Lymphatic Dissemination and the Role of Sentinel Lymph Node Biopsy in Early Gastric Cancer

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Gastric cancer remains one of the most important malignant diseases with significant geographical, ethnic, and socioeconomic differences in distribution. Early gastric cancer (EGC), defined as cancer limited to the mucosa or submucosa with or without lymph node metastases, is rarely seen in the Western world and often a chance finding. In Asia the incidence is much higher mainly due to mass screening programs in areas where there continues to be a high incidence of gastric cancer. Treatment of EGC has evolved in the last decades from invasive surgical approaches towards endoscopic and other minimally invasive techniques. Involvement of regional lymph nodes in patients with EGC largely determines the treatment of choice.

In this edition of *Digestive Surgery*, Dong et al. [1] report on the prevalence of lymph node metastases and the application of the sentinel lymph node biopsy (SNLB) in EGC. In breast cancer and melanoma surgery the sentinel lymph node procedure has proven to be a valuable tool in lymph node mapping with a sensitivity of more than 95%. When the SNLB is negative, lymphadenectomy can safely be omitted. Hence, SNLB is now routine practice in these cancer types.

In gastric cancer, lymph node status is one of the most important prognostic factors. The extent of gastrectomy and lymphadenectomy is largely based on the likelihood of lymph node metastases to first- (N1) and second-tier

(N2) lymph node stations. The applicability of SNLB in gastric cancer has been studied in recent years in an effort to accurately predict metastasis to (non)regional lymph nodes. The ultimate goal is to identify patients who truly need a lymphadenectomy and to identify patients in whom lymphadenectomy can be omitted. Obviously, patients with suspicious or proven lymph node metastases are not eligible for SNLB and a routine D2 lymphadenectomy is deployed. Also in patients with advanced tumours (T3 and more), SNLB does not seem appropriate [2]. These patients already have a high probability of having first- or second-tier lymph node metastases. Moreover, in advanced tumours, original lymphatic drainage routes might be obstructed or altered, resulting in a lower accuracy of the SNLB.

In EGC the prevalence of lymph node metastasis is relatively low. Lymph node metastases are found in approximately 3% of mucosal EGC. In submucosal EGC, lymph node metastases are found in approximately 20% but with a wide range from 10 to 64% [3–5]. In addition, approximately 5% of lymph node metastases in submucosal EGC are located in second-tier lymph nodes, mainly nodal stations 7, 8a and 9 [6, 7]. The article of Dong et al. [1] confirms the low prevalence of lymph node metastases (6 of 111 patients, 5%) in mucosal EGC and the relatively high prevalence of lymph node metastases (58 of 144 patients, 40%) in submucosal EGC in 255 retrospec-

tively analysed patients. In 11 of 64 lymph node-positive patients (17%), metastases occurred in second-tier lymph node stations, which is markedly higher compared to other studies. This may be due to the relatively high number of submucosal tumours with unfavourable features such as a depressed lesion and an undifferentiated histological type, which have a higher chance of lymphatic dissemination.

In most patients with mucosal EGC and in a subset of submucosal EGC, endoscopic mucosal resection or endoscopic submucosal dissection techniques are safely being performed. However, in a small percentage of these tumours, nodal metastases are present and these patients are not cured by a local resection of the tumour alone. In most submucosal cancers and mucosal EGC with unfavourable features, lymphadenectomy is performed because of the relatively high risk of lymph node metastases. However, radical surgery may be overtreatment since no lymph node metastases are found in the vast majority. In these patients, local or segmental resection without lymphadenectomy would probably have resulted in the same excellent disease-free survival rates, but without its surgical morbidity and mortality. In concordance with SNLB in breast cancer and melanoma, SNLB in EGC would provide a valuable tool in the decision to perform a lymphadenectomy or not.

The prerequisite before implementation of SNLB for EGC in clinical decision-making is a high accuracy, high sensitivity and a low false-negative rate of the procedure. In the study by Dong et al. [1], SNLB was performed in 23 patients before a standard D2 lymphadenectomy was performed. Lymph node metastases in the sentinel lymph node and lymphadenectomy specimens were detected in

4 patients without any false-positive or false-negative sentinel lymph nodes. They conclude that the accuracy, sensitivity and specificity of the SNLB in EGC was 100%. However, the number of patients who underwent a SNLB in this study is rather small and only 4 patients with positive lymph nodes are not representative for SNLB in EGC in general. Moreover, most patients had EGC confined to the mucosa with a very small chance of finding positive lymph nodes. The excellent false-negative rate is therefore not surprising.

Like this study by Dong et al. [1], other studies have also shown the technical feasibility of the sentinel lymph node procedure in gastric cancer. However, the accuracy of SLNB in gastric cancer still remains to be determined. A meta-analysis [2] of 38 studies including 2,128 patients with T1, T2 or T3 gastric cancer showed an identification rate of 95.6% and a sensitivity of 81.6% for EGC [2]. These data demonstrate that the reliability of SNLB in EGC is currently not comparable to SNLB in breast cancer or melanoma. The difficulty of performing SNLB in gastric cancer is that, unlike single-course lymphatic flow in breast cancer, the lymphatic flow of the stomach is multidirectional which can result in multiple sentinel lymph nodes located in different perigastric lymph node stations (greater and lesser curvature), but also in second-tier stations [8, 9].

In our opinion, the relatively low sensitivity and the high false-negative rate of SNLB in EGC do not justify the use of SLNB as a standard procedure in EGC. Although it has been suggested that SNLB is a useful tool for individualizing the extent of lymphadenectomy in patients [10], SNLB in EGC still has to be considered investigational.

References

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