Oncology Clinics Journal

RESEARCH ARTICLE

Sentinel lymph nodes status in endometrial cancers

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ABSTRACT

BACKGROUND: Lymphadenectomy carries the risk of intraoperative and postoperative complications, and selective lymphadenectomy provides reliable data about the lymph node status. There are conflicting data about the retroperitoneal lymphadenectomy during the treatment of endometrial cancers (ECs) and to what extent lymphadenectomy should be performed.

OBJECTIVES: This review article was designed to evaluate the diagnostic value and the methods of sentinel lymph nodes (SLNs) detection in ECs.

METHODS: PubMed search was performed for the articles published over the last 5 years from 2013 to 2017 using the following keywords: sentinel lymph nodes and endometrial carcinoma. Thirteen PubMed articles were retrieved: seven review article (one of them was systematic review), five studies (three prospective and two retrospective studies), and one society recommendation. The retrieved articles were critically analyzed to evaluate the diagnostic value and the methods of SLNs detection in ECs.

RESULTS: Lymph node status is one of the most important histopathologic features to determine the postoperative adjuvant treatment and the survival in ECs. The Society of Gynecologic Oncology recently recommended SLNs mapping into the surgical staging of ECs to reduce the morbidities associated with comprehensive or systemic lymphadenectomy. SLNs biopsy was considered accepted alternative to systemic lymphadenectomy for determining nodal spread in early-stage ECs. SLNs mapping and the lymphovascular space infiltration status can be used to select high-risk patients with ECs who would benefit from comprehensive staging. In addition, SLNs mapping would allow upstaging in low- or intermediate-risk patients in whom adjuvant therapy could be omitted. The sensitivity of SLNs mapping to detect metastasis was 96%. Although the current data favor the use of cervical injection of indocyanine green for SLNs detection, others argue that this technique is controversial because the distribution of SLNs in ECs is different from cervical cancers.

CONCLUSION: SLNs mapping is more accurate alternative to systemic lymphadenectomy for determining the nodal spread in early-stage ECs. The sensitivity of SLNs mapping to detect metastasis was 96%; SLNs mapping could allow upstaging in low- or intermediate-risk ECs; and women staged with SLNs mapping were more likely to receive adjuvant treatment compared with women staged with systemic lymphadenectomy.

KEYWORDS

sentinel, lymph, node, endometrium, carcinoma

Publisher Name: Medtext Publications LLC

Manuscript compiled: Monday 23rd April, 2018

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INTRODUCTION

Endometrial cancers (ECs) is the commonest gynecological cancer in Europe.[1] Lymph node status is the key point to detect the EC staging, prognosis, and adjuvant treatment.[2]

The International Federation of Gynecology and Obstetrics (FIGO) staging of ECs revised in 2009 include the pelvic and paraaortic lymphadenectomy as one of the most important prognostic factors in ECs.[3] There are conflicting data about the retroperitoneal lymphadenectomy during the treatment of ECs and to what extent lymphadenectomy should be performed.[4]

The authors argue that the retroperitoneal lymphadenectomy increases the intraoperative and postoperative complications, especially in women with comorbidities such as obesity, hypertension, and diabetes.[5] In addition, systemic lymphadenectomy is not necessary in women at low risk for lymph node involvement (stage 1a–1c ECs).[6]

Selective lymphadenectomy has been widely employed for staging evaluations of ECs because it is simple and provides reliable data regarding the lymph node status.[7]

Sentinel lymph node (SLN) is the first node receiving lymphatic drainage from the primary tumor, and the pathological status of SLN reflects the overall status of entire lymphatic basin. Thus, a patient with negative SLN for metastasis can be managed by SLN biopsy (SLNB) instead of systemic lymphadenectomy.[8]

The American Society of Breast Surgeons recommended a false-negative rate of ≤5% to abandon axillary dissection, and Kang et al.[9] suggested that a false-negative rate of ≤2% should be a goal for determining the clinical usefulness of preoperative or intraoperative prediction of low risk for lymph node metastasis. This review article evaluates the diagnostic value and the methods of SLNs detection in ECs.

MATERIALS AND METHODS

PubMed search was done for the articles published over the last 5 years from 2013 to 2017 using the following keywords: sentinel lymph nodes and endometrial carcinoma. Thirteen PubMed articles were retrieved: seven review article (one of them systematic review), five studies (three prospective and two retrospective studies), and one society recommendation. The retrieved articles were critically analyzed to evaluate the diagnostic value and the methods of SLNs detection in ECs.

