MINI-REVIEW

Fertility-Preserving Treatments in Patients with Gynecological Cancers: Chinese Experience and Literature Review

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Abstract

We conducted a retrospectively reviewed of the literature published of patients underwent fertility-preserving treatments for cervical, endometrial and ovarian cancers using the WANFANG database in Chinese. A majority were retrospective studies and case reports. With cervical cancer, radical trachelectomy(RT) in combination with pelvic lymphadenectomy could preserve the fertility of patients with early stage IA1-IB1 cancers, Tumor size ≤2cm should be emphasized as the indication of RT in considering of the higher recurrent rate in patients with tumor size >2cm. For endometrial cancers, there is much experience on it. Given accurate pretreatment assessment, hormonal therapy is feasible management option to preserve fertility in young patients with early stage lesions that limited to the endometrium and well differentiated. High dose progestin have been applied, oral medroxyprogesterone acetate (MPA), 250-500mg/day, megestrol acetate 160-480mg/day. Other therapies that have been used in a limited number of cases include GnRH analog, intrauterine devices (IUDS) containing progestogen, usually combination of these therapies. All patients should be followed up by ultrasound and/or MRI evaluation, and endometrial curettage at intervals of 3 months. With ovarian cancer, in China, fertility-preserving surgery in patients with stage IA (grade G1) of epithelial ovarian tumor and patients with germ cell tumor and borderline ovarian tumor have been successfully performed.

Keywords: Gynecological cancers - fertility preserving - treatment - recurrence - outcome

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Introduction

In recent years, fertility-preserving is rapidly expanding new field. Cancer may be detected at any age, thousands of reproductive-age women and girls are diagnosed with cancer every year (Howlader et al., 2014). Today Reduction of cancer-related mortality remains the main issue of the health-care provider, but the fertility-preserving ability in the increasing population of young and delaying childbearing women with gynecological cancers also is considerable. Fertility-preserving treatments have been successfully performed in early stage cases of cervical, endometrial and ovarian cancers, although the awareness and access to fertility-preserving was limited in the beginning (Mojgan Karimi Zarchi et al., 2011). Here, we report our present experience of fertility-preserving treatments in gynecological cancers and focus on new developments on the horizon in the literature.

Cervical Cancer

Cervical cancer is still the most common gynecological cancer in the world despite the popularization of screening program for cervical cancer and the adoption of vaccination against human papilloma virus(HPV) in many country (Jeong-yeol et al., 2015). In China, as the nationwide of screening for cervical cancer and releasing of family-plan, the young person with early-stage of cervical cancer is increasing, many of them desire for producing and raising own children.

The fertility-preserving treatment of Ia1 and Ia2 cervical squamous cell carcinoma is conization, which is conservative used only in cervical adenocarcinoma Ia1 (Yang et al., 2013). According to study, the procedure, such conization, is successfully therapy for pre-invasive lesions and some microinvasive carcinoma (limited to ≤3mm) without lymphovascular invasion (Baalbergen et al., 2011). The risk factor of recurrence or remains for conization is positive margin, lymphovascular invasion and multi-center lesions. In order to avoid remains, it is important that to choose appropriate range of conization. It is necessary that the width of conization is 0.3cm outside of the lesions, and the depth of conization is 2.0-2.5cm of cervical canal. The microinvasive cervical carcinoma with positive-margin, it is recommended that it is coned again or managed as stage Ib1 according to FIGO guideline for cervical cancer. But the treatment of stage Ia1 with lymphovascular invasion and stage Ia2 of cervical cancer is not only conization, but also total pelvic lymphadenectomy should be performed.

Radical trachelectomy (RT) is defined as removal of cervix and parametrium, preserving ovaries and uterus

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body and grafting uterus body to vagina at the end of the operation. RT could be completed through vaginal, abdominal and laparoscopically way, which is good option to preserve fertility meanwhile threatment of cancer (Dargent et al., 1994; 2000; Li et al., 2011; Chen et al., 2013; Yao et al., 2013; Cao et al., 2013).

Selection criteria for RT were as below: young patients desire for fertility without infertility factors, Tumor size ≤2cm, tumor stage Ia2-Ib1 without lymphovascular invasion, endocervix upper intact. Some believed that It is recurrence easily after RT if Tumor size is >2cm, tumor stage is Ib2 or higher with lymphovascular invasion (Dargent et al., 1994) . It is very important to evaluate tumor size, stage, lymphovascular and endocervix upper invasion or not, which can be measured aided through MRI and colposcopy before procedure.

Early detection of recurrent may impact not only survival of patient but also fertility wish undergo RT. Close follow-up is necessary in any patient after RT treatment. Follow-up should be done every month in first half year after RT, including: gynecological check, ultrasound, and serum SCC-Ag, CT, MRI and PET-CT at necessary, every 2 month for the last half year, then every 3 month for 3 years, and every half year after that. Cytology evaluation of vaginal vault should be done every 3 month, fertility could be suggested with twice negative cytology evaluation.

