

Medical management versus palliative surgery for bowel obstruction in ovarian cancer

Abstract

Of all gynecological cancers, ovarian cancer represents the major challenge for the clinician. In the ovarian cancer, epithelial tumors have the biggest prevalence, and because they are usually asymptomatic until the occurrence of metastases, in more than two thirds of the cases, the patients presents in advanced stages of the disease. Intestinal obstruction is developed either during initial diagnosis or more commonly, in combination with recurrent disease and may be due to mechanical blocks or carcinomatous ileus. Patients with intestinal obstruction are generally in tainted physical condition, treated intensive in the past with chemotherapy and surgery, in a short period of time. Due to the high morbidity and mortality of surgery in these patients, it is often difficult to decide to perform a surgical intervention. Therefore, a systematic review of surgical interventions is required to evaluate its effects on short-term regarding the control of symptoms and on long-term in order to prolong the life without symptoms and also the ability to further provide chemotherapy. The main goal that we evaluated for the management of bowel obstruction in women with ovarian cancer was to maintain quality of life with an effective control of symptoms.

Keywords: surgery, obstruction, chemotherapy, ovarian cancer, management

Introduction

According to Ferlay and contributors, ovarian cancer is the sixth most common cancer among women. A woman's cumulative risk of developing ovarian cancer by age 65 years is 0.5%: 0.4% in developed countries and 0.7% in less developed countries. According to the same research it is less common in women under the age of 35 years, and its incidence increases with age⁽¹⁾. Other study reveals that ovarian cancer is characterized by its insidious onset and absence of early specific symptoms. About 70% of patients are diagnosed in stages III and IV, having widespread tumor dissemination within the abdominal cavity with or without tumor spread to the liver, lungs or distant organs⁽²⁾. In Europe, just over a third of women with ovarian cancer are alive five years after diagnosis⁽³⁾, largely because most patients present with disease that has spread beyond the ovaries. Long term survival rates have improved little over the last thirty years: between the year 1971 and 1975, the relative five year survival rate for women diagnosed in England and Wales was 23% whereas in 1991 to 1993 it was 29%⁽³⁾. Although more than 70% of women with advanced cancer respond to initial chemotherapy, most patients suffer from recurrent disease within the peritoneal cavity and eventually become resistant to chemotherapy. Once the disease recurs, it usually becomes incurable despite further chemotherapy and surgery^(4,5).

The epithelial ovarian cancer arises from the tissues from the coelomic epithelium or 'mezotelium' and comprises 90% of all ovarian cancers in women, with the other 10% being non-epithelial such as sex-chord stromal and germ cell tumors⁽⁶⁾. The epithelial ovarian cancers primary disseminates by peeling of the cells in the peritoneal cavity and spreads through direct extension to adjacent organs such as the uterus, fallopian tubes, ovaries and, less frequent, the rectum. However, the mechanism of metastatic spread in epithelial ovarian cancer differs from other epithelial

cancers. Following direct extension, ovarian cancer cells are seeded in the peritoneal cavity and fluid and disseminated to other pelvic and abdominal organs by the trans-coelomic route, a route that provides direct access to the abdominal peritoneal cavity. Therefore, dissemination of the malignant cells into the abdominal cavity, largely contributes to the morbidity and mortality related to vital organs particularly gastrointestinal and genitourinary systems⁽⁷⁾.

Primary peritoneal and fallopian tube cancers are considered to have similar mechanisms of metastatic spread and the management of these cancers is almost identical to the management of ovarian cancer. Histological features and tumor biology of primary peritoneal and fallopian tube cancers are also very similar to those of the ovarian cancers⁽⁸⁾.

Bowel obstruction is a common feature of advanced or recurrent ovarian cancer. The presence of multiple locations of the occlusion occurs quite frequently in patients with recurrent epithelial ovarian cancer. More than half of patients experience small bowel occlusion, a third presents colon occlusion a sixth show both aspects by extrinsic compression by tumor mass and lymph nodes⁽⁹⁾. Other causes of obstruction include the tumor infiltration of mesentery, bowel muscle or nerves. Edema of bowel wall, fecal impaction, and constipating drugs can contribute to the development and severity of bowel obstruction. Occasionally, the obstruction may be due to benign causes such as adhesions, post radiation bowel damage, inflammatory bowel disease, or hernia. These patients, with occlusion due to benign cause, are usually suitable for surgical management⁽¹⁰⁾.

Although the true incidence of bowel obstruction in ovarian cancer is not known, several retrospective studies have suggested that it occurs in 25 to 50% of all ovarian cancers. Progressive external compression of the bowel and its mesentery by ovarian carcinoma results in obstruction and may eventually lead to death in these patients⁽¹¹⁾.