RESULTS

Lymph node status is one of the most important histopathologic features to determine the postoperative adjuvant treatment and the survival in ECs. The Society of Gynecologic Oncology recently recommended SLNs mapping into the surgical staging of ECs to reduce morbidities associated with comprehensive lymphadenectomy. SLNB was considered accepted alternative to comprehensive lymphadenectomy for determining the nodal spread in early-stage ECs. SLNs mapping and the lymphovascular space infiltration (LVSI) status can be used to select high-risk patients with ECs who would benefit from comprehensive staging. In addition, SLNs mapping would allow upstaging in low- or intermediate-risk patients in whom adjuvant therapy could be omitted. The sensitivity of SLNs mapping to detect metastasis was 96%. Although the current data favor the use of cervical injection of indocyanine green (ICG) for SLNs detection, others argue that this technique is controversial because the distribution of SLNs in ECs is different from cervical cancers. Previous studies showed no significant associations between the presence of risk factors (grade, myometrial invasion, cervical invasion, and LVSI) and the incidence of micrometastasis and/or isolated tumor cells (ITCs) foci in the SLNs.

DISCUSSION

Medical Research Council of Assam Science Technology and Environment Council (ASTEC) trail (a study in the treatment of EC) suggested that there was no benefit in performing systemic lymphadenectomy for early-stage EC regarding patients' survival and/or prevention of recurrence.[10]

In addition, Tara et al.[6] concluded that the noninvasive or the minimal invasive assessment of the lymph node status to target specific lymph nodes for sampling is more beneficial than complete or systemic lymphadenectomy in primary ECs.

Schmolze et al.[11] conducted a retrospective review of all high-grade ECs with serous histology, >50% myometrial invasion, or FIGO stage >2, and conventional systemic pelvic lymph node dissections to evaluate the value of conventional systemic (nonsentinel) lymph node dissections in high-risk ECs. Schmolze et al. found significant associations between node status and depth of myometrial invasion, LVSI, and FIGO stage and also found that there was no significant relationship between lymph node status and serous histology. No SLN biopsies were performed in the study by Schmolze et al.[11]

Suri and Arora[12] reviewed the role of lymphadenectomy in early-stage ECs including SLN status, and also they found that only few studies have assessed the place of SLNB in the management of ECs. Yordanov et al.[13] concluded that the lymph node status has important prognostic value in ECs for the postoperative adjuvant treatment and survival.

The Society of Gynecologic Oncology recently recommended SLNs mapping into the surgical staging of ECs to reduce the morbidities associated with systemic lymphadenectomy.[14]

Tschernichovsky et al. in their review article evaluated the diagnostic performance and the oncologic outcomes of SLNB versus comprehensive or systemic lymphadenectomy in ECs. Tschernichovsky et al.[15] concluded that SLNB was more accurate alternative to comprehensive lymphadenectomy for determining the nodal spread in early-stage ECs.

Regarding the diagnostic accuracy of SLNs in ECs, a retrospective multicentre study (n = 180 patients) was conducted by Naoura et al.[16] to evaluate the value of SLNs mapping in staging patients who were presumed high risk for ECs. Naoura et al. detected SLNs in 159 of 180 ECs patients (88%), and the SLNs were bilateral in 63% the cases. The false-negative rate of the SLNs mapping was 6% (9/159); 2.3% in the low/intermediate risk group and 20% in the high-risk group (p = 0.0008).[16] Naoura et al. concluded that the SLNs mapping and the LVSI status can be used to select high-risk patients with ECs who would benefit from comprehensive systemic staging.[16]

Ninety-three patients with type I and II ECs were submitted to surgery with SLNs mapping; in the study by Ferraioli et al.,[17] patients with a locoregional or distant relapse represented the case series (CS) and patients without locoregional or distant recurrences were the case controls (CC).

Ferraioli et al.[17] found that the detection rate of SLNs per hemi-pelvis was 17 (85%) of 20 and 33 (82.5%) of 40 for CS, and CC, respectively.

Ferraioli et al.[17] concluded that the lymph node status is one of the most important histopathologic features to determine the ECs adjuvant treatment.

Touboul et al. reported in their review a SLNs detection rate of 81.7% and a false-negative rate of 12.3%. Thirty-five percent of SLN metastasis were low-volume disease (micrometastases or ITCs).[18]

They concluded that the SLNB could allow upstaging in low- or intermediate-risk ECs patients in whom adjuvant therapy could be omitted.[18]

A systematic review conducted by Bodurtha Smith et al.[19] evaluated the diagnostic accuracy and the clinical impact of SLNs mapping on ECs. They identified 55 eligible studies (4915 women included), and the overall detection rate of SLN mapping was 81% with 50% bilateral pelvic node detection rate and 17% paraaortic detection rate.[19]

Bodurtha Smith et al.[19] concluded that the use of ICG increased the bilateral detection rate compared with that of blue dye, and the cervical injection increased the bilateral SLNs detection rate but decreased the paraaortic detection rate.

