The sentinel lymph node in gastric cancer

KEYWORDS: Stomach Neoplasms; Sentinel Lymph Node Biopsy

On the basis of studying physiology of the stomach lymph drainage system, as well as follow-up of metastases' incidence, Japanese Research Association for the Stomach Cancer (JRSJC), has given recommendations on the systematic lymph nodes dissection D2, which has been established as a standard in the surgical treatment. According to the tumor localization and the disease stage, recommendations have been given which group of the lymph nodes should be removed during the surgical intervention. The lymph nodes' mapping by the vital colors is considered a significant method for intraoperative planning of dissection level and it was introduced at our Institute as a routine method in the clinical practice 5 years ago. Recently, the lymph nodes' sentinel biopsy has been intensively tested with aim to decrease intervention radicalness and morbidity. Significance of this method in the stomach cancer has been still tested. Former experience indicates that the complex stomach lymph drainage is significantly decreased using this method.

The sentinel node hypothesis states that the histopathological status of the first node on the lymphatic drainage pathway from a primary tumor reflects the tumor status of the entire lymphatic drainage basin. Within this hypothesis is the assumption that the surgeon can correctly and consistently identify this node (1). The anatomical definition of the sentinel node as the lymph node closest to the primary lesion does not take into consideration the physiology of lymph drainage: the node closest to the primary tumor is the first one to be involved only when it receives direct drainage from the injecting site. Only a few studies have investigated the lymphatic flow system of gastrointestinal cancers from the point of view of the sentinel node (SN) concept. The validity of the sentinel node hypothesis is still controversial for gastrointestinal cancers including gastric cancer (2). It is important to determine the value of this procedure in an accurate staging and in minimally invasive approach to gastric cancers (3).

As Siewert and Sendler state, while the lymphatic flow on the surface of the body can be defined easily, the lymphatic drainage of the stomach is much more complicated (4). Namely, following rotation of the stomach during embryonic development, the lymphatic flow is not directed in a simple fashion. It is questionable whether a specific area of the stomach will drain into one lymph node echelon only (4). It is one of the essential obstacles for SLN biopsy (SLNB) in gastric cancer. Furthermore, skip metastasis seems to be quite common in cancer of the stomach (4).

Most of authors use the dye method instead of the radionuclide method to detect the sentinel node. Ichikura et al. used indocyanine green injected endoscopically into the gastric submucosa adjacent to the tumor (5). Some of the authors used isosulfan blue dye, as Tsoulas (6). Miwa used patent blue dye (7).

The perigastric nodes close to the primary tumor are generally the SNs and the use of the radionuclide method implies interference by the gamma rays emitted from the primary tumor located very close to these lymphatic metastases.

The dye is usually injected around the tumor and was soon bound to albumin and carried specifically through the lymphatic vessels. The green-stained nodes are removed.

Moreover in the blue dye technique the time of injection of blue dye needs a careful monitoring, because there is a short window of time during which selective identification of the SN is possible. That is why Kitigawa et al. affirm that a combination of intraoperative endoscopic injection of blue dye and gamma probe inspection is helpful for localizing sentinel nodes in gastric cancer (8). To confirm the complete resection of sentinel nodes a survey of the abdominal cavity by a gamma-detecting probe is essential (3).

Then gastrectomy with extended lymphadenectomy was performed. Both SNs and non-SNs are subjected to histological examination with hematoxylin-eosin.

In research of Kitagawa, using radio-guided method, SNs were identified in 138 of 145 patients (95.2%). The SN was positive in 22 of 24 patients with lymph node metastasis. The incidence of metastasis in the SNs was significantly higher than that in the non-SNs. The diagnostic accuracy according to SN status was 98.6%. Kitagawa underlined that radio-guided SN mapping is an accurate diagnostic procedure for detecting lymph node metastasis in patients with early-stage gastric cancer (2).

Hiratsuka reports that the success rate of SN detection is as high as 99%, with only one false negative (2).

A good basis for discussing the possibility of using the sentinel node mapping in patients with gastric cancers was done by Tsuburaya et al. (9). Namely, in order to examine the biology of sentinel lymph node of stomach cancer, they investigated solitary lymph node metastases that were hypothesized to represent sentinel lymph nodes. Out of 4620 patients with primary gastric cancers, 1271 cases with a localized tumor were selected and the localization of the solitary metastases in relation to the primary tumors were studied. They found that out of 130 tumors with a single basin metastasis, only 71% of the tumors in the upper third, 75% of the middle and 80% of the lower involved the node basins in the close vicinity (9). In the anterior wall and the greater curvature the rates of adjacent metastasis were more than 90%, while in the posterior wall and the lesser curvature they were 76% and 43%, respectively. Metastases of the remaining cases were identified at more distant basins (9).

