

Comparison of lymph node number and prognosis in gastric cancer patients with perigastric lymph nodes retrieved by surgeons and pathologists

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Abstract

Objective: To compare the numbers of positive and total lymph nodes and prognosis in gastric cancer patients whose perigastric lymph node retrieval was performed by surgeons and pathologists.

Methods: We conducted a retrospective analysis of clinical and follow-up data from 1,056 patients who underwent gastric cancer D2 radical lymph node resection between January 2008 and December 2010 in the Gastrointestinal Surgery Department of Yantai Yuhuangding Hospital. The follow-up ended in December 2015. Patients were divided into two groups according to the specialty of physicians who performed the postoperative perigastric lymph node retrieval: the surgeon group (475 cases) and the pathologist group (581 cases). The numbers of positive and total perigastric lymph nodes and the 3- and 5-year survival were compared between gastric cancer patients in the two groups overall and stratified by TNM stage (AJCC 7th Edition).

Results: Overall, the numbers of positive and total lymph nodes were significantly higher in the surgeon group than in the pathologist group (6.53 ± 4.07 vs. 4.09 ± 3.70 , $P=0.021$; 29.64 ± 11.50 vs. 20.71 ± 8.56 , $P<0.001$). Further analysis showed that the total number of lymph nodes in stage I patients (19.40 ± 9.62 vs. 15.45 ± 8.59 , $P=0.011$) and the numbers of positive and total lymph nodes in stage II (1.38 ± 1.08 vs. 0.87 ± 1.55 , $P=0.031$; 25.35 ± 10.80 vs. 16.75 ± 8.56 , $P<0.001$) and stage III patients (8.11 ± 6.91 vs. 6.66 ± 5.12 , $P=0.026$; 32.34 ± 12.55 vs. 25.45 ± 8.31 , $P<0.001$) were significantly higher in the surgeon group than in the pathologist group. The survival analysis showed that the 3- and 5-year survival of stage II and III patients was significantly higher in the surgeon group than in the pathologist group (82.0% vs. 73.1%, 69.5% vs. 61.2%, $P=0.038$; 49.2% vs. 38.9%, 36.3% vs. 28.0%; $P=0.045$).

Conclusions: Compared with retrieval performed by pathologists, postoperative perigastric lymph node retrieval performed by surgeons was associated with significant increase in the total lymph node number of stage I patients, the numbers of positive and total lymph nodes of stage II and III patients, and the survival of stage II and stage III gastric cancer patients.

Keywords: Gastric cancer; surgeon and pathologist; lymph node retrieval; prognosis

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Introduction

Gastric cancer is one of the most common neoplasms and causes millions of deaths worldwide each year. This

malignancy is one of the main causes of death in many developing countries, especially in China, where it is the cancer with the second highest annual incidence and the third leading cause of cancer-related mortality (1-4).

Combined treatment, including surgery, perioperative radiotherapy and chemotherapy, has been recommended for the treatment of gastric cancer, and gastric cancer surgery has gone through several stages of development, from D1 lymph node dissection to D2 lymph node dissection, followed by extended D2 lymph node dissection (5-9) and finally the standard D2 lymph node dissection which is used at present (10,11). However, lymph node dissection for gastric cancer is difficult and controversial, and has been identified as one of the important prognostic factors in gastric cancer patients. The application of lymph node dissection for gastric cancer is in accordance with the standard of evidence-based medicine and principles of maximizing survival and minimizing mortality in patients. In the past, American and European surgeons routinely performed D1 or D1 plus lymph node dissection combined with postoperative radiotherapy and chemotherapy (12,13) to treat gastric cancer due to poor surgical skills and obesity in patients. Nowadays, standard D2 lymph node dissection has become a mainstream surgical technique in Asia, especially in China, Japan and South Korea, and has been accepted gradually by European and American surgeons (14). According to the 7th edition of the American Joint Committee on Cancer (AJCC) TNM staging system for gastric cancer, the number of positive lymph nodes (15) is considered to be an important factor influencing gastric cancer staging. Thus, the method for postoperative lymph node retrieval may be a key factor in gastric cancer staging. In this study, we compared the numbers of positive and total lymph nodes and prognosis in gastric cancer patients whose perigastric lymph node retrieval was performed by surgeons and pathologists respectively.

Materials and methods

Data collection

Data were derived from Yantai Yuhuangding Hospital, the Affiliated Hospital of Qingdao University. We enrolled 1,107 patients who had undergone D2 radical lymph node resection for gastric cancer from January 2008 to December 2011. Ultimately, data from 1,056 cases including 654 males and 402 females were analyzed because 28 cases were lost to follow-up and 23 cases died from non-gastric cancer-related diseases. The median age of these patients was 58 (range, 31–89) years old. All operations were performed by experienced gastrointestinal surgeons.