In addition, they concluded that the sensitivity of SLNs mapping to detect metastasis was 96%, and women staged with SLNs mapping were more likely to receive adjuvant treatment compared with women staged with systemic lymphadenectomy.[19]

Bodurtha Smith et al. concluded that the SLNs mapping is feasible and accurately predicts nodal status in women with ECs, and the SLNs mapping may be considered an alternative standard of care in the staging ECs. The current data favor the use of cervical injection techniques with ICG for SLNs detection.[19]

Regarding the methods of SLNs detection in ECs, Favero et al.[20] conducted a prospective study to determine the feasibility and the accuracy of laparoscopic SLNB in ECs obtained through hysteroscopic injection of technetium-99 (Tc-99). Favero et al. found that among the 70 isolated SLNs, 35% (24) were exclusively identified in the paraaortic area. Nodal metastasis was confirmed in nine patients (22%), and SLNs was identified in seven of nine patients (78%), with 100% specificity, 89% negative predictive value (NPV), and 58% sensitivity. Favero et al.[20] concluded that endoscopic SLNB obtained through hysteroscopic injection of Tc-99 is a feasible and safe method with 73% (31/42) SLNs detection rate.

A prospective study was conducted by Kataoka et al.[21] to evaluate the diagnostic value of SLNs mapping using hysteroscopic subendometrial injection of 99m-Technetium-labeled phytate (radioisotope; radioisotope method) and subserosal ICG injection (dye method) in women with ECs.

Kataoka et al. detected at least one SLN in 100% of ECs cases, with 100% sensitivity and NPV. A total of 62.8% of SLNs were present in pelvic and 37.1% in paraaortic lymph nodes. Kataoka et al.[21] concluded that the SLNs mapping for ECs revealed high detection rate, with high sensitivity and NPV.

In addition, Nagai et al.[22] found that the one-step nucleic acid amplification assay using CK19 mRNA was applicable for detecting the lymph node metastasis in ECs.

Robova et al. conducted a review article to evaluate different techniques of injection and histopathologic elaboration of SLNs in ECs. They found that the hysteroscopic injection is not easy to learn, and the exact peritumoral injection in large tumors is often impossible.[23] In addition, they found that the subserosal administration of tracer is difficult during laparoscopic or robotic surgery, and the cervical injection is a controversial technique because the distribution of SLNs in ECs is different from cervical cancers.[23]

Regarding the SLNs and micrometastasis, Sawicki et al.[24] evaluated the association among SLNs, micrometastasis, and ECs relapse. They found no significant associations between the risk factors (grade, myometrial invasion, cervical invasion, and LVSI) and the incidence of micrometastasis and/or ITCs foci in the SLNs.[24] Sawicki et al.[24] concluded that the detection of SLNs micrometastasis may result in lower false-negative rate.

This review article concluded that the SLNs mapping is more accurate alternative to systemic lymphadenectomy for determining the nodal spread in early-stage ECs. SLNs mapping could allow upstaging in low- or intermediate-risk ECs in whom adjuvant therapy could be omitted. The sensitivity of SLNs mapping to detect metastasis was 96%, and women staged with SLNs mapping were more likely to receive adjuvant treatment compared with women staged with systemic lymphadenectomy. Although the current data favor the use of cervical injection of ICG for SLNs detection, others argue that this technique is controversial because the distribution of SLNs in ECs is different from cervical cancers.

SLN micrometastasis could help in modulation of the ECs adjuvant treatment, and future studies are needed to clarify the optimum method of lymphadenectomy in ECs and the optimum methods of SLNs detection.

CONCLUSION

SLNs mapping is more accurate alternative to systemic lymphadenectomy for determining the nodal spread in early-stage ECs. The sensitivity of SLNs mapping to detect metastasis was 96%; SLNs mapping could allow upstaging in low- or intermediate-risk ECs; and women staged with SLNs mapping were more likely to receive adjuvant treatment compared with women staged with systemic lymphadenectomy. Although the current data favor the use of cervical injection of ICG for SLNs detection, others argue that this technique is controversial because the distribution of SLNs in ECs is different from cervical cancers.

CONFLICT OF INTEREST

There is no conflict of interest related to this review article.

DISCLOSURE

This review article was funded by the authors themselves.

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