Endometrial Cancer

The number of endometrial cancer is increasing trend as the changing of life style and diet structure in Chinese women. It has been proving that the treatment of high effective progestin is good option for young person with endometrial cancer (Chiva et al., 2008; Dursun et al., 2012; Yu et al., 2009; Wang et al., 2014).

Complex atypical hyperplasia of endometrium is a precursor of endometrial adenocarcinoma, which is the most common histological type of endometrial cancer, although the ultimate treatment is surgery in early-stage lesions for them , hormonal therapy such as progestin has been suggested to young women age ≤40 who anxious to conserve their fertility (Yu et al., 2009; Wang et al., 2014). Besides, Selection criteria for progestin therapy have to be content with things as high grade, lesion limited to the location in the endometrium without involvement of myometrium, lymph node or the cervix. The express of progestin receptor is positive and patient's consent must be done fully before conservative therapy.

The evaluation before progestin therapy for early-stage endometrial cancer should be done, including: history of disease, check-up, all body status, Pathological review and the severe degree of lesion through ultrasound or MRI (Cade et al., 2010), PET-CT at necessary. The method of therapy is high dose progestin used, oral medroxyprogesterone acetate (MPA), 250-500mg/day, megestrol acetate 160-480mg/day. Other therapies that have been used in a limited number of cases include GnRH analog, intrauterine devices (IUDS) containing progestogen, usually combination of these therapies. The evaluation of curative effect is very important. All patients should be followed up by endovaginal ultrasound and/or MRI evaluation, and endometrial curettage at intervals of 3 months. The criteria of judgment for therapy end-point is divided by remission completely, remission partially, no response to progestin therapy or disease stable and deteriorate. The indication of termination for progestin therapy is one of them: disease deteriorate, no desire for fertility, remission completely, severe side-effect and no response to progestin therapy after six months.

For those patients with remission completely, the therapy purpose is to maintain normal period and prevent recurrence, if they have no plan for fertility in short-time, While the therapy purpose is to monitor ovulation and complete fertility as soon as possible for the patients who anxious to conceive and give birth to a child.

Ovarian Cancer

The highest mortality is caused by ovarian cancer in gynecological malignant tumor. They have different clinical expression in different type of ovarian cancer, so do different manage and prognosis. The decision of preserving-fertility treatment for patients with ovarian cancer depends on age, type and stage (Liu et al., 2013).

Epithelial ovarian cancer (EOC) is the most common histological type. Although most of them are diagnosed in postmenopausal women, 3-17% of EOC occurs in women under 40 years old and less than 30 years (Plaxe et al., 1993; Rodriguez et al., 1994; Schilder et al., 2002; Park et al., 2008; Anchezar et al., 2009). We need take discreet attitude to perform preserving-fertility surgery for women with EOC. To weigh the advantages and disadvantages, explain them to patients, and sign medical informed consent (MIC) before preserving- fertility surgery taken. Some criteria must be satisfied as below: young patient age ≤35 who desire to conserve their fertility, stage Ia, G1, the opposite ovary with good appearance and negative pathology, negative abdominal cavity cytology and lymph node in high-risk district , Compliance with follow-up.

But in malignant ovarian germ cell tumor (GCT), unilateral salpingooophorectomy with preservation of the contral lateral ovary and uterus is considered the appropriate surgical treatment to conserve fertility, without regarding to stage, even in the case of advanced germ cell tumor, particularly if the contra lateral ovary is normal (Ghaemmaghami et al., 2010; Wang et al., 2011; Liu et al., 2013), considering most GCT is unilateral ovary disease, sensitive to chemotherapy cisplatin+ etoposide + bleomycin (PEB) and cisplatin+ vincristine + bleomycin (PVB). For early-stage ovarian dysgerminoma and high differentiation ovarian immature dermoid tumor, preserving- fertility staging surgery including omentectomy and retroperitoneal lymph nodes dissection.

For young patient age ≤40 with borderline ovarian tumor, unilateral salpingooophorectomy with preserving-fertility is recommended, Staging surgery is not be suggested for them, considering pelvic cavity adhesion is caused by it (Wang et al., 2011). Bilateral borderline ovarian tumors is less happened, we can only perform removing the tumors with ovaries left as long as normal ovarian tissue existing. Preserving-fertility therapy is

adapted for advanced borderline ovarian tumor without contral lateral ovary and uterus involved and negative exogenous nipple structure and Invasive plant. Patients with borderline ovarian tumor are normally young with recurrent character easily after surgery, so provider should explain the advantage and disadvantage of Preserving-fertility therapy, sign informed consent.

Conclusion

Preserving-fertility treatment should be suggest for young patients with gynecological cancers who desiring future childbearing, but we should address the possibility of infertility with patients treated before cancer treatment, the discussion and informed consent should be documented. If any potential threats to fertility in the treatment process happened, the patient should be encouraged to consider consulting reproductive specialists. Sperm and embryo cryopreservation as well as oocyte cryopreservation are considered mature practice and widely available (Gurgan et al., 2008; Cao et al., 2009; Noyes et al., 2009; Cobo et al., 2011), ovarian tissue cryopreservation is only option for children without recourse to ovarian stimulation and sexual maturity. Other Preserving-fertility methods should be further investigated without recurrence danger.

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