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Effect of the number of lymph nodes harvested on the long-term survival of gastric cancer patients according to tumor stage and location: a 12-year study of 1,637 cases

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TNM stage;
Tumor location

Abstract

BACKGROUND: The effect of the number of lymph nodes harvested on the long-term survival of gastric cancer according to Tumor, Node, and Metastasis (TNM) stage and tumor location remains unclear.

METHODS: Patients who underwent gastrectomy for gastric cancer (1998 to 2009) were evaluated retrospectively (1,637 patients). The patients' clinicopathological variables, overall survival (OS), and progression-free survival (PFS) were recorded. The effect of the number of lymph nodes harvested on survival was analyzed according to TNM stage and tumor location.

RESULTS: Harvest of greater than 30 lymph nodes was associated with significantly better OS and PFS than less than or equal to 14 lymph nodes, but no significant difference was observed between less than or equal to 14 and 15 to 29 lymph nodes harvested. The number of lymph nodes harvested was significantly associated with the OS or/and PFS of late stage cancer (N+, T3 to T4, and stage III to IV), harvest of greater than 30 lymph nodes brought significantly better survival compared with the other 2 groups. A higher number of harvested lymph nodes was associated with significantly better PFS for gastric cancer of the body of stomach, but not for proximal, distal, and whole stomach cancer. When the tumor was located in the body of the stomach, the PFS was better with 15 to 29 lymph nodes than less than 14 lymph nodes; however, the OS and PFS were not significantly different between greater than 30 lymph nodes and 15 to 29 lymph nodes. TNM stage and number of lymph nodes harvested were the independent risk factors affecting the survival.

CONCLUSION: Tailored lymphadenectomy according to TNM stage and tumor location might be considered for gastric cancer patients.

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Almost 1 million new cases of gastric cancer have been estimated to have occurred in 2012, making it the fifth most common malignancy in the world, after cancers of the lung, breast, colorectum, and prostate (http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx). More than 70% of the cases occur in developing countries, and 50% of the

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worldwide cases have been reported in Eastern Asia (mainly in China).[1–4] Gastric cancer has become the third leading cause of cancer-related death in both men and women worldwide.[5] Clinicopathological characteristics and therapeutic strategies, including the number of harvested lymph nodes,[6] Tumor, Node, and Metastasis (TNM) stage,[7] tumor location,[8] tumor size,[9] and perioperative chemotherapy,[10] have been proven to affect the outcome of gastric cancer. However, the appropriate extent of lymph node dissection accompanied by gastrectomy for the treatment of cancer remains controversial.[11] In gastric cancer, the TNM stage and tumor location, which play a crucial role in the decision-making process for the primary operation, can be evaluated before surgery by a radiologist.[12] If the extent of lymph node dissection required can be judged before the surgery based on the TNM stage or tumor location, the lymphadenectomy protocol can be tailored to meet the needs of individual patients. However, little is known about the impact of the number of harvested lymph nodes on the long-term survival of gastric cancer patients with different TNM stage and tumor location.

In this study, we retrospectively reported the clinicopathological characteristics and survival in 1,637 cases of gastric cancer over a period of 12 years, and analyzed the relationship between the number of harvested lymph nodes and survival of the gastric cancer patients based on T stage, N stage, TNM stage, and tumor location. We found that the number of harvested lymph nodes was an independent risk factor affecting the postoperative outcome of gastric cancer patients. The findings from this study will lay the basis for tailor-made lymphadenectomy procedures that cater to the needs of individual patients.

Patients and Methods

Patients and their clinical characteristics

This study included 1,637 cases of patients (1,108 men and 529 women) diagnosed with gastric cancer and eligible for curative (R0) resection at Peking University People's Hospital, China, between 1998 and 2009. Patients who underwent curative intent resection (R0) but had no other history of cancer were considered to be eligible for the study. Patients were excluded if they underwent neoadjuvant chemotherapy, or if they underwent wedge resection or endoscopic mucosal resections.

The median age of the patients was 65 years (range 17 to 93 years). Among the patients, 134 (8.2%) had a family history of tumors. Of the 134 patients, 53% (71/134) had a family history of gastric cancer; D1 or D1 plus lymphadenectomy was used to treat early gastric cancer and D2 or D2 plus (D2 + #14v+#12p+#8p or +#16a) lymphadenectomy was used to treat advanced cancer. Among the 1,637 patients, 975 (59.6%) underwent postoperative chemotherapy according to the National Comprehensive Cancer Network guidelines or the wishes of the patient.

TNM classification was based on the 7th edition of the American Joint Committee on Cancer staging system. All patients underwent computed tomography scan or magnetic resonance imaging for preoperative clinical staging. All the patients underwent gastroscope to get pathological results. Endoscopic ultrasound was not performed routinely in all patients. If the tumor was suspected early gastric cancer, endoscopic ultrasound was recommended for preoperative T staging. The tumors were divided according to their grade into 3 categories: well, moderately, and poorly differentiated. Patient demographics, tumor factors, surgical factors, and survival (overall survival [OS] and progression-free survival [PFS]) were analyzed. Follow-up evaluation was performed every 3 months for the first 2 years, every 6 months from the third to fifth postoperative year, and then every year thereafter. Magnetic resonance imaging or computed tomography of the brain or chest, and positron emission tomography were performed only when indicated. Recurrences were categorized as local (anastomotic and gastric stump), lymphatic (regional and distant lymph node metastasis), hematogenous (liver, lung, bone, brain, and kidney), or peritoneal. The approval of the Institutional Review Board was obtained for this study.

Statistical analysis

Statistical Package for Social Science version 17.0 (SPSS, Chicago, USA) was used. The chi-square test was used to assess differences in categorical variables for clinicopathological data. Independent t test was used to evaluate differences in variable measurements. Univariate survival analysis (OS and PFS) was performed using Kaplan–Meier methods. The Cox proportional hazards model was used for multivariate analysis. P values less than .05 were considered to indicate statistical significance.

Results

Surgical and pathological characteristics of the gastric cancer patients

Distal subtotal gastrectomy was the most common surgical method used, followed by proximal subtotal gastrectomy and total gastrectomy. Billroth II gastrectomy was the most commonly performed procedure, followed by Billroth I, Roux-en-Y (esophagus–jejunum), and Roux-en-Y (stomach–jejunum). Furthermore, a higher number of patients underwent D2 lymphadenectomy compared with the number of patients who did not receive D2 lymphadenectomy.

Surgery-related complications occurred in 5.8% (96/1,637) of the patients. The complications included anastomotic leakage (.9%, 15/1,637), anastomotic stenosis (1.5%, 24/1,637), intra-abdominal bleeding (.7%, 12/1,637), postoperative ileus (2.1%, 34/1,637), and postoperative intra-abdominal infection (.6%, 10/1,637).