



# The Role of Lymphadenectomy in Patients with Endometrial Cancer

Georgios Androutsopoulos<sup>1\*</sup>, Ioannis C. Kotsopoulos<sup>2</sup> and Georgios Decavalas<sup>1</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, University of Patras, Greece

<sup>2</sup>Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, UK

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

## Editorial

Endometrial cancer (EC) represents the most common malignancy of the female genital tract in developed countries [1-10]. Current international guidelines (ACOG, FIGO, SGO, ESGO and ESMO), recommend systematic surgical staging as the initial treatment approach for all types of EC [type I (endometrioid) and type II (serous, clear cell, undifferentiated)] [2-4,6-15]. This is mainly because systematic surgical staging offers many diagnostic, prognostic and therapeutic benefits for these patients [2-4,6-13].

Pelvic and para-aortic lymphadenectomy represents an integral part of the systematic surgical staging [2-4,6-11,16]. Pelvic lymphadenectomy should include the remove of the nodal tissue from the distal half of the common iliac artery, the external iliac artery and vein (down to the deep circumflex iliac vein) and the obturator fat pad (anterior to the obturator nerve) [11]. In para-aortic lymphadenectomy the nodal tissue from the inferior vena cava and aorta (up to the level of either the renal vessels or to the inferior mesenteric artery) is dissected [8-11].

According to the revised FIGO staging system for endometrial cancer, lymphadenectomy represents the only way to accurately diagnose patients with FIGO stage IIIc disease [2-4,6-13,16-18]. Therefore, lymphadenectomy provides important information regarding the need for postoperative adjuvant treatment, in order to maximize the survival and minimize the morbidity of over-treatment (post-radiation effects, chemotherapy related toxicity) and the risks of under-treatment (recurrence) [8,11,18-20].

The implementation of pelvic and para-aortic lymphadenectomy in patients with early stage type I EC, does not affect the overall and the disease free survival [2-11,13,21-23]. According to the results of the ASTEC study, pelvic

lymphadenectomy should not be recommended as a routine procedure outside of clinical trials, in patients with early stage type I EC [22]. However, this requires an extensive intraoperative frozen section evaluation of the uterine specimen, an approach usually not available or feasible in many hospitals [11,20,22]. On the contrary, pelvic and para-aortic lymphadenectomy improves overall survival in patients with advanced stage type I EC as well as in all patients with type II EC [2-11,24-28].

There is an ongoing debate regarding the need and the extent of para-aortic lymphadenectomy in EC patients, mainly because the occurrence of isolated para-aortic lymph node metastases with negative pelvic nodes, is approximately only 1-3,5% [8,11,20,29]. Based on the results of the SEPAL study, combined pelvic and para-aortic lymphadenectomy should be recommended in intermediate and high risk EC patients (stage Ib or more in type I EC and any stage in type II EC), as there are essential survival benefits [8,30]. Furthermore, the implementation of para-aortic lymphadenectomy up to the level of renal vessels is preferable, because most patients with para-aortic lymph node involvement have metastases above the level of the inferior mesenteric artery [8,29,31].

The extent of pelvic and para-aortic lymphadenectomy should be confirmed pathologically in the tissue specimen [8,11]. Although there is not any limit regarding the number of the removed lymph nodes, the removal of more than 10-12 lymph nodes is directly correlated with improved prognosis [8,11,24,26,27,32]. Consequently, the total number of the removed lymph nodes, reflects the adequacy of lymphadenectomy [8,24,26].

The most common intraoperative and postoperative complications of pelvic and para-aortic lymphadenectomy, are vessel or nerve injury, pelvic lymphocysts, lymphoedema and

cellulitis [2-4,6,7,9-11,21,33,34]. Extended pelvic and para-aortic lymphadenectomy (more than 14 lymph nodes) increases significantly the risk for these perioperative complications [2-4,6,7,9-11,21,33,34]. This is the main reason why, surgeons should carefully balance the increased morbidity and the risk for perioperative complications with any survival benefit, especially in elderly patients and in patients with comorbidities (obesity, diabetes mellitus and coronary artery disease) [2-4,6,7,9-11,33,35,36].

In recent years, the sentinel lymph node detection and dissection has emerged as an attractive approach, mainly because it could potentially be related to reduced risk of perioperative complications compared to the systematic lymphadenectomy. Particularly in EC, sentinel lymph node dissection still remains experimental and represents a balance between systematic lymphadenectomy and no dissection in low and intermediate risk EC patients [8,37-42]. The approach is based on the theory that lymph drains away from the tumor in a specific centrifugal pattern [38,39]. Consequently, if the sentinel lymph node is negative for metastasis, then the chance that more distal nodes are involved by tumor is very low, and therefore the need for further lymphadenectomy is not necessary [38,39].

There are many arguments regarding the site of injection (cervix, uterine serosa or endometrium), the injection method and the used injected agent (<sup>99m</sup>Tc, patent blue and indocyanine green) [8,13,38,39,41,43-48]. Based on the results of the SENTI-ENDO study, sentinel lymph node mapping could play an essential role in the identification of lymph nodes with micrometastases, especially in EC patients with early stage disease [8,13,38,39,41,43,49,50]. Nevertheless, further prospective randomized clinical trials are needed [8,37,39,40,50].

In conclusion, pelvic and para-aortic lymphadenectomy plays an essential role in the systematic surgical staging of patients with EC [2-4,6-11,16]. Moreover, provides important information for the postoperative adjuvant treatment of these patients, in order to maximize the survival and minimize the morbidity of over-treatment (post-radiation effects, chemotherapy related toxicity) and the risks of under-treatment (recurrence). Provisional results of the sentinel lymph node dissection look promising and future studies would be able to show if this approach could replace the systematic lymphadenectomy.

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