

Systematic lymphadenectomy or sentinel lymph node dissection in endometrial cancer: A clinical dilemma

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Abstract

Endometrial cancer represents a common malignancy of the female reproductive system and systematic surgical staging is the primary therapeutic approach, as offers many advantages in diagnosis, treatment and prognosis.

Pelvic and para-aortic lymphadenectomy remains an integral part of the primary surgical therapeutic approach of endometrial cancer and provides substantial information concerning the need of postoperative adjuvant treatment, in order to improve survival, minimize side-effects and toxicity from over-treatment and avoid issues related to under-treatment. However, the extend of pelvic and para-aortic lymphadenectomy, has a direct correlation with the incidence of perioperative complications.

Sentinel lymph node mapping and dissection consti-

tutes a compromise between systematic and no lymphadenectomy especially in low or intermediate risk patients with endometrial cancer. It is a very popular and attractive approach in this patient subgroup and minimizes the incidence of perioperative complications compared to systematic lymphadenectomy.

In conclusion, sentinel lymph node mapping and dissection still remains an experimental approach in patients with endometrial cancer, but it could possibly have a more important role in the assessment of pelvic and para-aortic lymph nodes and finally substitute systematic lymphadenectomy in the near future.

Key words: systematic surgical staging; systematic lymphadenectomy; sentinel lymph node dissection; endometrial cancer

Introduction

Endometrial cancer (EC) represents the fifth most common malignancy in the general female population, after breast, colorectal, lung and cervical cancer^{1, 2}. The disease usually affects postmenopausal

women and is more frequent in developed countries (Northern America, Northern and Western Europe). However, the mortality rate in less developed countries (Northern Africa, Melanesia) is considerably greater compared to developed ones^{1, 2}.

Current recommendations and guidelines

According to the recently published recommendations and guidelines (ACOG, FIGO, SGO, ESGO and ESMO), systematic surgical staging represents a fundamental therapeutic approach, as it provides many advantages in diagnosis, treatment and prognosis of patients with either type I (endometrioid) or type II (serous, clear cell, undifferentiated) EC³⁻¹⁷. Postoperative adjuvant treatment plays also an essential role in EC patients with increased risk of recurrence or at advanced disease stage and could be either radiotherapy, chemotherapy or a combination of both^{3-8, 10, 12, 14, 18}.

Despite the provided benefits, the extent of surgical procedure and the type of postoperative adjuvant treatment should be thoroughly individualized according to disease stage, type of EC and patient's general performance status^{3-17, 19}.

The role of lymphadenectomy in endometrial cancer

According to the abovementioned, pelvic and para-aortic lymphadenectomy remains an integral part of the primary surgical therapeutic approach of EC, as patients with FIGO stage IIIC disease could be diagnosed accurately with this procedure only^{3-12, 14, 16, 17, 20}. This is the main reason why, the implementation of pelvic and para-aortic lymphadenectomy provides substantial information concerning the necessity of postoperative adjuvant treatment, in order to improve survival and control the morbidity of over-treatment (toxicity and side-effects) and the issues related to under-treatment (recurrent disease)^{3-8, 10, 12, 14, 16, 21}.

Systematic pelvic and para-aortic lymphadenectomy

In systematic pelvic lymph node dissection, the lymphatic tissue from distal half of common iliac vessels, external iliac vessels (down to the deep circumflex iliac vein) and obturator fossa (above to the obturator nerve) should be removed^{3, 16}. Likewise in systematic para-aortic lymph node dissection, the lymphatic tissue from aorta and inferior

vena cava (up to the level of renal vessels or inferior mesenteric artery) should also be dissected^{3, 6, 16}.

The extend of pelvic and para-aortic lymphadenectomy

Currently, there are many disagreements regarding the necessity and the extend of pelvic and para-aortic lymph node dissection in EC patients^{3, 6, 21, 22}. This is mainly based on the fact that the implementation of systematic pelvic and para-aortic lymph node dissection in low risk EC patients (stage IA in type I EC), does not improve overall and disease free survival.^{3-10, 12, 14, 16, 23-26} Moreover, the identification of isolated metastases in para-aortic lymph nodes is a very rare event (1-3,5%) in EC^{3, 6, 16, 21, 22}.

Based on the ASTEC study findings, pelvic lymph node dissection should be avoided in low risk EC patients (stage IA in type I EC) outside clinical trials.²⁴ Nevertheless, an thorough intraoperative frozen section evaluation of the entire uterine specimen is necessary, which is not attainable in many hospitals^{3, 16, 21, 24}.

On the other hand, the SEPAL study findings showed that pelvic and para-aortic lymph node dissection should be routinely performed in intermediate and high risk EC patients (stage IB or more in type I EC and any stage in type II EC), because there are survival benefits^{6, 27}. Additionally, para-aortic lymph node dissection should be extended up to the level of renal vessels, as metastatic disease usually involves para-aortic lymph nodes above the level of inferior mesenteric artery^{6, 16, 22, 28}.