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Description of the Intervention

Patients with bowel obstruction have been usually heavily treated with multiple chemotherapeutic agents and surgery, and the cancer may become resistant in some cases to chemotherapy. The aim of any further treatment is therefore to relieve the symptoms related to bowel obstruction and to improve the quality of life. The life expectancy is limited with a median survival of approximately four months⁽¹¹⁾. Management options are: surgery which may include the insertion of colorectal stents, gastro-stoma, chemotherapy or treatment with intravenous fluids and pharmacologic agents to relieve the symptoms related to obstruction. The purpose of palliative surgery is to relieve the symptoms of bowel obstruction by means of four procedures: stoma formation, bypassing the obstruction, resection of bowel and placement of colorectal stents⁽¹²⁾. The surgery is associated with a high incidence of morbidity (5 to 90%) and mortality (5 to 40%). Major surgical complications include entero-cutaneous or entero-vaginal fistulas, anastomosis leaks (leakage where two ends of bowel join together), short bowel syndrome, malabsorption disorder caused by the surgical removal of the small bowel) and sepsis. Once the obstruction is relieved, a small proportion of patients may become suitable for further treatment with chemotherapy⁽¹³⁾.

Percutaneous endoscopic gastro-stoma (PEG) placement, can be used to achieve intestinal decompression⁽¹⁴⁾. It is feasible to use PEG to relieve nausea and vomiting in palliative settings. It is considered for patients presenting with recurrent bowel obstruction and previously treated with surgery for small bowel obstruction. For selected patients, placement of PEG tubes can be followed by administration of chemotherapy⁽¹⁵⁾. Somatostatin and its analogues, octreotide and vapreotide, have been used to alleviate symptoms from malignant bowel obstruction in ovarian cancer. Somatostatin inhibits glucagon and insulin hormones, reduces acid secretion, slows bowel peristaltic and decreases bile flow⁽⁴⁾. Octreotide acts in a similar way to somatostatin but has a longer half-life. It inhibits growth hormone, glucagon, and insulin more potently. Octreotide also suppresses luteinizing hormone response to gonadotropin-releasing hormone and inhibits release of gastrin, secretin, vasoactive intestinal peptide, motilin, and pancreatic polypeptide. Steroids have also been used to relieve bowel obstruction. Their effect on bowel obstruction has been controversial: they may reduce the level of obstruction indirectly by reducing tumor edema⁽¹⁶⁾. However, a Cochrane systematic review the use of corticosteroids in bowel obstruction related to gynecological or gastrointestinal malignancies and showed no evidence in that corticosteroids were effective in treating bowel obstruction⁽¹⁷⁾.

The scientific research was accomplished by analyzing the following scientific registers 'Cochrane Gynecological Cancer Group Trials Register', 'The Cochrane Central Register of Controlled Trials (2009)', MEDLINE and EMBASE (2009). Also, were investigated the registers of clinical trials, abstracts of scientific meetings and discussions with experts.

Selection Criteria

For this study were searched comparative studies between palliative surgery and medical management, patients

included in the study were adult, diagnosed with ovarian cancer, with partial or complete bowel obstruction. Studies compared palliative surgery, medical interventions and complications⁽¹⁸⁾. We were able to identify 183 articles that made reference on the subject, of which only 22 were identified as potentially eligible for the title and abstract form. Only one study corresponded to our criteria and was included in the review. In this study, were identified 47 women for which management of their condition was palliative surgery (27 women) or medical management with Octreotide (20 women), which was able to report overall survival, pre-surgical morbidity and mortality⁽¹⁹⁾. Women with poor performance status have not undergone a surgery. Although six women (22%) who undergone surgical intervention had serious complications and three (11%) died of complications. A multivariable analysis identified that women which undergone surgical interventions and surpassed the complications had obviously a higher survival than the women treated with Octreotide. However, the magnitude of this effect was not reported, although, the quality of life was affected at the patients who undergone surgery⁽²⁰⁾. Palliative surgery compared to the non-surgical treatment for the improvement of the symptoms of bowel occlusion in the ovarian cancer⁽²¹⁾.

Ovarian cancer is usually asymptomatic until the occurrence of metastases and in more than two-thirds of the cases in patients in the advanced stages of the disease. Among the most common complications of advanced and recurrent ovarian cancer, the intestinal obstruction is included. Patients with intestinal obstruction are generally in altered physical condition with a short life period. Therefore, maintaining the quality of life with effective control of symptoms is the primary management of intestinal obstruction. It is possible that surgery for intestinal obstruction complicating ovarian cancer to be inopportune, in terms of surgical stress on a biological organism already affected by both cancer and intestinal occlusion. Hence, a serious restraint on surgery surgeon, but especially its consequences is important. Finally, the quality of life of patients with advanced ovarian cancer complicated by intestinal obstruction and operated, appears as a priority of the management described in the case⁽²²⁾.

