Rep Pract Oncol Radiother, 2005; 10(2):

Original Paper

Received: 2004.05.11
Accepted: 2004.08.06
Published: 2005.XX.XX

Sentinel node in gynaecological oncology

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Source of support: This study was supported by a KBN 3PO5E 05223 grant.

Proceedings from the I Symposium "Sentinel Node", Poznań 26 March 2004.

Summary

Background The concept of sentinel node biopsy has been widely invastigated in various malignant tumoures and has become a standard method in such neoplastic diseases as penile cancer or melanoma. In tumours, where the lymphatic flow is more complicated and difficult to analyze, this concept still needs to be verified.

Aim The aim of this paper is to present the validity of the above concept in sentinel node detection in vulvar, cervical and endometrial cancers.

Materials/Methods Sentinel node detection was performed in 127 women with gynaecological malignances; 39 patients with vulvar cancer, 52 patients with cervical cancer and 36 patients with endometrial cancer. In sentinel node detection we used radioisotopes and a dye technique. After sentinel node dissection, in all cases, radical surgery with systemic lymphadenectomy was performed. The number and localization of the nodes classified as sentinel nodes were analyzed.

Results The identification rate for sentinel node detection was 97.4% in vulvar cancer, 96.2% in cervical cancer and 88.9% in endometrial cancer. The sensitivity in this procedures was 100.0% in vulvar cancer, 94.0% in cervical cancer and 87.9% in endometrial cancer.

Negative predictive value was 96.2% for vulvar cancer, 97.0% for cervical cancer and 100.0% for endometrial cancer.

Conclusions The concept of sentinel node detection in gynaecological malignances requires more clinical date for its validation, but outcomes in vulvar cancer seem to be potentially most promising.

Key words **sentinel node • gynaecological neoplasms**

Full-text PDF: http:/www.rpor.pl/pdf.php?MAN=7338

Word count: 1352
Tables: 2
Figures: –
References: 12

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Background

The presence of metastases of neoplastic cells to lymph nodes, which are drained by lymph from the organ involved in neoplastic process, is one of the most important prognostic factors. Thus systemic pelvic and paraaortic, lymphadenectomy in uterine and cervical cancer, as well as bilateral inquinal femoral and pelvic lymphadenectomy in vulvar cancer, remain the treatment of choice.

Dissection of the lymph nodes involved in neoplastic process has two principle aims: it decreases the amount of tumour mass with possible subsequent therapeutic effect, and it enables proper clinical staging of the neoplasm of the female genital tract and adequate planning of postoperative treatment.

These objectives make systemic lymphadenectomy the most important part of radical surgery.

Histologic analysis of lymph nodes of cancer patients, dissected by radical surgery revealed metastases to the lymph nodes only in not more than 30% of all patients. Thus, more than 70% of patients, who underwent radical surgery, do not benefit from this procedure [1]. Therefore, it is reasonable to limit the extensiveness of surgical procedures in those patients. Needless to say radical surgery in cancer patients is potentially a source of morbidity that includes an increase in blood loss, wound breakdown, injury of large vessels and nerves, an increase in susceptibility to infections, formation of postoperative fistulas, lymphocoele, lymphoedema, restricted regional mobility, scar formation and further cosmetic, psychological and sexual disturbances.

According to some authors, removal of unaffected lymph nodes may have an unfavorable effect on the local immunological system, which may result in larger number of local recurrences of the disease. The hypothesis based on this fact would make some clinicians more willing to limit the extensivness of surgery [1].

There are several visualization techniques used in the evaluation of lymph node status in female gynaecological malignancies. Unfortunately, none of them make it possible to comprehensively evaluate morphologically lymph node status. In this context, there is considerable hope for progress in lymphatic mapping and sentinel node detection. According to Morton's definition, the sentinel node is a primary node which drains lymph directly from the tumour. Histological status of the sentinel node reflects the status of other lymph nodes in the regional lymphatic basin.

Sentinel node mapping using dyes and/or radioactive tracers has already been successfully implemented as a standard procedure in penile cancer and melanoma and will become, most probably, a standard procedure in breast cancer in the nearest future [2]. This has been possible because of the simplicity of the technique of mapping as well as a result of superficial lymphatic flow patterns in those tumours. Actually, many centers gather experience in the detection of sentinel nodes in gynaecological malignances [3]. The accuracy of both techniques is evaluated as well as that of traditional or laparoscopic surgery [4–6].

Aim

The aim of this paper is to present the possibility of sentinel lymph node detection in vulvar, cervical and endometrial cancer, and to provide a response to the original concept of sentinel node in those tumours.

Materials and Methods

Lymphatic mapping and sentinel lymph node detection was performed in 127 women with gynaecological malignancies: 39 patients with vulvar cancer stage I and II, 52 patients with cervical cancer stage IA2 to IIB, and in 36 patients with endometrial cancer stage I, according to FIGO.

For sentinel node detection were used:
1. a radioisotope technique: Nanocoll (Nycomed Amersham Sorin S.r.l.) marked with technetium 99m, preoperative lymphoscyntygraphy and intraoperative detection by hand – held gamma probe (Navigator GPS, USSC), and
2. a dye – Patent Blau (Guerbet GmbH) technique.

