

Trends in Extra-Ovarian Cancer Tissues and Organs Resection in Patients with Ovarian Cancer

Qingmiao Wang, Hua Linghu*

Department of Obstetrics and Gynecology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China
Email: linghuhua@cqmu.edu.cn

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Abstract

Ovarian cancer mostly presents with extensive peritoneal cavity and extraperitoneal dissemination. Satisfactory and complete resection of the lesions is one of the key factors to improve the prognosis. The trend of surgical resection of extra-ovarian tissues and organs invaded by the tumor has become obvious in order to remove all primary loci and all metastases as much as possible to minimize residual tumor lesions. This article provides a literature review on organ resection in ovarian cancer cytoreduction, summarizing the perioperative complications and survival outcomes at the time of different organ surgery, with the aim of providing guidance for clinical work.

Keywords

Ovarian Cancer, Organ, Surgery, Prognosis

1. Introduction

Ovarian cancer is the most common malignant neoplasm in gynecology, and the mortality rate is the highest among gynecologic malignancies [1] [2] [3]. The standard treatment is cytoreduction in combination with paclitaxel and platinum-based chemotherapy [4] [5]. Due to absence of early and effective screening methods, most patients have progressed to advanced disease with extensive metastases in the pelvic and abdominal cavities at the time of presentation. Except for patients with severe comorbidities or extensive metastases that preclude surgery, the standard treatment for advanced epithelial ovarian cancer is cytoreduction supplemented with paclitaxel and platinum-based combination chemotherapy [6] [7]. Following primary or interval debulking surgery and postoperative chemotherapy, most patients will achieve clinical remission, but the

vast majority will relapse within a short period of time. Currently, several studies have shown that the outcome of cytoreduction is an important factor affecting survival. Optimal and complete resection is one of the key factors to improve the prognosis of advanced ovarian cancer (AOC) [8] [9] [10] [11]. However, the complete reduction rate in epithelial ovarian cancer (EOC) is less than 50%, and residual lesions may be due to large intraperitoneal tumors, tumors that metastasized to critical anatomical sites, molecular pathologic features, severe medical complication, venerable age, and inexperience of the surgeon [12] [13].

Ovarian cancer is usually characterized by extensive peritoneal cavity and extraperitoneal spread. In order to minimize the residual tumor lesions, there has been a clear trend to surgically resect the extra-ovarian tissues and organs invaded by tumors [14] [15], including diaphragmatic resection, partial hepatectomy, partial pancreatectomy, partial intestinal resection or splenectomy. This article reviews the perioperative complications and survival outcomes of patients with ovarian cancer who underwent surgery on different organs.

2. Upper Abdominal Surgery

Peritoneal spread is the most common spread pattern of ovarian cancer, usually in the form of miliary loci that may involve the hepatic capsule and the right diaphragm. Extensive upper abdominal surgery can increase the rate of optimal debulking surgery [16] [17], and improve the survival of patients. However, difficulty in exposing the surgical site increases surgical complexity, and aggressive surgery increases postoperative complications [18]. Kuhn *et al.* reported an increased incidence of perioperative severe complications in patients undergoing upper abdominal surgery compared with standard surgery, but Chi *et al.* found that major postoperative complications and postoperative mortality were acceptable in patients undergoing extensive upper abdominal surgery [19] [20].

2.1. Diaphragm Surgery

Diaphragmatic metastases, especially to the right hemidiaphragm, are extremely common in patients with AOC, with up to 40% of patients presenting with massive metastatic diaphragmatic lesions [21] [22]. In recent years, many studies have emphasized the importance of diaphragmatic tumor resection. The tumor can be reduced by means of focal electrocoagulation, diaphragmatic peritoneal stripping, diaphragmatic resection, etc. The surgical method depends on the gynecologist's judgment of the lesion type and extent of spread. A thorough understanding of the upper abdominal anatomy is the basis for thorough exploration and cytoreduction, thereby reducing the risk of bleeding due to damage to major vessels. The most common complication after diaphragm surgery is pleural effusion. In a recent meta-analysis of 292 patients who underwent diaphragm surgery (197 diaphragmatic peritoneal stripping and 75 diaphragmatic full-thickness resection), the incidence of pleural effusion after diaphragmatic peritoneal stripping and diaphragmatic resection was 43% and 53%, respectively.

The requirements for postoperative pleural puncture or chest tube insertion were 4% and 9%, respectively. Patients with diaphragmatic resection were more likely to have pleural effusion, pneumothorax, pneumonia [22]. The MSKCC study showed that the incidence of ipsilateral pleural effusion was 58%, and the overall incidence of postoperative pleural puncture or chest tube insertion was 15% [23]. Diaphragm surgery is a critical step in cytoreduction in patients with advanced and recurrent ovarian cancer with an acceptable incidence, and rigorous postoperative pulmonary management can significantly reduce the incidence of chest complications [24], while the prediction, prevention and management of subsequent complications should also be emphasized [25].