The extent of pelvic and para-aortic lymph node dissection should be thoroughly confirmed during tissue specimen evaluation.^{3, 6} The total number of dissected lymph nodes, reflects the sufficiency of lymphadenectomy and affects patient's prognosis^{3, 6, 16, 29-32}.

Disadvantages of systematic lymphadenectomy

The extend of pelvic and para-aortic lymphadenectomy, has a direct correlation with the risk for perioperative complications (intraoperative and postoperative)^{3-5, 7, 8, 10, 12, 14, 16, 17, 23, 33, 34}. The most common perioperative complications in EC patients having

pelvic and para-aortic lymph node dissection are vascular or nerve injury, lymphocyst, lymphoedema and cellulitis formation^{3-5, 7, 8, 10, 12, 14, 16, 17, 23, 33, 34}.

When more than 14 lymph nodes are excised during pelvic and para-aortic lymph node dissection, then the incidence of perioperative complications is significantly increased^{3-5, 7, 8, 10, 12, 14, 16, 17, 23, 33, 34}. Especially in elderly or obese patients with either diabetes mellitus or coronary artery disease, the morbidity and risk for perioperative complications are substantially increased and should be carefully balanced with any survival benefit^{3-5, 7, 8, 10, 12, 14, 16, 17, 33, 35, 36}.

Sentinel lymph node mapping and dissection

Recent years, sentinel lymph node mapping and dissection has become very popular and attractive approach of EC patients^{16, 17, 32, 37-42}. This is mainly because the incidence of perioperative complications is considerably lower compared to systematic lymph node dissection^{16,17,32,37-42}. Moreover, sentinel lymph node mapping and dissection constitutes a compromise between systematic and no lymphadenectomy especially in low or intermediate risk patients with EC^{6, 16, 17, 37-41, 43-45}.

This approach is based on the on the fact that lymph follows a specific centrifugal pattern to drain away from the tumor^{17, 37, 43}. The tracer, either ^{99m}Tc Technetium, patent blue or indocyanine green (ICG), is injected directly to the cervix, endometrium or uterine serosa and the sentinel lymph nodes could be easily identified based on tracer concentration and signal production using the appropriate equipment^{6,9,16,17,37-41,43,44,46-48}.

Apart from the identified sentinel lymph nodes, enlarged or suspicious lymph nodes should also be removed based on the established surgical algorithm^{37, 49}. In case that the sentinel lymph node identification fails in one side, a side-specific systematic pelvic lymph node dissection should be performed^{37, 49}.

It is interesting to note, that all dissected sentinel lymph nodes should be ultrastaged by an experienced pathologist^{17, 37, 50-52}. Multiple sections from

every lymph node and immunohistochemistry are required, in order to identify which one has macrometastasis, micrometastasis or isolated tumor cells^{17, 37, 51, 52}. The procedure of ultrastaging is expensive, time consuming and difficult to be performed in large number of lymph nodes^{17,37,51}. However, ultrastaging could play an fundamental role in the accurate detection of lymph node micrometastases^{39, 41, 53-55}.

Further management after sentinel lymph node dissection

In case that the sentinel lymph nodes are negative, no further nodal excision is required, as the possibility for distal lymph node involvement is very low^{17, 37, 43}. Consequently, any unnecessary systematic lymphadenectomy could be easily avoided^{17, 19, 37, 38}. Furthermore, many surgical parameters such as total operative time, financial cost and perioperative complication rate could be significantly improved by using this innovative approach^{3-8, 10, 12, 14, 16, 17, 23, 33, 34, 37}.

If the sentinel lymph nodes are positive, then systematic pelvic and para-aortic lymph node dissection should be implemented and the lymphatic tissue from distal half of common iliac vessels, external iliac vessels, obturator fossa, aorta and inferior vena cava, should be dissected^{16, 19, 37, 43}.

Conclusion

In conclusion, pelvic and para-aortic lymph node dissection represents an essential part of systematic surgical staging in EC and sentinel lymph node mapping and dissection has become a very popular and attractive approach especially in low or intermediate risk patients with EC^{3-12,14,16,17,20,32,37-42 56}. Systematic lymphadenectomy provides substantial information concerning the utilization of postoperative adjuvant treatment^{3-8, 10, 12, 14, 16, 21}. Sentinel lymph node mapping and dissection remains an experimental approach in EC, but it could possibly have a more important role in the assessment of pelvic and para-aortic lymph nodes and finally substitute systematic lymphadenectomy in the

near future especially in patients with early stage disease^{6, 9, 16, 17, 37-41, 43, 44, 47, 55, 57}. ■

Conflict of interest

The authors declare no conflicts of interest.

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