Second Look Laparotomy for Ovarian Cancer: Past, Present and Future

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INTRODUCTION

Ovarian cancers are one of few solid tumors where multiple surgeries and debulking is found to be useful. There are various terms coined for surgical exploration at different periods of time - primary surgical cytoreduction, interval tumor reductive surgery, secondary surgical cytoreduction and second look laparotomy. A second-look laparotomy (SLL) specifically applied to laparotomy in patients who are clinically free of disease after primary cytoreductive surgery and completion of first line chemotherapy. The so-called second-look operation was first defined by Owen Wangenstein in the late 1940s with reference to exploratory laparotomy procedures in patients with colon cancer from whom he had previously removed all gross tumor but in whom there was a high risk of recurrence. In 1966, during an era when single-agent alkylating therapy for advanced ovarian cancer was standard, Rutledge and Burns first reported their experience of SLL in 288 ovarian cancer patients[1]. SLL is basically done to rule out recurrence of disease which is not routinely picked up by any other investigation and to decide regarding systemic therapy.

Technique of SLL

A second-look laparotomy includes re-exploration of the peritoneal cavity and selected retroperitoneal structures. Immediately prior to surgery, a pelvic examination under anesthesia is performed. The abdomen should be entered through a generous vertical excision, extending from the pubic symphysis to well above the umbilicus. If no obvious tumor is found, saline washings are obtained from multiple sites within the peritoneal cavity, usually including the pelvis, both paracolic gutters, and the undersurfaces of both hemi-diaphragms and a meticulous, systematic search for areas of occult tumor should be made. All adhesions should be lysed and portions submitted for histologic analysis. Any suspicious areas should be biopsied. The residual omentum should be palpated, as should the aortic lymph nodes. The intestines must be care-fully examined. Throughout this evaluation, particular attention should be paid to areas where residual disease was left at the initial operation. Peritoneal biopsies should be taken from multiple sites within the abdominal cavity, including the pelvis, paracolic gutters, and both hemi-diaphragms. Any remaining areas of omentum should be removed. Many surgeons remove the appendix if present. If obvious tumor is found, the goal of the operation becomes removal of as much tumor as possible.

With the introduction of platinum-based chemotherapy in the mid to late 1970s and the use of aggressive primary debulking, up to 50% of patients treated with chemotherapy for advanced cancer had no clinically detectable tumor at the completion of their chemotherapy and 50% will have pathological complete response. Since it was known that may of these women harbored occult residual cancer, various noninvasive methods for detecting such disease were tried.

Other methods (Non SLL group) to rule out residual/recurrent ovarian cancer: Role of Imaging :

Ultrasound, contrast enhanced CT scan and MRI all have been used to assess the response after completion of planned treatment. Imaging techniques such as CT, sonography, and MRI are generally unable to detect intra-peritoneal tumor masses smaller than 1 to cm and, in fact, may miss much larger masses. In one study, computed tomography failed to detect pelvic and abdominal masses up to 3 cm size, as well as larger omental tumor cakes and the overall diagnostic accuracy was only 58%[2].

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Biochemical Markers

Serum tumor markers, in particular CA-125, have proven to be clinically useful in monitoring the course of ovarian cancer. While an elevated CA-125 is highly accurate as an indicator of persistent disease, numerous studies have shown that, even with a normal serum CA-125, a significant number of patients in clinical complete remission will have residual disease at laparotomy. Rubin et al[3] found persistent disease in 62% of patients who had a normal CA-125 level at the time of surgery. These findings have been confirmed in other studies[4] Raised CA-125 levels suggest a residual disease but lacks sensitivity. Recently Senapd et al reported combined CA-125 and polypeptide specific antigen (TPS) had a negative predictive value of 88.9% for pathological complete response[5].

Culdocentesis

Some authors[6] have suggested that the cytologic analysis of peritoneal fluid obtained by culdocentesis may be a means of assessing response in women under treatment for ovarian cancer. However the accuracy of this technique in detecting residual disease is quite low.

Laparoscopy

Several groups have used laparoscopy as an alternative to second-look laparotomy. At the NCI, laparoscopy was routinely used to assess response to chemotherapy[7]. In 66 restaging laparoscopies, residual tumor was found in 33 (50%) and provided the only evidence of disease in 24 cases (36%) These latter patients were spared an unnecessary second-look laparotomy. However, 55% patients with negative laparoscopy found to have residual disease at laparotomy. Hussain et al studied 150 patients, who underwent laparoscopic second-look operations, found the rate of negative evaluations and the rate of recurrences in patients with negative second look are equivalent to those described in studies of second-look assessment by laparotomy with 2.7% complication rate[8].

As of today laparoscopy is still considered a investigative modality for detection of residual disease in ovarian cancer and further studies with large number of patients is need before any definitive conclusions could be drawn.

