

Surgery for ovarian cancer – is it a job for the generalist?

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Ovarian cancer makes a significant contribution to deaths due to cancer in women. Of the gynaecological malignancies ovarian cancer has the highest mortality rate. Optimal cyto-reductive surgery followed by taxane/platinum based chemotherapy has made a big difference in the prognosis of the disease. Lack of effective screening tests and the non specific symptoms of the disease contributes to it being diagnosed at an advanced stage, resulting in overall low cure rates¹⁻³. Majority of the women have advanced stage disease at the time of diagnosis. Hence the surgery is difficult and demands special skills. The purpose of this article is to examine if surgery for ovarian cancer should be carried out by general gynaecologists or by trained gynaecological oncologists.

Introduction

Epithelial ovarian cancer is the fifth commonest cause of deaths due to cancer in women in Sri Lanka. Incidence of epithelial ovarian cancer is 6.8/100000 population⁴. Ovarian cancer is the sixth most commonly diagnosed cancer among women in the world and has the highest mortality rate out of all cancers of the reproductive system^{5,6}. Almost 50% of the case load of surgery for ovarian cancer in the National Cancer Institute of Sri Lanka comprise of secondary surgery due to suboptimal primary surgery or inadequate staging performed elsewhere. Stage of disease with International Federation of Obstetrics and Gynaecology (FIGO) criteria is closely associated with survival. Of patients with ovarian cancer, 75% present with advanced disease (FIGO stage III/IV) globally.

Epithelial ovarian cancer spreads in several ways. Symptoms when present are often vague and most reflect the effects of tumour filling the abdomen/pelvis. The disease often spreads extensively throughout the peritoneal cavity and to the lymphatics before causing any symptoms. Surgery is the cornerstone of management of epithelial ovarian cancer for several reasons. It allows the histological

conformation of the disease type and grade and is the key component in staging of the disease. Surgery is also carried out after neoadjuvant chemotherapy or as an interval debulking procedure. While it can be curative in early stage disease, optimal cytoreductive surgery has been shown to optimize adjuvant chemotherapy and the overall survival. Overall the 5 year survival rate is about 45%¹. This article will be looking at the surgical aspects of epithelial ovarian cancer in primary and recurrent disease.

Primary disease

Conventional surgical treatment for epithelial ovarian cancer includes total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy and sampling of para-aortic lymph nodes, except in early stage disease.

Nearly all retrospective and prospective studies have confirmed that the extent of cytoreductive surgery and the amount of residual disease after primary surgery are the most important factors that influence the survival of patients with advanced ovarian cancer, as reviewed in the meta-analysis by Bristow et al^{7,9}.

According to the Gynaecological Oncology Group (GOG) optimal cytoreduction is defined as residual tumour tissue of less than 1cm in maximum tumour diameter. This threshold has been further evaluated by Hoskins et al⁹. In order to achieve optimal cytoreduction more aggressive surgical procedures such as rectosigmoidectomy, extensive peritonectomy, partial liver resection, excision of enlarged lymph nodes are sometimes needed in advanced ovarian cancers. Various reports have demonstrated the feasibility and acceptable complication rates associated with rectosigmoid resection¹¹⁻¹⁴. At our institution a rectosigmoidectomy with stripping of pelvic peritoneum is carried out routinely for patients with advanced stage disease with involvement of the cul-de-sac and the sigmoid colon.

The correlation between surgical cytoreduction and outcome was first assessed by Griffiths in 1975¹⁵. In his retrospective analysis of 102 patients, he noted that those with no gross residual disease had a mean survival of 39 months, patients with residual disease

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≤ 0.5 cm had a mean survival of 29 months, patients with residual disease greater than 0.5 cm but ≤ 1.5 cm had a mean survival of 18 months, and patients with residual disease greater than 1.5 cm had a mean survival of 11 months. Residual disease greater than 1.5 cm had no correlation with survival. This study clearly demonstrated an inverse correlation between the residual tumor volume and patient survival.

