

Editorial

Fertility Preservation in Young Patients with Endometrial Cancer

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Endometrial cancer (EC) represents the most common malignancy of the female genital tract in developed countries [1-10]. Based on recent data, the average life time risk for EC worldwide is approximately 1.71%.¹¹ Although the disease mainly affects postmenopausal women, approximately 4% of patients are younger than 40 years [1-10, 12-15]. In the majority of the patients, abnormal uterine bleeding remains the most common symptom [1-7, 9, 10, 12, 13].

According to the recommendations of many international scientific societies (ACOG, FIGO, SGO, ESGO and ESMO), systematic surgical staging represents the initial treatment approach in all patients with EC [2-4, 6-10, 12, 16, 17]. This is mainly because systematic surgical staging offers many diagnostic, prognostic and therapeutic benefits in these patients [2-4, 6, 8, 12, 16, 17]. The extent of surgery should be carefully individualized according to the type of EC and the patient's general medical status [8].

In this light, patients younger than 40 years who wish to preserve their fertility, should be carefully counselled that fertility sparing treatment is a non-standard approach and the available data on outcomes is limited [8, 12, 15, 18, 21]. Moreover, they should be able to accept close follow-up during and after the fertility sparing treatment [8, 12, 19]. Furthermore, they should be informed about the need of systematic surgical staging in case of treatment failure or after childbearing [8, 12, 15, 18, 19, 21].

In particular, only patients with FIGO stage IA, grade 1 and type I (endometrioid) EC are eligible for fertility sparing treatment [8, 12, 14, 15, 22]. These

patients should have strong desire for fertility preservation, no contraindications for medical treatment and informed consent about fertility sparing treatment [8, 12, 15]. Additionally, they should be referred to specialised centres [8, 12, 18].

An appropriate endometrial specimen should be obtained with dilatation and curettage, hysteroscopy or office endometrial biopsy [8, 12, 15, 23-26]. However, dilatation and curettage is superior to office endometrial biopsy, because it provides a better specimen [8, 12, 23, 24, 26]. The specimen should be examined by an expert pathologist, in order to diagnose accurately the grade and the type of EC [8, 12, 15, 26]. Additionally, the assessment of hormone receptor status (estrogen, progesterone) and the expression of molecular prognostic markers (p53, Ki-67, HE-4), might provide useful information regarding the biologic behavior of tumor [8, 12, 14, 15, 27]. Patients with highly aggressive tumors are not eligible for fertility sparing treatment [8, 12, 15].

Furthermore, the presence of myometrial invasion and/or extrauterine disease (synchronous ovarian tumor, ovarian metastases, suspicious retroperitoneal nodes) should be evaluated with magnetic resonance imaging (MRI), ultrasound and/or computing tomography (CT) [8, 12, 15, 26, 28-30]. Magnetic resonance imaging is superior to ultrasound and computing tomography, in evaluating the depth of myometrial invasion in these patients [8, 12, 15, 26, 28-30]. Laparoscopy, although it is optional, might provide useful data regarding disease stage [12, 15].

Fertility sparing treatment in young patients with FIGO stage IA, grade 1 and type I (endometrioid) EC, is based on oral progestins [8, 12, 15, 31-33]. The most commonly used progestin regimens are medroxyprogesterone acetate and megestrol acetate [8, 12, 15, 26, 31-33]. The combined use of

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levonorgestrel releasing intrauterine device with GnRH-analogues, shows promising results and represents an alternative choice [8, 26, 32, 34]. The average daily dosage of medroxyprogesterone acetate is 400-600 mg, while that of megestrol acetate is 160-320 mg [8, 12, 15, 35]. Moreover, the average duration of treatment with oral progestins is approximately 6 months [8, 12, 15, 26]. In the past, many patients were treated for more than 6 months [15, 36, 37]. Nevertheless, there are no evidence to support the prolonged use of oral progestins, in order to achieve late response [15, 26, 36, 37].

During the treatment, all patients should be evaluated with endometrial sampling (dilatation and curettage or hysteroscopy) every 3 months [8, 12, 15, 26, 32, 38]. After completion of the 6-month treatment, they should be further evaluated with magnetic resonance imaging in order to assess the response to the fertility sparing treatment [8, 12, 15, 26, 29, 38].

If there is no response after the 6-month treatment with oral progestins, then patients should have systematic surgical staging according to the recommendations of the international scientific societies (ACOG, FIGO, SGO, ESGO and ESMO) [2-4, 6-10, 12, 15-17, 26].

On the other hand, if there is a complete response after the 6-month period, then patients should be referred to a fertility clinic in order to achieve pregnancy as soon as possible [8, 12, 15, 39-42]. Worth to notice that pregnancy significantly associated with a lower risk for recurrence [8, 12, 15, 32, 39]. If they do not wish pregnancy at this time, they should continue the treatment with oral progestins and they should have a re-evaluation every 6 months [8, 12, 15, 26, 32, 39].

Based on recent studies, the overall response rate in EC patients having fertility sparing treatment is approximately 75% [8, 12, 15, 20, 26, 39, 43]. However, the overall recurrence rate ranges between 30% and 40% [8, 12, 15, 20, 39, 43]. This is the main reason why, all young EC patients should have systematic surgical staging after childbearing [8, 12, 15, 26].

In conclusion, fertility sparing treatment using progestins is a promising treatment approach for well selected young patients diagnosed with FIGO stage IA, grade 1 and type I (endometrioid) EC. Nevertheless,

this management still represents a non-standard approach for them [2-4, 6-10, 12, 16, 17]. In this light, all patients should be carefully informed about the effectiveness of that innovative treatment approach and the need of systematic surgical staging in case of treatment failure or after childbearing [8, 12, 15, 20, 39, 43].

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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