A radiotracer of 2,5 mCi activity was applied peritumorally in vulvar and cervical cancer patients from 14 up to 18 hours before planned surgery. In early advanced cervical cancers and in endometrial cancer, the radiotracer was injected into 4 sites of the ectocervix: at 12, 3, 6 and 9 hours. Preoperative orientation of the lymphatic basin was based on lymphoscyntygraphy, performed 2 hours after radiotracer injection. Then, intraoperatively, 2 to 4 ml of Patent Blau dye was injected, in the same way as was the radiotracer, 20–30 minutes before planned lymphatic mapping. Additionally, in endometrial cancer cases, Patent Blau was injected subserosly around the uterus fundus, and in the central of the anterior and posterior walls of the uterus (Table 1).

Sentinel lymph node(s) were searched for their tinge or radiation emission, detected by a hand-held gamma probe, after obtaining access to the retroperitonium. Node(s) characterized by 10 fold radiation emission to the surrounding background and a bluish tinge in compared to the other lymph nodes were qualified as sentinel nodes.

Then, all patients underwent radical surgery by systemic lymphodenectomy. The number and localization of the nodes classified as sentinel nodes were analyzed in each patient.

All the dissected lymph nodes were, then, examined by pathologists, but sentinel nodes were additionally immunohistochemicaly stained for micrometastasis. The identification rate, sensitivity and the negative predictive value of the method were also determined.

Results

In 39 patients with vulvar cancer, where both detection techniques were used, accumulation of the radiotracer was revealed in 38 (94.7%) cases (Table 2). Lymph nodes stained with blue dye were detected in 32 (82.1%) cases. In all cases, except one where the sentinel node was found in a region of deep inguinal lymph nodes, sentinel nodes were localized in a superficial inguinal lymph node group. Metastases to inguinal lymph nodes were found in 12 patients in complete agreement with the sentinel node status in these cases.

Table 1. Lymphatic mapping and sentinel node detection techniques.

Method of detection	Vulvar cancer	Cervical cancer	Endometrial cancer
Patent Blau (1)	–	–	23
Radiotracer (2)	–	–	–
Both (1+2)	39	52	13
Total	39	52	36

Table 2. Results of lymphatic mapping and sentinel node detection in vulvar, cervical and endometrial cancer.

Method of detection	Vulvar cancer n/N(%)	Cervical cancer n/N(%)	Endometrial cancer* n/N(%)
1. Only stained (1)	–	2/52 (3.8)	19/36
2. Only radiation emission (2)	6/39 (15.4)	7/52 (13.5)	2/13
3. Both (1+2)	32/39 (82.1)	41/52 (78.8)	11/13
4. All cases with identified sentinel node(s) (1+2+3)	38/39 (97.4)	50/52 (96.2)	32/36 (88.9)
5. Identification failure	1/39 (2.6)	2/52 (3.8)	4/36 (11.1)
6. Total	39 (100.0)	52 (100.0)	36 (100.0)
7. Identification rate	97.4	96.2	88.9
8. Sensitivity	100.0	94.0	87.9
9. NPV	96.2	97.0	100.0

* Radiotracer was used in 13 cases;
NPV – negative predictive value.

In 52 women with cervical cancer, sentinel nodes were detected using both techniques in 41 (78.8%) cases. In two (3.8%) cases the sentinel node was only blue stained; in 7 (13.5%) cases only emission of the radiation was detected. In two cases both techniques failed.

Metastases to lymph nodes were found in 18 cases, but in one case sentinel nodes were found free of neoplastic cells. This case was classified as false negative.

In about 80% cases with metastases to lymph nodes, sentinel nodes were located in the bifurcation of common iliac vessels.

Out of 36 patients with endometrial cancer both detection techniques were applied only in 13 cases. The remaining 23 cases were mapped only by the dye technique. In 19 cases sentinel nodes were only stained, in two cases only emission of the radiation was detected, and in 11 cases both methods were efficient. In 4 women sentinel node detection failed. Metastases to lymph nodes were found in three patients, where sentinel nodes showed neoplastic cells as well.

The use of preoperative lymphoscyntygraphy has enable us to establish approximate localization of sentinel nodes in all cases.

Discussion

The concept of a sentinel nodes has created a new quality in optimizing lymphatic system evaluation, and may bring about positive clinical results. Most probably, in many cases systemic lymphodenectomy will be replaced by selective lymphodenectomy [1]. This make it possible to limit the number of lymph node dissections, reduce the extent of surgery and, as a consequence, the number of perioperative complications. Based on our data, it seems that lymphatic mapping and detection of sentinel nodes in vulvar cancer may become well accepted [7–9]. This is due to the uncomplicated lymphatic basin and the simplicity of the technique. Lymphatic pathways in cervical and endometrial cancer are much more complicated [10,11]. The standardization of the technique, especially in endometrial cancer unlike tumours, will also be more difficult [12]. Judging from preliminary data, the best results could be obtained using both, the dye and the radioactive methods simultaneously. Moreover, it seems that preoperative lymphoscyntygraphy would improve surgeon's knowledge of the location of sentinel nodes. On the other hand, sentinel node biopsy is a minimal invasive technique which efficacy depends on experience and quality of surgery team. Thus, it may put in different light the place of laparoscopic surgery in gynaecological oncology, where it becomes possible obtaining larger magnification and where instrumentations allow become more precise.

Conclusions

The concept of sentinel nodes in gynaecological malignancies needs clinical confirmation for every kind of tumour. It also requires determination of false negative results, which may have an impact on clinical results.

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