Ovarian cancers are often advanced, hence surgery is difficult and demands special skills. Certain techniques can make the approach to advanced ovarian cancer more efficient and safer. A sound knowledge of the pelvic and the abdominal anatomy is an essential prerequisite for this kind of surgery. It is important for the surgeon to be familiar with the abdominal/pelvic cavity compartments, for these provide access to metastasis and serve as a plane for resection. When the normal anatomy of the pelvis is completely distorted by large tumour masses, these anatomic spaces become important as they will provide the most avascular pathway for circumscribing the tumor. The surgeon should be mentally and technically prepared to aggressively resect large cancers within the pelvis, as well as large metastatic deposits that involve organs in the upper abdomen.

When multiple metastasis at different sites are present usually the largest and the most troublesome ones are in the pelvis. Multiple organs are often fused together, i.e. the left ovary and the sigmoid colon, omentum with the transverse colon, right ovary and the ileo-caecum. On initial assessment resection of these cases may seem impossible. Yet, persistent dissection often achieves satisfactory debulking.

There are certain techniques that facilitate this kind of dissection. The tendency of ovarian cancer to involve the peritoneum along the pelvic wall, the bladder, and the sigmoid colon are advantageous in approaching the resection through retroperitoneal spaces. Although the cancer is adherent to the peritoneum, it seldom penetrates, and the best method of removing the tumour is through a retroperitoneal approach¹⁶. The ureters need to be exposed at a very early stage of the procedure to avoid the risk of ureteral injury. The anterior and posterior cul-de-sac are often filled with the tumour, and the conventional approach for separating the bladder from the uterus and the vagina from the rectum cannot be used. Very often patients with advanced ovarian cancer are declared inoperable before resectability has been amply tested when the procedure is carried out by a surgeon without appropriate training.

A meta-analysis of 6885 patients with stage III or IV epithelial ovarian cancer evaluated various

prognostic factors for survival¹⁷. This study too reiterated correlation between maximal cytoreduction and median survival. Each 10% increase in cytoreduction correlates with a 5.5% increase in median survival¹⁸. All patients were treated with adjuvant platinum based chemotherapy. Patient cohorts who had >75% maximal cytoreduction had a median survival of 34 months, compared with 23 months for patient cohorts with ≤25% maximal cytoreduction.

Numerous studies have shown that many women with ovarian cancer undergo suboptimal surgery¹⁹⁻²¹. Many studies have shown that specialized surgeons, gynaecological oncologists are more likely than general surgeons to perform optimal surgery for ovarian cancer²¹⁻²³. As a result, the National Institute of Health, American College of Obstetricians and Gynaecologists and Society of Gynaecological Oncologists all recommend that women with ovarian cancer be referred to a gynaecological oncologist for their initial management¹⁹.

According to FIGO, when ovarian malignancy is suspected preoperatively, the following procedures need to be carried out to accurately stage the disease²⁴. Midline incision for adequate exposure, careful evaluation of all peritoneal surfaces, 4 washings of the peritoneal cavity (diaphragm, right and left sides of the abdomen, and pelvis), omentectomy, complete or selected lymphadenectomy of the pelvic and para-aortic lymph nodes, biopsy and/or resection of any suspicious lesions and random blind biopsies of normal peritoneal surfaces²⁵.

When the cancer is less advanced, the surgeon's knowledge of spread pattern and common sites for subclinical metastatic deposits improve the accuracy of staging by discovery of microscopic size metastasis. In patients with disease apparently confined to the pelvis, meticulous staging is essential to define the correct extent of the disease at the time of diagnosis²⁴. As much as 30% of the early stage cancers are upstaged by a restaging procedures^{25,29}. Inadequate surgical staging will result in understaging and will lead to inadequate postoperative treatment, which will have a negative impact on the patients' prognosis.

In early stage disease, it is recommended to have an average of five random peritoneal biopsies as 7% of diaphragmatic peritoneal biopsies, 5% of omentectomy specimens and 10% of biopsies taken from other peritoneal sites are positive for tumour deposits. Twenty percent of restaging procedures have positive peritoneal cytology³⁰.

