





Editorial

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# Management Of Endometrial Cancer

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Endometrial cancer (EC) is the most common malignancy of the female genital tract.1 It occurs primarily in postmenopausal women [1,2]. Overall, about 2.64% of women develop EC during their lifetime [1]. In those patients, the most common presenting symptom is abnormal uterine bleeding [2].

Based on clinical and pathological features, sporadic EC is classified into 2 types [3,4]. Type I EC, represents the majority of sporadic EC cases (70-80%) [3,4]. It is usually well differentiated and endometrioid in histology[3,4]. Type II EC, represents the minority of sporadic EC cases (10-20%) [3,4]. It is poorly differentiated and usually papillary serous or clear cell in histology[3,4].

Systematic surgical staging is the baseline therapy, for most patients with EC[2,5-9]. Moreover, that therapeutic approach allows a more clear decision for stage related postoperative adjuvant therapy [8].

In those patients, systematic surgical staging includes: total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and complete resection of all disease [8]. Especially in patients with type II EC, systematic surgical staging requires additional omentectomy and biopsy of any suspected lesion [10]. Pelvic washings are no longer part of FIGO surgical staging system for EC, but may be reported separately[9].

Appropriate surgical staging provides prognostic and therapeutic benefits for women with EC [2,8]. It facilitates targeted therapy that maximize survival and minimize the morbidity of overtreatment (radiation injury) and the effects of undertreatment (recurrent disease, increased mortality) [8].

Pelvic and para-aortic lymphadenectomy is essential for surgical staging in patients with EC [5,8]. It has diagnostic and prognostic

value[5,11]. It defines accurately the extent of disease and determines the prognosis of EC patients[5,11]. Undoubtedly, it is the only way to identify EC patients with stage IIIc disease [8,9,12,13]. Also, it provides a rationale for the need, type and extent of postoperative adjuvant treatment[5,11,14].

Additionally, pelvic and para-aortic lymphadenectomy seems to have a therapeutic effect in patients with EC [15-17]. It is associated with improved survival in patients with type II EC and in patients with advanced stage disease [2,15,16,18,19]. However it has no effect on survival in patients with early stage type I EC. [2,20,21].

It seems that pelvic and para-aortic lymphadenectomy can be safely omitted in patients with early stage well differentiated type I EC[8,20-23]. However pelvic and para-aortic lymphadenectomy should be performed in all patients with advanced stage type I EC or with type II EC [18,24,25]. Also in any case of doubt, lymphadenectomy should be performed rather than abandoned [24].

The extension of pelvic and para-aortic lymph node dissection (more than 14 lymph nodes) is an independent risk factor for postoperative complications[20,23,26]. Moreover in elderly patients and in patients with relevant comorbidities (obesity, diabetes, coronary artery disease), morbidity must be carefully weighed against any survival advantage [8,27,28].

Traditionally, systematic surgical staging in EC patients performed through a laparotomy [29,30]. However in EC patients with early stage disease, it may be performed with minimally invasive techniques (laparoscopy, robotic-assisted surgery)[2,29-32]. Minimally invasive surgery associated with smaller incisions, shorter hospital stay, quicker recovery and lower risk of complications (blood loss, wound infection, herniation and ileus) [8,29-32]. Moreover, it offers many advantages especially in overweight and elderly patients [8,29-33]. Compared with laparotomy, it is associated with similar overall and disease-free survival [29,30]. However, there are relatively small differences in recurrence rates [29,30].

Especially in EC patients at increased risk for recurrence or with advanced stage disease, required a more aggressive management with postoperative adjuvant radiotherapy and/or chemotherapy [2,5,7,24].

Postoperative adjuvant radiotherapy includes external pelvic radiotherapy and/or brachytherapy. Vaginal brachytherapy in EC patients with early stage disease, reduces the risk of local recurrences but has no impact on overall survival [34]. However, it is well tolerated and associated with less side effects than external pelvic radiotherapy[34]. It is the adjuvant treatment of choice for high-intermediate risk EC patients[34,35]. External pelvic radiotherapy in EC patients with early stage disease, also reduces the risk of local recurrences but has no impact on overall survival [8,34,36,37]. Also, it is associated with significant morbidity and a reduction in quality of life [34,36]. It is used only in high risk EC patients or at advanced stage disease[35,38].

Adjuvant chemotherapy is the mainstay of treatment for EC patients with locally advanced or metastatic disease [2,5,39]. The most active chemotherapeutic agents are: taxanes, anthracyclines and platinum compounds [39,40]. Although adjuvant chemotherapy achieve high response rates, it has only modest effect in progression free survival and overall survival [39].

Moreover, the combination of adjuvant chemotherapy and radiotherapy is promising in high risk EC patients or at advanced stage disease[39,41]. It seems that the combination of chemotherapy and radiotherapy is more effective than the radiotherapy alone [39].

Recent years, molecular targeted therapies have still shown modest effect in unselected EC patients [39]. They usually target the inhibition of EGFR, VEGFR and PI3K/PTEN/AKT/mTOR signal pathways [42]. Perhaps they may be clinically active as adjuvant therapy in well-defined subgroups of type II EC patients with EGFR and ErbB-2 overexpression [43,44].

## **Conflict of Interest**

We declare that we have no conflict of interest.

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