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Review

Conservative treatment of early stage ovarian cancer: Oncological and fertility outcomes

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Abstract

Background: Ovarian cancer may appear in young women during their reproductive age. As a result of late childbearing nowadays, fertility preservation has become a major issue in young women with gynecological cancer. The aim of this review is to update the current knowledge on conservative treatment and fertility preservation of women affected of early stage epithelial ovarian cancer.
Material and methods: A web-based search in Medline and CancerLit databases on conservative treatment for early stage ovarian cancer has been carried out. All relevant information has been collected and analyzed.
Results: Less than 40% of ovarian cancers are diagnosed at early stages. Conservative treatment may be considered in young patients with a relapse rate that ranges from 9% to 29%, and a 5-year survival ranging from 83% to 100%. Recurrences in the controlateral ovary has been reported to be less than 5%, with most of these patients being alive after savage treatments. Moreover, it has been reported good fertility outcomes after conservative treatment with a successful conception rate that ranges from 60% to 100%, with an abortion rate under 30% in all series reported.
Conclusions: Conservative treatment for early epithelial ovarian cancers could be a safe option for women younger than 40 years who wish to preserve their childbearing potential. We need a strict case selection such as FIGO stage I grade 1 and 2, although grade 3 cases could be considered.

Keywords: Ovarian cancer; Early stage; Clinical management; Conservative treatment; Fertility sparing surgery

Introduction

Malignant ovarian neoplasms represent the first cause of death among all gynecological malignancies. Although the majority of ovarian neoplasms occur in elder women, ovarian cancer may appear in young women during their reproductive age.[1] As a result of late childbearing nowadays, fertility preservation has become a major issue in young women with gynecological cancer. Fertility-sparing treatments have been successfully attempted in selected cases of cervical, endometrial and ovarian cancer, and gynecological oncologists should be familiar with fertility-preserving options in women with gynecological malignancies.

A new discipline termed "oncofertility" has emerged; however, several informational gaps exist. Main concerns are the safety of conservative treatments, the uncertain efficacy of fertility options, the detrimental effects of chemotherapy to remaining reproductive organs, and when to undergo fertility treatments. Options to preserve fertility include fertility preservation when undergoing cytotoxic treatments, cryopreservation, assisted reproduction techniques, and fertility-sparing surgical procedures. Gynecologic oncologists should incorporate into their decision-making processes the patients' wish for fertility preserving alternatives, ideally without compromising oncologic safety.[2] Appropriate patient selection, and careful oncologic, psychologic, reproductive and obstetric counseling, is mandatory.[3]

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The aim of this review is to update the current knowledge on conservative treatment and fertility preservation of women affected of early stage epithelial ovarian cancer (EOC). The recurrence rate, overall survival (OS), disease-free survival (DFS), fertility outcome and the number of pregnancies were reviewed. A web-based search in Medline and CancerLit databases has been carried out. All relevant information has been collected and analyzed.

Conservative surgery

Ovarian cancer has the highest fatality-to-case ratio of all gynecologic cancers, as less than 40% of cases are diagnosed in early-stage disease.[4] The lack of an effective screening method and of early symptoms when tumor is confined to the ovary/ies, and the absence of sensible tumor markers and imaging techniques at early stages are the main reason of this high rate of diagnosis at late stages.

The standard surgical treatment of patients with FIGO stage I– II epithelial ovarian cancer is based on staging procedures including total hysterectomy, bilateral salpingo-oophorectomy, peritoneal sampling (washing and directed biopsies), omentectomy, and pelvic and para-aortic lymphadenectomy.[5]

Conservative treatment in order to preserve fertility in young patients has been proposed in selected patients with EOC.[5,6] Fertility sparing surgery includes unilateral salpingo-oophorectomy on the side of the ovarian tumor and complete staging including peritoneal sampling, pelvic and para-aortic lymph node dissection and omentectomy. Biopsy of the remaining ovary and an appendectomy are optional. It should be noted that the rate of microscopic tumor in the contralateral ovary is very low, ranging from 0 to 2.5% if the macroscopic appearance is normal.[7,8] Furthermore, a biopsy of the remaining ovary may potentially cause adhesions and reduce fertility in these patients. Appendectomy is recommended as part of the surgical staging in mucinous tumors (same as borderline ovarian tumors), in order to rule out a primary appendicular cancer with ovarian metastasis.[9] Uterine curettage could be considered in patients with endometrioid histology, as concomitant uterine cancer might be present.

Results of conservative management in EOC are still under debate in the literature. According to the 2007 guidelines of the American College of Obstetrics and Gynecology (ACOG), this treatment was initially proposed in case of nulliparous young patients, stage IA disease and always with a close follow-up.[10] The European Society for Medical Oncology (ESMO) agreed in 2008 with ACOG indication.[11] Moreover, the Fertility Task force of the European Society of Gynecological Oncology also supports the conservative management in stage IA grades 1 and 2 (excluding clear cell histology).[12] However, there is a limit to conservative surgery depending on FIGO stage, although precise cut-off remains unclear.

Besides the final decision on being conservative once the final pathologic report is available, in every case where the suspicion of invasive disease is present but frozen section is not available intraoperatively, conservative surgery should be carried out in order to give the opportunity to the patient to decide about her reproductive future. Once final pathology confirms the presence of an invasive ovarian cancer apparently limited to the ovary, these patients should be referred to a tertiary center for the definitive treatment.

Moreover, the influence of the route of surgery needs to be considered. Although for some authors[3] laparotomy is the preferred approach to avoid spillage, rupture or morcellation of the ovarian cyst, laparoscopic approach has been shown to be feasible. For some authors ovarian cyst rupture is significantly higher by laparoscopy among tumors measuring over 10 cm diameter. And spillage may occur in 88% vs. 9% when comparing laparoscopy to laparotomy, although nowadays it tends to happen inside a protected bag.[13,14]

One controversy has arisen lastly concerning completion of surgery after childbearing. Some authors[15] suggest that radical surgery should be considered after childbearing. The risk of recurrence in the contralateral ovary is low but not negligible and seems to support this approach. Among stage IA the reported recurrence rate is near 8%, if we consider stage IC it increases up to 10% and when we include stage II up to 13%.[16] However, in very young patients, preservation of the endocrine function is as important as preservation of fertility. In selected patients, after an appropriate counseling, delay of definitive surgery with a close follow-up may be a reasonable option.

Furthermore, these patients with ovarian cancer at young age should be tested for BRCA 1-2 mutations in order to undergo breast and ovarian cancer (in the controlateral if spared) appropriate screening or prevention.

Oncological outcomes

It is mandatory to take into account the oncological outcomes in any case of EOC that we consider for conservative management. For these reasons two main issues need to be addressed:

1. What is the prognosis of patients with early stage ovarian cancer undergoing conservative surgery?
2. What is the pattern of recurrence in these patients, and which is the rate of recurrence on the controlateral ovary?

Due to the rarity of diagnosis of early ovarian cancer in young patients, no randomized trial has been performed. We will address these issues separately, by analyzing the results of different retrospective series.

Several retrospective series addressed the prognosis of patients undergoing conservative surgery for early ovarian cancer in terms of overall survival and recurrence rates. The results are summarized in Table 1.

Interestingly, if we consider all the series taken together, 53% of the patients had mucinous tumors, indicating that