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Feasibility of Sentinel Node Concept in Gastric Carcinoma: Clinicopathological Analysis of Gastric Cancer With Solitary Lymph Node Metastases

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Abstract. *Background: The feasibility and diagnostic reliability of sentinel lymph node biopsy of gastric carcinoma are still unclear and controversial. Patients and Methods: To assess the applicability of the sentinel node concept to gastric carcinoma, we retrospectively analyzed the location of metastatic lymph nodes in patients with only one or two lymph node metastases. Results: A total of 135 patients, who underwent gastrectomy with D2 lymphadenectomy for primary gastric adenocarcinoma between 1997 and 2001, were enrolled in this study. An average of 39 lymph nodes were resected and analyzed for each patient. Of the 135 patients, 88 (65%) were subtyped as pN+ (with lymph node metastasis); of the latter, 15 cases (pT1-3; 17% of N+ cases) showed one or two lymph node metastases. In 14 (93%) of these patients, lymph nodes directly adjacent to the primary tumor were involved. Skip metastases were only seen in one patient with cardia carcinoma and lymph node involvement of compartment II (left gastric artery). Conclusion: In patients with gastric carcinoma, especially in early stage carcinoma, the phenomenon of skip metastasis is infrequent. Therefore, the sentinel node concept may be feasible in gastric cancer.*

Total or subtotal gastrectomy with systematic lymph node dissection has been considered as a standard procedure for the treatment of early gastric cancer with potential for micro-lymph node metastases (1, 2). However, an extended D2 lymphadenectomy may be an excessively aggressive lymph node dissection for early gastric cancer because only a few patients have lymph node metastases (3). Several studies have shown higher morbidity and mortality rates after D2 gastrectomy with extended lymphadenectomy compared to D1 resection (4, 5). Additionally, a formal, anatomic gastrectomy may be associated with a number of postgastrectomy disorders (6). Therefore, not only a lesser lymph node dissection but also a less extensive resection of the stomach may be satisfactory for treating early stage gastric carcinoma. Up to now, diagnostic imaging techniques, including computed tomography and endosonography, are still unsatisfactory and do not provide an accurate prediction of metastasis in the lymph nodes draining gastric cancer (7-10). Therefore, the development of novel diagnostic methods for assessing lymph node status is crucial for accurate preoperative lymph node staging (10). This would permit individualized, minimally invasive surgery such as a laparoscopic wedge resection for patients with early gastric cancer (6, 11).

Increasing evidence supports the sentinel node concept for malignant melanoma and breast cancer. The feasibility and diagnostic reliability of sentinel node biopsy of gastric carcinoma, however, are still unclear and controversial (12-14).

To assess the applicability of the sentinel lymph node (SLN) concept to gastric carcinoma, we retrospectively analyzed the location of metastatic lymph nodes in patients with metastatic involvement in one or two lymph nodes in a large series of patients with gastric adenocarcinoma after standardized D2 lymphadenectomy.

Patients and Methods

Patients. The gastrectomy specimens included in this morphological study were obtained between 1997 and 2002, from 135 consecutive patients who were treated surgically for primary gastric adenocarcinoma at the Department of Surgery, University of Cologne, Germany. Eighty-two specimens were obtained from men and 53 from women. The mean age was 64.2 years (range: 32 - 87). One hundred and twenty patients (90.4%) underwent total

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Table I. *Clinicopathological features of 135 patients with gastric carcinoma.*

Total number of patients	135
Age in years (mean)	64.2
T status	
pT1	28 (20.7%)
pT2	45 (33.3%)
pT3	51 (37.8%)
pT4	11 (8.2%)
N status	
pN0	47 (34.8%)
pN1	42 (31.1%)
pN2/3	46 (34.1%)
M status	
M0	112 (83.0%)
M1 lymph	23 (17.0%)
R classification	
R0	124 (91.9%)
R1 / 2	11 (8.1%)
Dissected LN number (mean, range)	39 (18 – 80)

LN, lymph node

Table II. *Localization of the gastric carcinoma and the metastatic lymph nodes in the 15 patients with one or two lymph node metastases: skip metastasis to compartment II in patient 13.*

Patient	pT	pN	pM	+ nodes	Tumor localization	Lymph node stations
1.	3	1	0	2	Lesser curvature	2, 3
2.	2	1	0	1	GE-junction type II	1
3.	2	1	0	1	Antrum, great curvature	4
4.	2	1	0	1	Corpus, lesser curvature	1
5.	1	1	0	1	GE-junction type II	3
6.	3	1	0	1	GE-junction type III, lesser curvature	5
7.	1	1	0	1	Antrum, lesser curvature	5
8.	2	1	0	2	Antrum, greater curvature	3, 4
9.	1	1	0	2	Antrum, lesser curvature	3
10.	2	1	0	1	Antrum, greater curvature	6
11.	2	1	0	1	GE-junction type II	2
12.	2	1	0	2	GE-junction type II	3, 7
13.	1	1	0	1	GE-junction type II	7
14.	3	1	0	2	Antrum, greater curvature	4, 5
15.	2	1	0	1	GE-junction type III, lesser curvature	1

GE, gastro-esophageal

gastrectomy and 13 patients (9.4%) subtotal gastrectomy with standardized D2-lymphadenectomy. The clinicopathological data are shown in Table I.