The goal in cytoreduction has changed from optimal towards maximal cytoreduction. Several studies have shown that no gross/macroscopic

residual disease should be the goal of surgery in primary cytoreduction in surgery for epithelial ovarian cancers^{18, 31-33}. Hoskins et al reported on stage III epithelial ovarian cancer patients enrolled in two multi-centre randomized clinical trials, a survival rate of 60% in patients with no gross residual disease¹⁰. More recent studies such as Chi et al³¹, and du Bois et al³³ report median survival of 106 months and 99 months respectively, in patients with no gross residual disease. Analysis by Chi et al. reported no gross residual disease had the longest survival compared with residual disease <1cm and residual disease >1cm.

The principle of radical debulking has come under some criticism³⁴. Some argue that tumour biology is more important in determining prognosis than surgical effort³⁵. The ability to successfully perform optimal cytoreduction (to <1cm) or maximal cytoreduction (no visible disease) ranges from 20% to 90% in advanced epithelial cancer. The former rate has been when the patients are managed by non trained specialists and the latter when they are managed by experienced specialist surgeons³⁶.

Evidence from the literature shows that the surgery is inadequate in 75% of the cases when it is performed by a person not trained in gynaecological cancer surgery. This could translate into a 50-100% of difference in the overall 5 year survival³⁶. Surgery performed by a trained gynaecological oncologist has been shown to increase survival³⁷. Impact of surgery may improve the 5 year survival rate of less than 20% to 50%³⁸.

Interval debulking surgery (IDS)

Interval debulking surgery is defined as a second operation which is performed after 3 to 4 cycles of chemotherapy in women who had suboptimal debulking at the first surgery. Primary aim of this procedure is to reduce the volume of residual tumour so as to increase the response to chemotherapy. Improved survival in secondary cytoreduction was first noticed by Bereck et al in the eighties³⁹. Subsequent studies had conflicting results which failed to show a clear survival benefit. However, the European Organization for Research and Treatment of Cancer (EORTC) trial⁴⁰ showed a significantly increased median survival in the IDS group compared to those who had not undergone this procedure.

Recurrent Disease

Place of surgical cytoreduction in epithelial ovarian cancer in the recurrent setting is controversial. Multiple retrospective studies have reported

improved survival with optimal cytoreduction⁴¹. In recurrent disease, secondary surgical cytoreduction should be considered if optimal debulking can be achieved. Patient selection is the critical factor in determining candidates for secondary cytoreduction. Selection criteria used would depend on the unit. In general, patients who are selected for this should have platinum sensitive disease (recurrence beyond 6 months after completion of platinum-based chemotherapy).

Conclusion

Post-operative residual tumour is one of the most important independent prognostic factors for survival^{42,6}. One series of patients with stage I and II disease showed that survival was improved if surgery was performed by a trained gynaecological oncologist²⁹. Similar results were reported by Eisenkop et al (1992) in patients with stage III and IV disease.

Evidence from the literature is sufficient to justify a recommendation that all patients with an ovarian cancer should be treated by a trained gynaecological oncologist. There is ample data in the literature to support that adherence to such a policy could improve patient survival in ovarian cancer.

Since the overall prognosis for patients with ovarian cancer is poor, the management of this condition should be carried out by multi-disciplinary teams in gynaecological oncology. Apparent early stage disease requires accurate staging. Inadequate staging will have a significant impact on the survival rates. Our experience at the National Cancer Institute of Sri Lanka suggests that ovarian cancer surgery carried out by 'Generalists' often leaves the patient with inaccurate staging and suboptimal debulking. These are crucial determining factors of survival. Since it is impossible to satisfactorily predict the stage of the disease by any method short of laparotomy, it is imperative that optimal treatment for these women can only be dispensed by trained gynaecological surgeons.

These are strong enough to override the convenience factor of having the surgery performed in a facility closer to the patient's home.

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