

SENTINEL LYMPHNODE BIOPSY IN STAGING ENDOMETRIAL CANCER

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Abstract

One of the most common gynecological cancers is endometrial cancer, with an incidence of 188.000 newly diagnosed cases each year, increasing because of rising obesity rates. The most important predictor factor for survival is represented by the status of the lymph nodes, and it also guides the postoperative treatment. Even if the evaluation of lymph node is included in the surgical staging criteria cancer since 1988, still, the optimal procedure for lymph node assessment is controversial. In some cohort studies, performance of pelvic and paraaortic lymphadenectomy (LND) has been associated with higher rates of overall survival, but there are also some other studies which demonstrated no change on survival. Although lymphadenectomy is commonly performed as part of the surgical treatment of endometrial cancer, its role still remains controversial. Node dissection provides really important information for prognostic, can help the guidement of adjuvant treatment, and has also been suggested to have a therapeutic effect. However, recently, some randomized trials failed to demonstrate a survival benefit for lymphadenectomy. Importantly, these studies also demonstrated that lymphadenectomy was associated with an increased risk of complications and called into question the value of the procedure. To limit the potential short- and long term morbidity of lymphadenectomy, sentinel lymph node (SLN) biopsy has been proposed for endometrial cancer.

Rezumat: Biopsierea ganglionului santinelă în stadializarea cancerului endometrial

Cancerul endometrial este una din cele mai frecvente malignități din lume, având o incidență în creștere datorită creșterii ratei obezității, de 180.000 de cazuri noi apărute anual. Starea ganglionilor limfatici este cel mai important predictor al supraviețuirii și ghidează protocolul de tratament postoperator. Deși evaluarea ganglionilor limfatici pelvini a fost inclusă încă din 1988 în criteriile de stadializare chirurgicală a cancerului endometrial, managementul acestora rămâne încă controversat. Limfadenectomia pelvină și paraaortică s-a dovedit a crește supraviețuirea în cancerul endometrial, fapt dovedit în unele studii, deși există studii care au demonstrat că nu influențează supraviețuirea. Deși limfadenectomia este efectuată frecvent ca parte a tratamentului chirurgical în cancerul endometrial, procedura rămâne încă controversată. Disecția ganglionară are un rol important în ceea ce privește prognosticul acestor pacienți, ghidând terapia adjuvantă. Mai recent, studii clinice randomizate au arătat că limfadenectomia nu influențează supraviețuirea. Mai mult, aceste studii au arătat că disecția ganglionară se asociază cu o rată crescută a complicațiilor postintervenționale. Pentru a reduce morbiditatea pe termen scurt sau lung determinată de această procedură, s-a propus biopsierea ganglionului santinelă în cancerul endometrial.

Cuvinte cheie: cancer endometrial, biopsie ganglion santinela, limfadenectomie

Introduction

Sentinel lymph node (SLN) detection, has been proposed as an alternative technique to identify lymphadenectomy. A sentinel lymph node is represented by the first node that receives drainage metastases of the lymph node, while reducing the morbidity associated with complete lymph node to harbor metastases in cancers with

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lymphatic spread. SLN biopsy can also detect abnormal lymphatic drainage from the main tumor that can be missed on routine lymph node dissection. SLN biopsy is already an established standard of care in staging of breast cancer and cutaneous melanoma among other cancers [12][13]. The complexity and bilaterality of the nodal basins of the uterus has made the applicability of the procedure in endometrial cancer a real challenge among practitioners. The result for SLN detection appeared to be promising, but some recent research has raised concerns about the adequacy of nodal detection, especially for paraaortic nodes [14]. The spread of the tracers through lymph node system can be limited by body mass index (BMI), so the efficacy of the procedure is being limited. For the reasons mentioned above, current guidelines do not yet recommend SLN biopsy as the standard of care in the staging of this type of cancer, although national societies and organizations that define treatment standards are more and more starting to recognize the utility of this staging approach [15].