According to Kitagawa, radical lymphadenectomy is the standard surgical approach even for early-stage gastric cancer with a relatively low incidence of lymph node metastasis because of the limited sensitivity of diagnostic imaging to detect micrometastases in regional lymph nodes (3).

In T1 gastric cancer (depth of cancer invasion limited in the mucosal or submucosal layer) the incidence of nodal involvement is reported to be as low as 2% to 18%, and in the T2 gastric cancer (cancer invading the muscular or subserosal layer) the incidence is about 50%.

Therefore Hiratsuka et al. consider that if D2 lymphadenectomy is larger than necessary in a considerably high proportion of T1 and T2 gastric cancer patients, than sentinel node concept is reliable indicator that could predict the absence of lymph node metastases with high accuracy, thus eliminating major operations (proximal, distal or total gastrectomy) and the lymphadenectomy (2).

Miwa stated in his research that extensive lymphadenectomy (D2) in 295 patients with early gastric cancer resulted in a significantly lower 10-year recurrence rate than limited lymph node dissection (D1) in 97 patients (7).
Among node-positive patients, the recurrence rate following D2 was significantly lower than that after D1. Among node-negative patients, there was no difference in recurrence rate between two groups. Miwa therefore suggests that we should always dissect the lymphatic basins even in cases with no sentinel node metastasis. In addition, patients with sentinel nodes containing metastasis should be treated with the D2 procedure (7).

Alkou et al. also stated that wide and complicated lymphatic system from a gastric tumor contributed to the relatively high (23%) incidence of micrometastases and the frequent occurrence of skip metastasis (10).

A similar view was reported by Kosaka et al. Namely. According to their survey, not every sentinel node is located in the perigastric region near the primary tumor and that, if the preoperative examination indicates submucosal invasion, then a systematic regional lymph node dissection should therefore be carried out (11). Kosaka reports skip metastases in 15% of 51% patients with gastric cancer (11).

Finally, according to Maruyama opinion, the ability to identify a tumor free SN might enable the surgeon to avoid the morbidity associated with radical lymphadenectomy in patients with gastric cancer (12). But he concludes that it is too early to apply sentinel node biopsy for reducing the extent of lymphadenectomy for gastric cancer because of the complicated anatomy of lymphatic streams from the stomach, and because of the frequent skip metastasis and micrometastasis (12).

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Ivan MARKOVIC
Radan ĐZODIĆ
Momčilo INIĆ
Neven JOKIĆ
Srdan NIKOLIĆ
Stevan JOKIĆ
Aleksandar ČELEBIĆ
Zorka MILOVANOVIĆ

Institute for Oncology and Radiology of Serbia, Belgrade, Yugoslavia

The sentinel lymph node concept in thyroid carcinoma - Preliminary results

KEYWORDS: Thyroid Neoplasms; Sentinel Lymph Node Biopsy

Sentinel lymph node was defined as the first lymph node that the tumor would drain to, within the regional lymphatic basin of that tumor. The concept of sentinel lymph node (SLN) being predictive of the status of the regional lymphatic basin is commonly attributed to Ramon Canadas, a South American surgeon, following his pioneering work on the lymphatic drainage in carcinoma of the penis in 100 patients back in 1977 (1). Gould and his colleagues from the Washington Hospital Center published their work and first introduced (sentinel node, in tumors of a parotid gland in 1951 (2). In 1992, Morton and his colleagues introduced the concept of SLN in to 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 (3). In the early nineties, SLN concept was applied to breast cancer using a blue dye and later using a radioactive collod 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). In 1998, Kelemen and co-workers have published the first results on SLN lymphadenectomy in thyroid carcinomas in 17 patients (7).

Different methods have been used for lymphatic mapping. First it was the application of vital color and later the concept lymphoscintigraphy and gamma probe was established. The vital dye and radiocolloid are applied intratumorally. Lymphoscintigraphy is performing preoperatively, while additional gamma probe and injection of vital dye are performed intraoperatively. After thyroidectomy marked sentinel lymph nodes are dissected and sent to frozen section and subsequent definitive histopathology.

The ideal radiotracer should have particles small enough to enter the lymphatics. All radio tracers that have been used are tagged to Technetium 99 with half-life time of 6 h, which enables the radioactive source to decay rapidly after injection (8). The optimal dose of radioactivity is still not established and ranges from 22 to 37 MBq per injection (9,10). Different vital dye was used in different studies - Metilen Blau, Patent Blue V, Isosulphan blue dye, in doses of 0.1 to 0.8 ml (mean 0.5 ml) per injection (7,11,12).

From 2001 to 2002, we performed SLN biopsy in 14 patients with thyroid