2.2. Liver Surgery

Approximately 40% of patients diagnosed with AOC have substantial metastatic lesions in the upper abdomen (diaphragm, liver) [26]. For patients with FIGO IV ovarian cancer, liver is the most common distant metastasis organ, about 37% - 57%, followed by distant lymph nodes, lung, bone and brain, and the median overall survival of patients with liver metastasis is 30 months [27]. In a study of ovarian cancer patients with liver metastasis, partial liver resection had a significant survival benefit compared to liver biopsy [28]. Similar results were reported in a multicenter study of 2655 patients with liver metastases from ovarian cancer who underwent cytoreduction of upper abdominal tumors [29]. Previous study emphasized the equal importance of complete cytoreduction not only in the lower abdomen, but also in the case of liver involvement [30]. Wang *et al.* found that patients with hepatic metastatic ovarian cancer who underwent partial liver resection up to R0 during cytoreduction had an OS of 50.1 months, compared with 20.0 months in patients who underwent partial liver resection up to non-R0 after during cytoreduction [31]. Studies have demonstrated the safety of liver surgery as part of cytoreduction surgery [31] [32] [33]. Chi *et al.* reported the most common postoperative complications after liver surgery, including pancreatic leakage, ascites, pleural effusion, with a morbidity and mortality of 22% and 1.4%, respectively [19]. Liver surgery for metastatic ovarian cancer is safe, and resection of liver lesions does not increase the rate of surgery-related complications for experienced surgeons. Hepatectomy should only be performed if complete cytoreduction to no residual lesions and the excision margin is negative, both at initial diagnosis and in the case of recurrence.

2.3. Splenectomy

Splenic involvement in patients with AOC is mainly manifested as the involvement of parenchyma, splenic hilum and peritoneum [34]. Splenectomy is required when the tumor involves the splenic surface, hilum, parenchyma, or when peritoneal involvement cannot be removed alone. The main complications after splenectomy include abdominal complications (such as peritoneal effusion, anastomotic leakage, abscess, pancreatic leakage, etc.) and pulmonary complica-

tions (such as pleural effusion, pneumonia and pulmonary embolism) and infectious complications (such as sepsis, and overwhelming post-splenectomy infection) [35]. Patients with splenectomy had longer time to postoperative adjuvant chemotherapy due to higher rates of postoperative complications (e.g., postoperative infection, reoperation, and length of postoperative hospital stay) [36], and delayed chemotherapy after cytoreduction is an independent prognostic factor for survival, with a median duration of adjuvant chemotherapy after splenectomy recommended at 5 - 6 weeks postoperatively [37]. Optimal debulking surgery was achieved in 34 patients who underwent splenectomy had a better survival in Sun's study [38]. There is a common indication for splenectomy for tumor involvement, rarely due to splenic injury. Splenectomy should be attempted in all patients with splenic involvement who can achieve optimal cytoreduction, whether primary or interval debulking surgery, after adequate preoperative evaluation.

3. Intestinal Surgery

Ovarian cancer is prone to involve the small intestine or colon, so resection of intestinal metastases is a key part of cytoreductive, and intestinal surgery includes intestinal resection, intestinal tumor stripping. The decision of whether to perform intestinal resection and the extent of resection often needs to be made in conjunction with the intraoperative situation [39]. Reports of intestinal resection have been published to increase optimal debulking surgery rates and improve patient survival [40] [41], however, extension of the surgical scope is associated with higher rates of intraoperative and early postoperative complications (e.g., bleeding, anastomotic dehiscence, and infection) [42]. The long-term sequelae of perioperative morbidity of intestinal resection may lead to increased mortality, and intestinal resection may be a negative prognostic factor [43]. Fistulas are sometimes performed after intestinal resection, which significantly reduces the comfort of the patient. In Abdul's study it was suggested that intestinal resection should only be performed if it can achieve complete cytoreduction or if it can reduce or prevent impending bowel obstruction [44]. A Korean multicenter study showed that the survival outcome of patients undergoing intestinal resection was not inferior to that of patients undergoing low anterior resection if optimal debulking could be guaranteed [45]. In patients suffering from intestinal metastases with ovarian cancer, the impact of postoperative complications and fistulas on patients' distant survival should be taken into consideration before deciding whether to perform intestinal resection [46].

4. Lymphnode Surgery

Lymphnode involvement in ovarian cancer is approximately 44% - 46%, and pelvic and para-aortic lymphnode dissection contributes to maximal cytoreduction in advanced EOC and has been performed as an important surgical procedure [47]. Common postoperative complications include fever, lymphatic cysts, and lymphedema, and severe cases may require reoperation [48] [49]. Contro-

versy remains regarding the impact of lymphnode dissection on survival. Several studies suggest that lymph node dissection is associated with a better prognosis [50]. Andreas's analysis of advanced ovarian cancer patients with primary debulking surgery showed that lymphnode dissection was associated with higher survival in patients with complete cytoreduction [51]. In Maggioni's randomized controlled trial for early-stage EOC, lymphnode dissection did not benefit either overall survival or progression-free survival, although more metastatic lymphnodes were removed in the lymphnode dissection group [52]. A different perspective was presented by the LION trial, which included patients with negative lymphnode metastases who achieved complete cytoreduction randomized into lymphnode dissection group and non-lymphnode dissection group, showing that lymphnode metastases were pathologically present in 55.7% of cases in the lymph node dissection group and that lymph node dissection did not provide any survival benefit [48]. Whether to perform lymphnode surgery, gynecologic oncologists should formulate an individualized surgical plan, correctly identify patients who can benefit from it, choose an appropriate surgical route, and minimize postoperative complications.

5. Conclusion

Ovarian cancer is prone to extensive metastasis to adjacent organs. With the advancement of surgical oncology, most gynecologic oncologists advocate an aggressive approach to remove involved tissues as much as possible. The trends of extra-ovarian cancer tissues and organs resection have been obvious, but the impact of aggressive surgery on patients' perioperative complications and quality of life still needs attention. Various factors such as the general physical condition of the patient and the degree of tumor dissemination influence the surgical plan of the gynecologic oncologist, and the use of targeted drugs such as PARP inhibitors also influence the choice of treatment plan. Surgery is still the basis of ovarian cancer treatment. For patients with multiple organ involvement, a multidisciplinary discussion should be conducted before surgery, and the surgical approach should be selected comprehensively by combining the patient's general condition and his own technical level during surgery, so as to avoid the discomfort of life and survival benefits brought by highly invasive surgery.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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