FERTILITY PRESERVATION IN UTERINE ENDOMETRIAL CANCER

ISAR FERTILITY PRESERVATION SPECIAL INTEREST GROUP

Introduction

Gynecologic malignancies often affect young women who are still in their reproductive years. Women are postponing childbearing and the incidence of cancer in those who still want to get pregnant has somewhat increased. Endometrium is the inner lining of the uterus. Endometrial cancer (EC) is the most common malignant tumor of the female reproductive tract in developed countries and the second most common gynecologic malignancy in China. Although EC is most often diagnosed in postmenopausal women, there is now an increased prevalence in younger women, which may be attributed to higher obesity rates and life-style changes. Approximately 4% of patients are diagnosed before the age of 40 years and before having given birth. Such patients may have a strong desire to preserve their fertility despite oncologic risks and thus may be reluctant to undergo standard treatment for EC, which includes hysterectomy, bilateral salpingo-oophorectomy, and surgical staging. Therefore, more conservative treatment approaches may need to be discussed, along with their associated oncologic and reproductive outcomes. In fact, various studies have confirmed the effectiveness and safety of conservative treatment in EC.

What is the incidence rate for Endometrial Cancer?

Cancer still represents an enormous global health burden, and published data reveals about 14.1 million new cancer cases and 8.2 million cancer deaths in 2012 worldwide. Endometrial cancer (EC) is the most frequent gynecologic cancer in developed countries killing 34,700 women in 2012.[1&2] Although it is primarily a disease of postmenopausal women, 25% are premenopausal and 3-5% are under age 40.[3] Almost 5% of women with endometrial cancer are under age 40, and they often have well-differentiated endometrioid estrogen-dependent tumors.

What is ideal treatment for women with endometrial cancer?

The standard treatment for cancer of endometrium includes an operation called Staging Laparotomy, where the extent of the disease is studied. It involves the removal of the uterus with both the ovaries & tubes and removal of the lymph nodes to see how far the disease has spread. The 5-year survival rate after this approach is approximately 94%.[4] Conservative treatment approaches, with uterine and ovarian preservation may be considered if there is a strong desire to preserve fertility. Currently, fertility preservation options in endometrial cancer are limited to hormonal methods.[5] Patients desiring to proceed with conservative hormonal management should be extensively counselled regarding potential risks as no scientifically proven optimal progestin regimen exists. Response to treatment may vary depending on tumor receptor status, ranging from 26 to 89% in estrogen and progesterone positive tumors but can be as low as 8-17% when these receptors are absent.[6]

Can pregnancy influence endometrial cancer recurrence?

There are reports of many pregnancies after conservative management of endometrial carcinoma, some after Assisted Reproductive Technique (ART). Combining conservative treatment with ART may result in healthy infants without an adverse effect on oncologic prognosis.[7] Introduction of infertility treatment (ART) soon after achieving tumor remission by high dose progesterone therapy would be beneficial for patients in this setting. Although preliminary results are encouraging, the. majority of the series reported so far have included only a small number of patients, and used different treatment methods, making the extraction of useful conclusions rather difficult.

Prerequisite for conservative approach:

The conservative treatment of endometrial carcinoma may be recommended when patient desires to preserve fertility, the tumor is endometrioid, its clinical stage is IA FIGO (i.e., the cancer is confined to the minor layers of the womb) and histological FIGO grade I (early stages of cancer). It is important to emphasize that such an approach is not standard and should be considered only if the patient insists. Careful and thorough counseling is mandatory in this setting. Thus, selection of women suitable for such conservative management, as well as treatment options, follow-up, recurrence, obstetric outcomes, and survival rates are vital parameters when counseling these women.

Adequate clinical staging of endometrial cancer remains a challenge while surgical staging is the gold standard. Prognosis is established based on histological grade, depth of myometrial invasion, cervical involvement, vascular space involvement, pelvic and aortic lymph node metastases, adnexal metastases, and positive peritoneal cytology

Establishing accurately the extent of tumour spread is extremely important if one is considering saving the uterus for future fertility and this can be done with a combination of various modalities like Ultrasound, CT Scan and MRI.

What are the available strategies of fertility preservation?

Hormonal therapy:

Most patients described in the literature received treatment with either MPA or megestrol acetate (MA), but there are controversies about the efficacy of these progestogens. Whereas MA treatment was previously reported to be associated with higher remission rate and lower recurrence rate. High dose progesterone therapy is still the only available best option. Long-term oral administration of large doses of progesterone has adverse side effects, which restricts its use in certain populations and limits compliance among young women. Therefore, research efforts have focused on developing a more effective and convenient treatment to help improve compliance and alleviate the side effects associated with oral progesterone. Other strategies including levonorgestrel-releasing intrauterine system (LNG-IUS) and gonadotropin-releasing hormone agonist (GnRH-a) therapy, used alone or in combination, have been explored as alternative options for conservative therapy in women with EC because the effectiveness of such strategies is comparable to that of high-dose oral progesterone

Hysteroscopic resection and progesterone therapy:

Hysteroscopic resection combined with progesterone therapy is a new type of conservative treatment. Hysteroscopic resection involves resection of the tumor, of a small layer of the myometrium underlying the lesion (two-step technique), and of the endometrium adjacent to the tumor (three-step technique).

If radical surgeries need to be performed, and the uterus cannot be saved, embryo and oocyte cryopreservation with future option of gestational surrogacy is an alternative.

Conclusion:

Selected patients with endometrial cancer may be candidates to a safe fertility-preserving management strategy. Two issues are extremely relevant when a conservative approach is considered:

- first, the evaluation of the tumor's individual pathology biology (histological type, grade, myometrial invasion, and presence of lymphovascular space invasion); and
- second, choosing the optimal approaches for fertility sparing and follow up.

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