New Insights in Endometrial Cancer Treatment

Androutsopoulos G*, Michail G and Decavalas G

Department of Obstetrics and Gynecology, University of Patras, Medical School, Rion, Greece

Editorial

Nowadays, endometrial cancer (EC) represents the most common malignancy of the female genital tract in developed countries [1-5]. The estimated average lifetime risk for EC in the United States, is approximately 2.64%. EC most commonly occurs in postmenopausal women [1-5]. The sporadic EC based on its clinical and pathological features is classified into 2 different types (type I EC and type II EC) and the classification has a crucial role for the entire management of EC patients [6,7]. It is interesting to note, that the international scientific societies (ACOG, FIGO, SGO and ESMO) recommend the systematic surgical staging as the initial treatment approach in patients with EC [3-5,8-12]. More specifically, the systematic surgical staging in patients with type I EC (endometrioid) includes: total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy and complete resection of any suspicious lesion [2-5,8-15]. On the contrary, the systematic surgical staging in patients with type II EC (poorly differentiated, papillary serous, clear cell) includes: total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, total omentectomy, appendectomy and complete resection of any suspicious lesion [3-5,10,11,14-16]. Additionally, pelvic washings are necessary for both types of EC, although they do not affect FIGO staging [9]. The systematic surgical staging in patients with EC can be performed either with laparotomy or laparoscopy [2-5,8,10-12,17-20]. When applied in EC patients, both of them have similar results in recurrence rates and they associated with similar overall and disease-free survival rates [10,12,17,18]. Nevertheless, minimally invasive techniques have significant advantages especially in overweight and elderly patients (smaller incisions, improved visualization, shorter hospital stay, less postoperative pain, quicker recovery and low risk for postoperative complications) [3-5,8,10,12,17-21]. Laparotomy is the most preferable approach for systematic surgical staging in patients with EC [3-5,10,11,17,18]. In sharp contrast, minimally invasive techniques (laparoscopy and robotic-assisted surgery) are significantly more difficult and time consuming and require special surgical skills [2-5,8,10-12,17-20]. This is the reason why, minimally invasive techniques are less popular and we use them only in EC patients with early stage disease [2-5,8,10-12,17-20]. It is also worth noting, that pelvic and para-aortic lymphadenectomy has an essential role for systematic surgical staging in patients with EC [3-5,11,14,15] It is the only way to diagnose EC patients at stage IIIC [3-5,8,9,11-13,22,23]. Furthermore, pelvic and para-aortic lymphadenectomy improves survival in patients with advanced stage type I EC and in all patients with type II EC [2-5,11,24-28]. In contrast, pelvic and para-aortic lymphadenectomy do not improve survival in patients with early stage type I EC [2-5,11,12,29,30]. Nevertheless, the extent of pelvic and para-aortic lymphadenectomy (>14 lymph nodes) in patients with EC, increases significantly the risk for postoperative complications [3-5,11,29,31,32]. As a consequence, in elderly patients and in patients with relative comorbidities (obesity, diabetes and coronary artery disease) we should carefully weigh the increased intraoperative and postoperative morbidity with any survival advantage [3-5,8,11,31,33,34]. On the other hand, according to the recommendations of the international scientific societies (ACOG, SGO and ESMO), postoperative adjuvant treatment (radiotherapy and/or chemotherapy) plays a very important role in EC patients with increased risk for recurrence or at advanced stage disease [2-5,8,10,11,13,35,36]. To begin with, the postoperative adjuvant radiotherapy in EC patients includes vaginal brachytherapy and external radiotherapy [3-5,10,11,36]. Vaginal brachytherapy is the treatment of choice in intermediate risk EC patients (stage IA grade 3 endometrioid type EC, stage IB grade 1-2 endometrioid type EC) [3-5,10,11,36-41]. The application of vaginal brachytherapy is well tolerated and it is associated with less side effects and better quality of life [10,36-40,42]. Moreover, vaginal brachytherapy minimizes the risk for local recurrences, but it does not affect overall survival [36,37,40,42]. Especially in intermediate risk EC patients, vaginal brachytherapy and external pelvic radiotherapy have an equal role for the local control of disease [3-5,10,11,36-39].

Similarly, external pelvic radiotherapy is the adjuvant treatment of choice in high risk EC patients (stage IB grade 3 endometrioid type EC, stage I non-endometrioid type EC) [3-5,10,11,38,39,42].
The application of external pelvic radiotherapy is not well tolerated and it is associated with significant morbidity and reduction in quality of life [3-5,11,37,43]. Although external pelvic radiotherapy minimizes the risk for local recurrences, it does not affect overall survival [8,36-38,40,43,44]. In contrast, whole abdomen radiotherapy is an alternative treatment option in EC patients with advanced stage disease [45]. However, whole abdomen radiotherapy should be used only in patients with completely resected disease [45]. Furthermore, it has tolerable toxicity and may improve overall survival [3-5,11,45].

On the other hand, postoperative adjuvant chemotherapy is the adjuvant treatment of choice in EC patients with advanced stage disease [2-5,10,11,13,36,46,47]. Nevertheless, adjuvant chemotherapy is more effective than whole abdomen radiotherapy, in EC patients with advanced stage disease [3-5,11,35-48]. The most common used chemotherapeutic agents in EC patients are: taxanes, anthracyclines and platinum compounds [46,49]. The application of postoperative adjuvant chemotherapy achieves high response rates, but it has only modest effect in progression free survival and overall survival [3-5,11,46]. Nowadays, the postoperative combination of adjuvant radiotherapy with adjuvant chemotherapy shows promising results, particularly in high risk EC patients and in EC patients at advanced stage disease [3-5,11,36,46,50]. Especially in EC patients with systematic surgical staging, the combined application of adjuvant radiotherapy and adjuvant chemotherapy reduces the risk of relapse or death and increases overall survival [3-5,10,11,36,51]. Additionally, the combined application of adjuvant radiotherapy and adjuvant chemotherapy is more effective than the isolated application of adjuvant radiotherapy [3-5,11,36,46,51].

Recent years, molecular targeted therapies are very popular in the treatment of various types of cancer [3-5,11]. Those therapies, usually target essential signaling pathways (EGFR, VEGFR and PI3K/PTEN/AKT/mTOR). However, they have not studied well in EC and they have only modest effect in unselected EC patients [3-5,11,46,55,57]. In this light, ErbB-targeted therapies can be used as an adjuvant treatment in well-defined subgroups of EC patients (type II EC) with EGFR and ErbB-2 over expression [3-5,11,14,15,58-68]. Moreover, their efficacy in those subgroups of EC patients, should be further evaluated with prospective clinical trials and adequate number of patients [3-5,11,14,15,58-68]. In conclusion, the systematic surgical staging plays an essential role in the treatment of EC patients and offers many diagnostic, prognostic and therapeutic benefits [2-5,8,11,14,15]. Moreover, it clearly affects the decision for the appropriate postoperative adjuvant treatment in EC patients, in order to maximize survival and minimize the morbidity of over-treatment (radiation injury) and the effects of under-treatment (recurrent disease, increased mortality) [2-5,8,11,14,15].

References
al. Pelvic lymph node count is an important prognostic variable for FIGO stage I and II endometrial carcinoma with high-risk histology. Gynecol Oncol. 2006; 102: 92-97.


62. Roque D, Santin A. Updates in therapy for uterine serous carcinoma. Curr