PET Scan

PET has been useful in differentiating the malignant from benign tumors and residual disease from post treatment fibrosis[9]. Its value has been demonstrated in a variety of cancers including ovarian, breast, colon, lung and cervical tumors[9]. Huber et al[10] found positive and negative predicitive value of 86% and 76% in 51 cases studied. They evaluated[14] patients for recurrence and all patients with positive scan had evidence of recurrence and negative scan patients remains free of disease. In another study Rose et al[11] reported only 10% sensitivity and 42% specificity[5] for PET scan in detection of residual/ recurrent ovarian cancer. They found low sensitivity of PET especially in small volume disease. To conclude early reports with PET scan are conflicting and further studies are needed.

Review of SLL Experience

Over the last 10 years, there have been many published series on second-look laparotomy. Findings at second-look laparotomy from 71 combined series of 5,190 patients showed no residual disease in 47% and presence of disease in 53% patients[12]. These findings are a clear indication of our current inability to identify persistent cancer by noninvasive means. However, clinical impact of SLL has been considered limited as 40-60% patients with negative SLL relapse within 5 years[13]. The value of a SLL with or without secondary surgical debulking of residual disease remains controversial. Some studies have reported advantageous effects on survival after secondary cytoreduction[14,15] where as others studies could not confirm these advantageous results despite secondary surgical cytoreduction and additional chemotherapy[16,17]. There is no evidence that second-look laparotomy per se is a therapeutic procedure. While there are no prospective trials in which patients in a clinical complete remission have been randomized to either a second-look operation or to medical follow-up retrospective studies comparing the survival of patients in whom a second-look was not performed have failed to show any difference in survival[18]. Consequently, it has been proposed

that a second-look laparotomy no longer be considered a routine procedure in patients who achieve a complete remission. Such a recommendation has been further strengthened by the absence of a randomized study that has demonstrated that second-line therapy is effective in prolonging survival. Recent data from GOG 1589, comparing carboplatin and paclitaxel versus cisplatin and paclitaxel in optimal-residual Stage III ovarian-cancer patients, has bearing on the issue to second-look laparotomy[19]. Although not randomly allocated to second-look, approximately half of the patients in this study elected the procedure, with no improvement in overall survival seen. Patients found to have complete pathological response at SLL have excellent prognosis. Hence it is reasonable to presume that SLL has more prognostic value rather than therapeutic value and complete pathological responders do well and secondary surgical cytoreduction does not result in improved survival.

Several clinical and histologic factors have been shown to relate to the likelihood of tumour being found at the time of second-look laparotomy. The most important factors are stage and the volume of tumor remaining following initial cytoreductive surgery. Patients with Stages III and IV disease had a substantially lower proportion of negative second-look operations than did those with stages I and II, 33% versus 70% respectively[20].

The amount of residual disease remaining following the initial operation for ovarian cancer is also a major determinant of the likelihood of disease being found at the time of second-look laparotomy. Patients with suboptimal residual disease after primary surgery had only 23% likelihood of a negative second look, as compared to 50% those with optimum residual and 72% in those with no known residual, tumor[21].

Rubin et al[22] reported the long-term follow-up of 91 platinum-treated patients who achieved a negative second-look. A multivariate analysis demonstrated that stage, histologic grade, and extent of residual disease remaining after primary cytoreduction were significant predictors of recurrence following a negative second-look. Patients who do recur have a poor prognosis, and few, if any, can be cured by currently available salvage therapies. Patients who have a prolonged disease-free interval (> 12 months) have a 30% to 50% likelihood of responding to second-line therapy. There is presently no evidence that any type of therapy can decrease the relapse rate in patients who do achieve a surgically confirmed complete remission. However, consolidation therapy is currently being studies in prospective trials. Treatments under investigations in patients who do achieve a complete remission include: intra-peritoneal chemotherapy, radioisotopes, immunotherapy, and systemic chemotherapy with noncross-resistant agents, and whole abdominal radiation.

SLL is the most accurate currently available method to detect residual disease. However, even the most carefully performed second-look operation may miss microscopic areas of tumor and because ovarian cancer may occasionally spread beyond the areas assessed at surgery. On the contrary, second - look laparotomy is highly invasive diagnostic procedure that results in significant expense, discomfort, and time in the hospital for the patient and post operative morbidity with no significant impact on long term survival.

Conclusions

SLL still remains the most accurate method to detect residual disease after ovarian cancer therapy. Current literature suggests that SLL provides more prognostic information and its therapeutic value in prolonging survival is not adequately proven It has been proposed that a second-look laparotomy no longer be considered a routine procedure in patients who achieve a complete remission. Currently in a non clinical trial situation, there appears to be little justification for a second-look laparotomy merely to obtain prognostic information. If, on the other hand therapeutic decisions will be based upon findings at second look, such a procedure may be justified. As far as other less invasive modalities including CA-125, CT scan, PET scan and Laparoscopy are concerned for detection of residual disease, the results of initial experience are encouraging and further studies including large number of patients is needed in future before they could replace SLL completely.

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