Therefore, there were searched other ways of solving these cases that once, in a classic way, had precise surgical indication. An option to discuss regarding management of these serious cases is drug therapy, its goal being to control symptoms such as nausea and vomiting, and avoiding occlusion⁽¹⁹⁾.

Octreotide is the drug used for this purpose. It is a synthetic analog of somatostatin, and has been shown to have the same biological effects as somatostatin, but it has greater specificity and potency in inhibiting the release of certain hormones and a longer duration of action (half-life, 90-120 minutes), with a peak at 2 hours and an overall duration of 12 hours. Octreotide can be administered by continuous subcutaneous or intravenous infusion or in bolus parenteral injection. The inhibitory activity of octreotide on gastro-intestinal motility and secretions seems to offer an advantage in both the perioperative management of bowel obstruction, and the medical management of inoperable malignant bowel obstruction, as well as the reversal of intestinal transit^(17,18).

Octreotide acts at the intracellular level of the intestinal epithelium to decrease secretion of water, sodium, and chloride, and can increase the absorption of water and electrolytes. Octreotide improves ion and water absorption, inhibits carbonic anhydrase, and suppresses gastrointestinal and pancreatic secretions by inhibiting stimulatory peptides. Moreover, octreotide reduces mesenteric flow and pressure. Finally, submucosa somatostatin-containing neurons inhibit excitatory nerves when activated by octreotide, primarily due to an inhibition of acetylcholine output. Relaxation occurs as a result, ameliorating the non-propulsive spastic activity. These effects may be due to the inhibition of vasoactive intestinal polypeptide, which has been shown to be increased in experimental bowel obstruction and is known to have unfavorable effects on intestinal secretion, splanchnic flow, and peristalsis⁽²⁰⁾. Thus, the inhibitory effect of octreotide on gastrointestinal secretions appears to break the vicious circle of secretion, distention, and contractile hyperactivity producing a hypertensive state in the lumen and consequent damage to intestinal epithelium and inducing a sort of artificial 'bowel silence'. A systematic review of published and unpublished studies was achieved that compared surgical and non-surgical methods of managing bowel obstruction in women with ovarian cancer⁽²¹⁾.

Women who are recommended for surgery are usually in better health than those who are not, therefore it can be difficult to disentangle the effects of surgery and the effects of their basic health. Therefore we only looked at studies that used statistical adjustment for the differences in underlying health between women who did and who did not receive surgery. We found only one relevant study which included only 47 cases: 27 had an operation to relieve bowel obstruction and the 20 who did not have an operation were given a drug called Octreotide to control the amount of vomiting that often results from bowel obstruction. Among the 27 women who had an operation, six women could not have their bowel obstruction corrected because the cancer had spread too far, six women had serious complications of surgery and three died of these complications. The women treated medically had a survival rate from 2 to 6 months⁽²²⁾.

We were therefore unable to reach definite conclusions about the relative benefits and harms of the two forms of

treatment including to identify sub-groups of women who are likely to benefit from one treatment or the other.

Why it is Important to Do this Review?

These patients are generally in poor physical condition with a limited life expectancy. Therefore, maintaining their quality of life with effective symptom control is the main purpose of the management of bowel obstruction. Given the high morbidity and mortality of surgery in these patients, it is often difficult to decide whether to perform surgery. The practice of surgical management of these patients varies between different countries, cancer centers and hospitals⁽²¹⁾. Therefore, a systematic review is needed to evaluate the evidence relating to surgery and its effects on short term symptom control and, in the longer term, prolongation of life, symptom free survival and ability to offer further chemotherapy. Such a review will provide guidance for clinicians and specify the areas for further research in this field. Previous reviews have considered the role of surgery⁽²²⁾ and separately the value of corticosteroids⁽¹⁹⁾ for the resolution of symptoms of malignant bowel obstruction in advanced gynecological and gastrointestinal cancers. More importantly, is the pathophysiology of the development of bowel obstruction in ovarian cancer and gastrointestinal cancers, that is very different and, for this reason, we believe that the role of palliative surgery in ovarian cancer related bowel obstruction should be evaluated separately⁽²¹⁾.

Conclusions

Recent studies do not showed strong evidence when comparing palliative surgery and medical management for bowel obstruction in ovarian cancer. Only one small non-randomized study found that women receiving surgery had longer survival than those receiving medical management, after adjustment of the prognostic factors. The medium survival rate after a surgical intervention on bowel obstruction is usually between 2.5 and 7 months. Therefore we are unable to show strong evidence regarding the relative benefits and harms of the two forms of treatment. Therefore, having in the view the available research studies, we are unable to identify sub-groups of women in which the management and benefits after the palliative surgical treatment of medical treatment could be susceptible. ■

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