Sentinel lymph node biopsy in epithelial malignant tumors

KEYWORDS: Sentinel Lymph Node Biopsy; Carcinoma; Surgery

The curative surgery of the epithelial malignant tumors is consisted of surgery of the primary tumor as well as lymph nodes in the regional lymphatic basin.

The role of lymph node dissection in locoregional treatment of patients with epithelial malignant tumors is still controversial.

Is a dissection of lymph nodes more therapeutic or diagnostic procedure?

Lymph node dissection enables removal of metastatic lymph nodes as potentially sites of new metastatic spread. Therefore it has a therapeutic and prognostic role. Also, lymph node dissection provides the most precise information on stage of the disease as well as decision on further therapeutic approach.

The extent of lymph node dissection - Where should we stop?

The extent is based on our actual knowledge of spreading of every type of carcinoma to the lymph nodes: breast cancer, thyroid cancer, skin melanoma, cervical cancer, gastric and rectal carcinoma, etc. It is still a matter of numerous actual controversies. Randomized clinical trials must provide the answers to these questions.

The optimal time for lymph node dissection

Initial, with the operation for primary tumor, when it has therapeutic, prognostic and staging importance.

Delayed, as loco-regional relapse in lymph nodes, when it also has therapeutic and curative importance.

The surgical removal of lymph nodes followed by histopathological analysis, using standard as well as techniques of immunohistochemistry, is the only way to confirm or exclude the presence or absence of lymph nodes metastases.

The clinical examination, ultrasonography, computed tomography, nuclear magnetic resonance, and positron emission tomography are not able to provide a safe diagnosis of lymph nodes metastases.

Sentinel lymph node (SLN) concept

Sentinel lymph node was defined as the first draining lymph node for epithelial malignant tumors. Ramon Canabas, a South American surgeon, introduced the concept of sentinel lymph node (SLN) for predicting the regional lymphatic node status in penile carcinoma in 1977 (1). Nevertheless, Gould and his colleagues from the Washington Hospital Center have published their work and first introduced (sentinel node) in tumors of a parotid gland in 1951 (2). The concept of SLN in the management of melanoma especially those affecting the trunk where the lymphatic drainage could be ambiguous, using a blue-dye (isosulphan blue) injected around melanoma or the biopsy scar, is attributed to Morton and his colleagues back in 1992 (3).

In the early nineties, SLN concept was applied to breast cancer using a blue dye and later using a radioactive colloid to localize the sentinel node (4, 5). Recent published literature seems to support the fact that a combination of blue dye and radioisotope gives better results than either substance on its own. (6). Kelemen and co-workers have published the first results on SLN lymphadenectomy in thyroid carcinomas in 17 patients in 1998 (7).

Is dissection of lymph nodes not involved by metastases useless and may it jeopardize patient's health?

Techniques of sentinel lymph node mapping

* The use of a vital blue dye (Methyl Blue, Isosulphan Blue, Patent Blue V, etc.) by intratumoral or peritumoral injection.
* The use of radioactive colloid (Tc 99) with preoperative and intraoperative (gamma probe) scintigraphy (8).
* Techniques of histological and immunohistochemical confirming, including PCR for detection of malignant cells without formed metastatic tissue in lymph nodes (9).

In which way is it possible to obtain the best results - a combination of vital dye and lymphoscintigraphy?

In the current literature the average rate of SLN identification is 91% (66%-100%) and when identified, the SLN accurately predicts the disease status of the neck in most patients (80%-100%) (10). The study from Roman group of SLN in thyroid malignancy showed the identification rates 66%, 50% and 83% for preoperative lymphoscintigraphy, vital dye and gamma probe scanning, respectively, as well as 100% using a combination of all three methods (11).

Where is the problem?

* "Skip metastases", another draining nodes (internal mammary in breast cancer, skin melanoma of the trunk, mediastinal SLN in thyroid cancer, D2-3 levels in gastric carcinoma, etc).

In which way these problems may be solved?

Postoperative lymphoscintigraphy one day after surgery could be an answer to this question.

Current studies on SLN

The concept of SLN is the most commonly used for skin melanoma and breast cancer. After the first clinical trial for stage I skin melanoma, made by Donald Morton back in 1992 (3), numerous studies were investigated the feasibility and accuracy of SLN mapping in almost all epithelial malignant tumors.

There are few ongoing studies that should be mentioned at this time:

1. Intraoperative lymphatic mapping by the sentinel node technique in clinical stage I melanoma patients. WHO Melanoma Programme, 1997; Study Chairman: N. Cascinelli

2. A study investigating the diagnosis and treatment of early lymph node involvement in patients with primary cutaneous melanoma by sentinel lymph node biopsy with or without completion lymphadenectomy and molecular markers. NCR/MSG SLNB in Melanoma Feasibility Study, 2001; Tim Eisen, Mo Kostilgar, David Ross, Christoebel Saunders

3. After mapping of the axilla: Radiotherapy or Surgery AMAROS. EORTC 10961, 2001, Randomised Phase III (No of patients 3485), EORTC BCG


What can be enhanced after the SLN concept?

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Sentinel node biopsy in the breast cancer: Possibility of the avoidance of axillary node dissection

KEYWORDS: Breast Neoplasms; Sentinel Lymph Node Biopsy

INTRODUCTION

Surgical treatment of early breast cancer includes the removal of the primary tumor and the removal of axillary lymph nodes, which drain the lymph from the tumor site.

Apart from the removal of the whole breast and dissection of the lymph nodes, the early breast cancer treatment, according to Halsted and Meyer method, became more extensive and culminated with hyper-radical interventions of Urban in the middle of 20th century. Their aim was to eradicate the malignant tissue and in this way to eliminate the possibility of disease spreading into the body (1,2). In the meantime, the significance of lymph nodes involvement for disease staging and prognosis was recognized, influencing also the extent of further systemic treatment and radiotherapy.

Completely different surgical approach to the disease, in the early eighties, was introduced by Veronesi, with the idea of conserving the breast and removal only the quadrant of the breast where the tumor is situated. Since noninvasive diagnostic procedures could neither confirm nor deny the lymph nodes involvement, axillary dissection remained the "gold standard" of these operations, and they have always been performed together with conserving operations. The term "sentinel node" (SN) (guard node), indicating the first lymph node which drains the tumor region, was introduced by Donald Morton (3).

Concept of the sentinel node biopsy (4) is dated in 1977, when Cabanas (4,5) performed the first operation of this type in the penile cancer. The largest number of studies in this field was conducted on malignant melanoma. Sentinel nodes were also studied on thyroid gland tumors, vulvar and uterine cervix cancer, and on gastrointestinal and colorectal tumors.

In 1994, Guilliano introduced SN biopsy and lymphatic mapping (determination of lymph paths) in the breast cancer (4). Considering significant analogy with the malignant melanoma (predictability of the lymph drainage), the concept has become easily applicable and widely accepted. Numerous large

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