The patients were divided into two groups according

to the specialty of physicians who performed the postoperative perigastric lymph node retrieval: the surgeon group (475 cases) and the pathologist group (581 cases). For patients in the surgeon group, the surgeons sequentially retrieved lymph nodes postoperatively within half an hour according to lymph node station (*Figure 1*) and then submitted the lymph node specimens to the Pathology Department for further examination. For patients in the pathologist group, the pathologists retrieved lymph nodes postoperatively. TNM staging was determined according to the Union for International Cancer Control (UICC)/AJCC guidelines (2010, 7th Edition). This research protocol was approved by the Ethics Committee of Yantai Yuhuangding Hospital, the Affiliated Hospital of Qingdao University.

Follow-up

Follow-up was carried out by outpatient review and telephone interviews, including obtaining medical history, performing physical examinations and determining the presence of tumor markers every 3 to 6 months over the first 3 postoperative years, every 6 months during the third, fourth and fifth postoperative years, and every year after 5 postoperative years. Abdominal CT scans or gastric endoscopy examinations were carried out when necessary according to clinical judgement. The follow-up interval was from the operation date until December 2015, and the median follow-up duration was 54 months. The longest

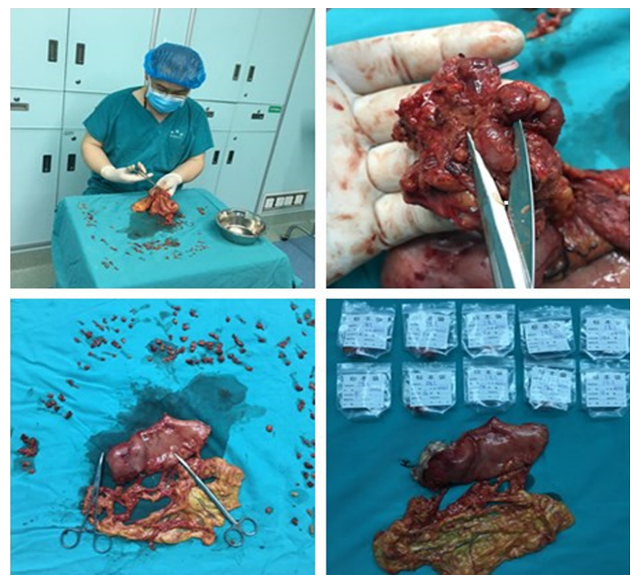


Figure 1 Steps of lymph node retrieval by surgeons.

time is 94 months, and the shortest time is 1 month.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (Version 19.0; IBM Corp., New York, USA). We compared the differences between two groups using *t*-test, χ^2 or Fisher's exact probability tests. The Kaplan-Meier method was used to calculate the survival rates, and log-rank tests were used to test for survival differences between the two groups. Two-tailed $P < 0.05$ was considered statistically significant in all tests.

Results

General information of patients

There were no significant differences in gender, age, family history of gastrointestinal malignant tumors, tumor location, resection margin, type of Lauren classification, degree of differentiation, tumor diameter, TNM stage, or the use of postoperative radiotherapy or chemotherapy between the two groups. Only the digestive tract reconstruction method differed between the two groups ($P = 0.017$) (Table 1).

Number of lymph nodes

In all, the data of positive and total lymph nodes in each group are in accord with normal distribution. We compared the number of lymph nodes by *t*-test. As shown in Table 2, the numbers of positive and total lymph nodes were significantly higher in the surgeon group than in the pathologist group ($P = 0.021$, $P < 0.001$, respectively). Further analysis showed that the total number of lymph nodes in stage I patients and the numbers of positive and total lymph nodes in stage II and stage III patients were higher in the surgeon group than in the pathologist group, and these differences were statistically significant (all $P < 0.05$). The number of positive lymph nodes in stage I patients and the numbers of positive and total lymph nodes in stage IV patients were also higher in the surgeon group than in the pathologist group, however, these differences were not statistically significant (all $P > 0.05$).

Survival analysis

In all, the 3- and 5-year survival rates of patients in the surgeon group were higher than those in the pathologist group, but the difference was not statistically significant

($P = 0.168$). Further analysis showed that the survival rates of stage II and III patients were significantly higher in the surgeon group than in the pathologist group ($P = 0.038$, $P = 0.045$, respectively). Patients with stage I and IV gastric cancer in the surgeon group also had higher survival rates than those in the pathologist group, but these differences were not statistically significant ($P = 0.224$, $P = 0.268$, respectively) (Table 3, Figure 2-6).

