clinical issue, being encountered in up to 35% of patients with recurrent disease and is usually associated with poor outcomes[23]. The main patho-physiological incriminated mechanism seems to be widespread carcinomatosis, intra-abdominal and/or

locoregional recurrences causing extrinsic compression. Retroperitoneal disease (i.e. nodal involvement and involvement of mesenteric plexus) or postoperative adhesions[24].

Kolomainen and contributors[25] introduced in their study 90 women diagnosed with bowel obstruction secondary to relapsed ovarian cancer who were submitted to surgery at Royal Marsden Gynaecology Unit. The initial FIGO stages were: stage I in 10 cases; stage II in two patients; stage III in 69 cases and stage IV in 9 cases. Suboptimal cytoreductive surgery was performed in 25 of the 77 patients with advanced disease atthe moment of primary treatment. The median time from ovarian cancer diagnosis to documented bowel obstruction was 19.5 months. Intraoperatively the main sites of obstruction were large bowel (22%), small bowel (42%) or an association of both causes (29%). Forty-nine patients were submitted to emergency surgery, one of them being operated during the first 24 hours after admission; in all the other cases a pre-operative hydro-electrolytic re-equilibration was needed. The main surgical procedures included bowel resection and anastomosis in 40 patients, internal derivative procedure including stoma in 5 patients, and stoma in 56 patients. Postoperative complications were seen in 24 cases. Therefore, only 1 patient necesitated emergency re-operation for entero-vaginal fistula, while another case was submitted to re-operation for laparostomy closure. In the other 22 cases the postoperative complications were treated by conservative approach. The authors reported a postoperative mortality rate of 18%. The median overall survival rate from the moment of bowel obstruction surgery was 90.5 days[25].

In order to assess the outcomes and morbidity following diaphragmatic peritonectomy for patients with advanced or recurrent ovarian cancer, Dowdy and contributors[26] conducted a study on 56 patients. In 19 cases diaphragmatic peritonectomy was part of secondary cytoreduction. The authors also reported an association of other visceral resections in 82% of cases, the most frequently seen procedures being large bowel resection (52%), splenectomy (21%) and small bowel resection (19%). An R0 resection was achieved in 95% of cases. The most common complication was pleural effusion, in 12 cases. However only 5 of them necessitated a thoracocentesis or placement of a chest tube. All the other cases were solved by conservative management. The authors reported a 5 year survival rate of 16% for cases submitted to diaphragmatic peritonectomy at the moment of secondary cytoreduction and a median overall survival of 23 months after the moment of secondary cytoreduction[26].

In another study conducted by Fanfani and contributors[27] 87 patients underwent diaphragmatic surgery for ovarian cancer: in 21 of the patients diaphragmatic surgery was performed at the moment of secondary cytoreduction. Diaphragmatic resection was performed in 13 patients while diaphragmatic peritonectomy was performed in 56 of the patients. In twelve patients bilateral diaphragmatic involvement was found. The most frequently seen postoperative complication remained pleural effusion in 37 cases and necessitated pleural drainage in 10 cases. The overall survival for patients who underwent diaphragmatic resection at the moment of secondary cytoreduction was 24 months. The authors concluded that diaphragmatic resection represent a safe method which might increase the rate of complete cytoreduction and secondary the overall survival without significant increase of postoperative morbidity[27].

Conclusions

An aggressive surgical approach is perfectly justified at the moment of secondary cytoreduction in order to increase the rate of complete resection. Our recommendation is that the association of extended procedures such as diaphragmatic resection, splenectomy or segmental enterectomy might increase the overall survival without significant increase of postoperative complication rates. ■

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