



Editorial

Volume 2 Issue 3 - February 2017
DOI: 10.19080/JGWH.2017.02.555586

J Gynecol Women's Health

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Conservative Management of Young Patients with Early Stage Endometrial Cancer

Georgios Androutsopoulos^{1*}, Ioannis C Kotsopoulos², Georgios Adonakis¹ and Georgios Decavalas¹

¹Department of Obstetrics and Gynecology, University of Patras, Greece

²Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, UK

Submission: February 06, 2017; **Published:** February 08, 2017

*Corresponding author: Georgios Androutsopoulos, Department of Obstetrics and Gynecology, University of Patras, Medical School, Rion 26504, Greece, Tel: +306974088092; Email: androutsopoulos@upatras.gr; androutsopoulosgeorgios@hotmail.com

Editorial

Endometrial cancer (EC) represents the fifth most common malignancy in women worldwide, after breast, colorectal, lung and cervical cancer [1,2]. The disease is more common in developed countries (Northern America and Northern and Western Europe), but the mortality rate is significantly higher in the developing ones (Northern Africa and Melanesia) [1,2]. It mainly affects postmenopausal women and abnormal uterine bleeding remains the most common symptom [3-14]. However, up to 14% of cases are premenopausal and almost 4% of patients are younger than 40 years [3-16].

Based on the recent recommendations and guidelines, systematic surgical staging represents the primary therapeutic approach in all patients with EC as offers various diagnostic, prognostic and therapeutic benefits in them [3-10,12,17-20]. However, the extent of this procedure should be carefully individualized according to the disease stage, the patient's performance status and the desire of fertility preservation [5,8,10,12,13,19,20].

In this light, conservative management should be offered in well selected young patients with early stage disease and strong desire for fertility sparing treatment [5,8,11,13,21-24]. Only patients with FIGO stage IA, grade 1 and type I (endometrioid) EC, are eligible for this approach [5,8,11,13,15,25]. Moreover, they should have strong desire for fertility preservation, no contraindications for medical treatment and informed consent about conservative management [5,8,11,13].

Patients should be informed that conservative management is a non-standard treatment approach and they should also be able to accept a very close follow-up during and after fertility sparing treatment [5,8,11,13,21,24]. Furthermore, they should be carefully counselled regarding risks for recurrence, anticipated future fertility and pregnancy issues [5,8,11,13,21-

24]. Additionally, they should be aware about the need of systematic surgical staging in case of treatment failure or after childbearing and be referred to specialised oncologic centres [5,8,11,13,21,22,24].

To begin with, a proper endometrial specimen should be taken from all patients either with office endometrial biopsy, hysteroscopy or dilatation and curettage [5,8,11,26-31]. Nevertheless, dilatation and curettage provides better specimens compared with office endometrial biopsy and it is preferable [5,8, 26,27,29-31]. An expert pathologist should assess the endometrial specimen, in order to provide an accurate diagnosis of the grade and the type of EC [5,8,11,13,29]. Moreover, hormone receptor status (estrogen, progesterone) and expression of molecular prognostic markers (p53, Ki-67, HE-4) should also be evaluated in order to identify tumors with aggressive or potentially aggressive biologic behavior, where the conservative management is contraindicated [5,8,11,13,15,32].

The depth of myometrial invasion and the identification of extrauterine spread (ovarian metastases, retroperitoneal lymph nodes, omental disease) should be evaluated with either magnetic resonance imaging (MRI), ultrasound and/or computerized tomography (CT) [5,8,11,13,29,33-35]. Among them, magnetic resonance imaging assess better the depth of myometrial invasion, when compared with ultrasound and computerized tomography and it is usually preferred [5,8,11,13,29,33-35]. Apart from that, useful data regarding disease stage might be obtained with laparoscopy, although it still remains an optional evaluation method [5,11,13].

The conservative management of young patients with FIGO stage IA, grade 1 and type I (endometrioid) EC, is mainly based on oral progestins [5,8,11,13,36-38]. In daily practice, medroxyprogesterone acetate and megestrol acetate, are the most common used progestin regimens [5,8,11,13,36-38].

The average daily dosage of medroxyprogesterone acetate is 400-600 mg, while that of megestrol acetate is 160-320 mg [5,8,13,39]. The treatment with oral progestins usually lasts 6 months, although in the past many patients treated for longer periods of time [5,8,11,13,29,39-41]. Recently, the combined administration of GnRH-analogues with intrauterine devices releasing levonorgestrel, showed promising results and represents an alternative treatment approach [8,13,29,37,42].

During the conservative management, endometrial sampling (dilatation and curettage or hysteroscopy) should be performed every 3 months, in order to assess the response to treatment [5 8 11 13 29 37 43]. At the end of 6-month period with oral progestins administration, the overall response to treatment should be re-evaluated with MRI [5,8,11,13,29,34-43]. If there is no response, systematic surgical staging should be performed as there is no evidence of prolonged (more than 6 months) hormonal treatment to achieve late response [3-13,17-20,29,40,41].

In case of complete response to the conservative treatment, the patient should be referred to a fertility centre and offered an assisted conception protocol [5,8,11,13,44-47]. Interestingly, there is evidence that pregnancy substantially reduces the risk of disease recurrence [5,8,11,13,37,44]. However in case that the pregnancy is not immediately desirable, then the treatment with oral progestins should be continued and the patients should be reassessed in 6 months intervals [5,8,11,13,29,37,44].

According to recent data, the overall response to the conservative management of EC patients is about 75% [5,8,11,13,23,29,44-48]. However, all these patients who treated with oral progestins, should have systematic surgical staging after childbearing as the overall recurrence rate ranges between 30% and 40% [5,8,11,13,23,29,44,48].

In conclusion, only well selected young patients with FIGO stage IA, grade 1 and type I (endometrioid) EC are eligible for conservative management with oral progestins [5,8,11,13,15,25]. Although this is a promising approach, it cannot be used as a standard treatment [3-10,12,13,17,18]. Consequently, patients should be thoroughly counseled and informed about the feasibility of that innovative treatment approach and the necessity of systematic surgical staging in case of no response, recurrence or after childbearing [5,8,11,13,23,44,48].

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DOI: [10.19080/JGWH.2017.02.555586](https://doi.org/10.19080/JGWH.2017.02.555586)

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