



Sentinel Lymph Node Mapping in Gynecological Malignancies-Are We Ready for Routine Clinical Use?

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Abstract

Sentinel lymph node mapping over a period of time has gained popularity in gynecological cancers. In case of vulvar and cervical cancers, results are quite convincing. Combined mapping methods along with ultrastaging and immunohistochemistry of sentinel nodes has shown higher detection rate with negligible false negative results. But, still to validate the place of sentinel lymph node mapping in management of gynecological cancers more multicentric studies are required.

Keywords: Sentinel lymph node; Gynecological cancers; Immunohistochemistry

Background

Lymphatic metastasis is one of the commonest routes of spreading of gynecological malignancies and therefore, no doubt that the status of lymph nodes has got vital role in the management and planning of these tumours. The first lymph node draining the lymphatic flow with the highest possibility of involvement is called sentinel lymph node (SLN). In accord with lymphatic mapping hypothesis, it is likely that negative sentinel lymph node biopsy rules out the probability of involvement of non-sentinel nodes, however there is possibility of false results as cited in literature [1]. Role of sentinel lymph node mapping concerning vulvar & cervical cancer has place in the current American & European guidelines, whereas in case of endometrial cancer it is still investigational. The purpose of index article is to review & discuss the state of art of sentinel lymph node mapping & its various approaches in gynecological malignancies. The search strategy for this included relevant articles related to SLN biopsy, their cross references, keywords and meta-analysis published.

Mapping Methods

Sentinel lymph node mapping is done by various techniques like dye labeling, use of radioactive substance or combined modality. Inert vital dye, Isosulphan blue is injected at the junction of tumour and healthy tissue in case of vulvar cancer

and in peritumoral cervical stroma circumferentially with median staining time of 20 minutes [2,3]. Another technique of mapping with radioactive substance involves peritumoral injection of Technetium -99 (Tc-99) labelled colloids such as Sulphur, Carbon or Albumin. Sulphur colloids are injected 2-4 hours prior, while albumin labelled ones are used one day prior to surgery. Identification of SLN is done usually with gamma probes. First draining lymphatics are located in groin in case of vulvar cancer while in cervical and endometrial cancer they are deep around iliac vessels, sometimes with complex anatomy. Therefore, preoperative use of single photon emission tomography/computed tomography (SPECT/CT) or intra operative portable gamma camera can guide the surgeon during the surgery in cervical or endometrial cancers. Other recent advances like hybrid tracers and 3-D navigation devices may represent complementary tools by improving the intra operative visualization of sentinel lymph nodes.

Sentinel lymph node biopsy in vulvar cancer

Vulvar cancer accounts for 3-5% of gynecological malignancies [4]. As the pattern of dissemination in vulvar cancer is lymphogenic, therefore the lymph node metastasis represents the most important prognostic factor. Standard treatment of vulvar cancer includes radical vulvectomy and inguino-femoral

lymphadenectomy, however only a third of patients in early stage will have lymph node involvement. So a standard protocol of elective inguofemoral lymphadenectomy in patients with early stages may not benefit all, but risking significant morbidity in terms of wound infection and breakdown, lymphedema and cellulitis [5-9]. So, accurate identification of sentinel lymph node in early stage vulvar cancer may potentially spare the patients from common morbidities of the inguofemoral lymphadenectomy (IFL) but on the other hand unrecognized disease in the lymph nodes may prove fatal. The sentinel lymph node obtained by injecting blue dye or /and using radiolabeled colloid is histologically examined (ultra staging) and also subjected to immunohistochemistry (IHC).

In a meta-analysis of 29 studies (1779 women), SLN detection rate was 68.7% with blue dye, 94% for Tc-99 and highest up to 97.7% with combined mapping method. Pooled sensitivity upto 95% with negative predictive value of 97.9% were seen in studies using 99mTc/blue dye, ultrastaging and immuno histochemistry with IFL as reference. No doubt, patients undergoing SLN biopsy experienced less morbidity than those who had IFL. So they concluded that sentinel lymph node biopsy with combined mapping method (dye+Tc 99) along with ultra staging and IHC is highly accurate in properly selected patients and they should be followed cautiously [10]. Furthermore omission of IFL where sentinel lymph node is negative may be better understood after the results of on-going multicenter studies (GOG-0270 and GROINSS V11).

Sentinel lymph node biopsy in cervical cancer

Cervical cancer is the commonest gynecological cancer of the developing countries & like vulvar cancer lymph node metastasis is the most important factor for recurrence and mortality. A number of studies have been carried out in an attempt to investigate the usefulness of SLN biopsy in cervical cancer. Pooled sensitivity of 80% with methylene blue and up to 92% with Tc-99 has been reported in literature. Detection rate of up to 97% has been found with combined methods [11,12]. A study by Roca et al has shown very high negative predictive of sentinel lymph node biopsy in early stage cervical cancer & strongly recommend the incorporation of this simple technique in the routine clinical use [13]. Some authors has advocated the usefulness of this technique in only cervical tumors of less than 2 cm with common histological subtypes [14,15]. Sentinel lymph node mapping in selective group of patients combined with accurate intra operative histological assessment could reduce surgical related morbidity in patients of early stage cervical cancer [16-18].

Sentinel lymph node biopsy in endometrial cancer

Increased rate of complications because of extensive lymph node dissection to stage patient's disease in endometrial cancer has led to concept of sentinel lymph node mapping. Out of described mapping techniques, hysteroscopic injection has

shown good results in endometrial cancers. Because of technique difficulties to assess the injection area due to the complexity of lymphatic drainage in endometrial cancer limited studies of sentinel lymph node mapping are available.

Conclusion

No doubt, over a period of few years multiple studies on sentinel lymph node mapping has shown promising results, still there are few aspects that needs to be emphasized. Incorporation of new technical modalities to improve detection rate, ultra staging along with immunohistochemistry of sentinel nodes and innovative management approaches need to be developed. Furthermore prospective multicentric studies are required to validate the place of sentinel lymph node mapping in management of gynecological cancers.

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