The specimens were examined macroscopically and microscopically to determine tumor localization. The carcinomas were classified according the pTNM classification of the International Union Against Cancer (15) including lymph node status.

Lymph node analysis. The specimens were removed *en bloc* and the lymph nodes of compartment II (groups 7-11), including lymph node number 12, were dissected from the specimens on a back table by two surgeons according to a standardized protocol (1). The lymph nodes of compartment I (groups 1-6) were dissected by the pathologist during the preparation of the stomach. The specimens were fixed in 5% formaldehyde and embedded in paraffin. A series of sections from six levels of each dissected node was selected and routine staining with hematoxylin and eosin as well as PAS was performed. All lymph nodes were analyzed microscopically for metastatic infiltration. The number and site of all lymph node metastases were recorded. Histological findings were classified according to the TNM classification established by the UICC (15).

Statistical analysis. Only descriptive means were used to analyze the pattern of nodal metastases. Continuous variables were expressed as mean±s.d. and were analyzed according to the Student's *t*-test. Frequencies were analyzed by the Chi^2 test. A $p<0.05$ was considered significant. All calculations were performed using the statistical software SPSS/P + (SPSS Incorporated, Chicago, Illionois, USA).

Results

The clinicopathological characteristics of patients enrolled in this study are summarized in Table I. The distribution of the tumor localization and the groups of lymph node metastases are depicted in Table II. On average, 39 (range, 18 – 80) lymph nodes were resected and analyzed for each patient. Of the 135 patients who underwent gastrectomy with D2 lymphadenectomy, 88 (65%) were subtyped as pN+. Among 88 patients with lymph node metastasis, 15 cases (17%) showed one or two lymph node metastases. Of the latter group, 4 were classified as pT1, 9 as pT2 and 2 as pT3, according to the TNM classification. In 14 (93%) of these patients, the primary tumor spread directly to the local lymph nodes.

Skip metastasis was only seen in one (7%) of the 15 patients, with one infiltrated lymph node of a cardia carcinoma in lymph node station 7 (left gastric artery, compartment II).

Discussion

Determination of the extent of lymph node dissection required in patients with gastric carcinoma on the basis of actual node involvement is important as less extensive dissection may reduce postoperative morbidity and mortality rates (4, 5). However, diagnostic imaging techniques, including computed

tomography (CT) and ultrasonography, are still unsatisfactory and do not provide an accurate preoperative prediction of metastases in the regional lymph nodes draining gastric cancer (9, 16). Considering the intraoperative assessment of lymph node metastases, it is accepted that it is not valid to diagnose lymph node metastases by size and palpation. Several authors have demonstrated the low sensitivity of the surgical diagnosis of nodal involvement (17-21). Usually, lymph node metastases were evaluated by the size and consistency of the nodes during surgery. However, increased size does not necessarily indicate the presence of metastasis (7).

As a novel diagnostic method for assessing lymph node metastatic status, the sentinel node concept has been developed in order to individualize the indication for lymph node dissection and thus permit individualized, minimally invasive surgery (6, 11 ,13). Recently, a wedge resection with limited lymphadenectomy was attempted by Ohgami et al. (22) to improve the quality of life in patients with early gastric cancer.

SLN, the first draining node from a tumor, should theoretically be the first site of lymph node metastases. The feasibility of SLN biopsy has been studied extensively for cancers in the colon (23, 24), head and neck (25), thyroid (26), prostate (27), cervix (28), breast (29, 30) and skin (31, 32). The clinical implications of SNL biopsy in gastric carcinoma, however, remain controversial (12, 33). This is due to the multidirectional lymph drainage resulting from the diversified organogenetic evolution of the stomach and the connections between coeliacal, retroperitoneal and also mediastinal lymph nodes (1, 2, 34, 35). As a result, nodal metastasis is thought to occur randomly. An isolated involvement of compartment D2 (positions 7 – 11) or even compartment D3 was found in patients with a tumor-free compartment D1 (36-38).

The so-called skip metastasis in gastric cancer has been considered an obstacle to the utilization of the SLN concept (12, 39). However, in our study, skip metastasis was only seen in one patient out of 15 patients (7%) with one or two lymph node metastases. Thus, according to our study and the literature, the low incidence of skip metastases in patients with gastric carcinoma, especially in early stage carcinoma, supports the sentinel node technique to be a promising concept in this carcinoma as well. The first clinical studies (11, 13, 33, 39, 40-44) of lymphatic mapping and SLN biopsy in gastric carcinoma confirm our results. The incidence of skip metastases in gastric cancer was found to be 0 – 10% in other retrospective studies (41, 45) and 5.1% in another SLN biopsy study (11, 46).

In conclusion, based on our data, the SNL concept may be feasible in gastric carcinoma due to the low frequency of skip metastases. In order to establish standard guidelines for determining the extent of lymphadenectomy in gastric cancer, multicenter studies of SLN biopsy should be performed. Furthermore, forthcoming studies should investigate the prognostic impact of the sentinel node concept in gastric carcinoma.

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