The most common type of endometrial cancer that women will be diagnosed with will be the endometrioid type, grade 1 or 2. Risk of nodal involvement in this group of women is low. A historic case series, [16] which included 180 women with grade 1 cancers, reported the incidence of node positivity as 0%, 3% and 11% in women with no, inner third and outer third myometrial invasion respectively. The risk of extra uterine spread also increases with tumor grade. The preoperative grade based on endometrial biopsy may not always reflect the final grade of the hysterectomy specimen, with between 15% and 27% of women being upgraded [17]. In the UK, the majority of cancer centers and units will not offer such women a lymph node dissection as there is a low risk of finding a positive node. Instead the administration of adjuvant treatment for apparent stage I disease is based on the woman's age, the presence of lymphovascular involvement and the depth of myometrial invasion on the hysterectomy specimen. Unfortunately, a number of women with positive lymph nodes may not benefit of the adjuvant treatment chemotherapy, as outlined in a Cochrane data review. Women with grade 3 endometrioid cancer and more aggressive tumor types, including

serous cancers and clear cell cancers, are at much higher risk of extra uterine spread. Stage III or IV disease will be found in 70% of the women with serous carcinoma and in 50% of the women with clear cell cancers [18] using the International Federation of Gynecology and Obstetrics (FIGO) staging system. 10–20% of endometrial carcinomas are type II and cause 40% of deaths [19]. These women will be offered some form of lymph node dissection if the histopathological type is known before the surgery.

There are more methods for injecting the tracer. These include cervical injection, hysteroscopic injection and subserosal myometrial injection. The most used method is cervical injection because of easy access to the cervix. It is similar to the technique used for cervical cancer SLNB. Some studies [20][21] have reported cervical injection at a single site and others in conjunction with subserosal myometrial injection. Injecting the tracer in the cervix has the disadvantage is the fact that metastatic spread, through the ovarian drainage route to paraaortic lymph nodes, can be missed. However, Abu-Rustum et al. [20] demonstrated that the addition of a fundal injection to the cervical injection did not appear to produce a higher detection rate. Rossi et al. [22] injected indocyanine green (ICG) either into the cervix or the endometrium (through the hysteroscope) and concluded that a higher detection of the sentinel lymph node is reached proceeding cervical injection. The depth or the specific site of the injection of the tracer is not yet standardized, but the most used area for injecting the tracer into the cervix by practitioners worldwide is into cervical stroma just under the cervical epithelium. The detection rate of the sentinel lymph node in endometrial cancer using cervical injection is between 80% and 100%.

This reliability of this procedure is based on the detection rate of the sentinel node, the sensitivity of the procedure and the false-negative rate. Within the context of SLNB, it is almost impossible to find false positives and the specificity is therefore considered 100%. The importance of how detection, sensitivity and false negative rates are measured is due to the three potential nodal basins for lymphatic

drainage in endometrial cancer. The majority of studies report pelvic SLNB data based on the procedure performed: i.e. two sides of the pelvis counts as two procedures. If a sentinel node is not detected on one side it is often recommended that a full pelvic lymphadenectomy to be performed on that side [23].

A recent meta-analysis made by Bodurtha Smith et al [24] on 55 studies concluded that the sentinel lymph node detection rates are relatively high, almost 81%, with 51% bilateral detection, and sensitivity of 96%, similar with those observed in breast cancer and melanoma, in which SLN mapping is the standard care. Also, the bilateral detection rates were observed to be higher when using indocyanine green compared to blue dye.

Discussion

Sentinel node detection in endometrial cancer is feasible and has reasonable test performance. It can be a good replacement for the controversial pelvic lymph node dissection in endometrial cancer [25]. Current protocols for SLNB recommend that if a sentinel node in one side of pelvis is not identified then a full pelvic node dissection should be carried out on that side. This would be a significant change of practice for some in the world, especially in low risk women. For medical centers that are against pelvic lymph node dissection not detecting a sentinel node in endometrial cancer allows to avoid the pelvic lymphadenectomy.

It is unclear whether the sentinel lymph node status could replace or complement indications for adjuvant treatment based on uterine factors or a woman's age. It is likely it would become an additional factor in a similar manner to breast cancer management. The problem remains choosing the best group of patients that would benefit the most from this procedure Determining the risk of lymph nodal involvement preoperatively is difficult and lymph nodal involvement is one of the best prognostic factors and criteria for adjuvant treatment. With the low morbidity of the SLNB procedure, it might be desirable if all women could undergo SLNB to help in the selection of those who require chemotherapy or radiotherapy.

Conclusion

Detecting the sentinel lymph node is easily becoming an alternative standard of care in the treatment and staging of some categories of patients diagnosed with endometrial cancer. The patient selection criteria remains a difficult task, while the procedure is considered to be a secure one. Mapping the sentinel lymph is a suitable procedure to assess clinical stage I endometrial cancer. Physicians worldwide should consider adding the SLN biopsy to their staging techniques prior to exclusively adopting the new technique. They should take care to adhere to SLN algorithms and monitor outcomes.

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