Discussion

In most gastric cancer centres, lymph nodes are retrieved by pathologists (16). However, pathologists always simply report the positive and total numbers of greater and lesser curvature lymph nodes because they are less familiar with gastric lymph node stations. The UICC guidelines recommend that the total number of harvested lymph nodes in gastric cancer patients should be not less than 16, and lymph node retrieval should be considered incomplete if less than 16 lymph nodes are retrieved (17). But it did not recommend the details of perigastric lymph node retrieval. Radiotherapy and chemotherapy have been recommended to prevent recurrence in patients with less than 16 lymph nodes harvested. However, most gastric cancer surgeons think that those cases with less than 16 lymph nodes harvested occur due to insufficient postoperative gastric lymph node retrieval by pathologists rather than their poor surgical skills. En bloc lymph node dissection is often used in patients with gastric cancer (18). It is difficult to determine the number of positive and total lymph nodes in each station if surgeons do not retrieve lymph nodes by station. At present, only the total lymph node number and the positive lymph node number are considered in the National Comprehensive Cancer Network (NCCN) staging guidelines; therefore, pathologists may be satisfied when the number of retrieved perigastric lymph nodes is more than 16. In China, Huang *et al.* have advised the number of lymph nodes should be more than 21 in radical total gastrectomy to ensure the standard D2 radical lymph node dissection for gastric cancer (19).

However, when lymph node retrieval is performed by surgeons, the surgeons may not only divide lymph nodes into stations but also count sectioned lymph nodes as a single lymph node at each station. This methodological change may greatly reduce the workload of pathologists, increase the total number of perigastric lymph nodes and the number of positive perigastric lymph nodes, improve quality control in the surgical treatment of gastric cancer, and promote the implementation of standard D2 radical lymph node dissection for gastric cancer (20,21). This

Table 1 Patients' clinical and pathological characteristics

Characteristics	No. of cases		χ^2	P
	Surgeon group (N=475)	Pathologist group (N=581)		
Gender			3.387	0.066
Male	321	361		
Female	154	220		
Age (year)			0.078	0.780
≤60	251	302		
>60	224	279		
Family history of gastrointestinal malignant tumors			0.089	0.766
Yes	40	46		
No	435	535		
Tumor location			4.944	0.423
Upper (U)	22	38		
Middle (M)	120	142		
Lower (L)	251	288		
M+L	24	42		
U+M	22	32		
U+M+L	36	39		
Reconstruction method			8.147	0.017
Billroth I	214	215		
Billroth II	172	256		
Roux-en-Y	89	110		
Resection margin			0.950	0.622
Proximal	21	19		
Distal	365	452		
Full stomach	89	110		
Type of Lauren classification			3.113	0.211
Intestinal type	281	358		
Diffuse type	153	189		
Mixed type	41	34		
Degree of differentiation			0.468	0.494
High and middle	164	189		
Low and undifferentiated	311	392		
Tumor diameter (cm)			0.975	0.323
≤4	342	401		
>4	133	180		
TNM stage			0.746	0.862
I	71	99		
II	108	126		
III	247	305		
IV	49	51		
Postoperative radiotherapy and chemotherapy			1.694	0.429
Radiotherapy and chemotherapy	79	103		
Chemotherapy	283	359		
Neither radiotherapy nor chemotherapy	113	119		

Table 2 Comparison of positive and total numbers of lymph nodes between two groups

Variables	Lymph node number ($\bar{x}\pm s$)		P
	Surgeon group	Pathologist group	
All			
Positive	6.53±4.07	4.09±3.70	0.021
Total	29.64±9.64	20.71±8.56	<0.001
Stage I			
Positive	0.18±0.35	0.17±0.56	0.353
Total	19.40±9.62	15.45±8.59	0.011
Stage II			
Positive	1.38±1.08	0.87±1.55	0.031
Total	25.35±10.80	16.75±8.56	<0.001
Stage III			
Positive	8.11±6.91	6.66±5.12	0.026
Total	32.34±12.55	25.45±8.31	<0.001
Stage IV			
Positive	9.27±6.64	8.93±7.12	0.881
Total	25.08±6.97	23.82±9.40	0.186

Table 3 Comparison of survival rates between two groups

Variables	Overall survival (%)		P
	Surgeon group	Pathologist group	
All			0.168
3-year	62.2	55.6	
5-year	52.8	46.5	
Stage I			0.224
3-year	93.1	86.2	
5-year	87.2	79.2	
Stage II			0.038
3-year	82.0	73.1	
5-year	69.5	61.2	
Stage III			0.045
3-year	49.2	38.9	
5-year	36.3	28.0	
Stage IV			0.268
3-year	24.0	9.1	
5-year	11.2	8.8	

methodology may also cause the pathological stages of gastric cancer to shift, resulting in patients initially diagnosed with stage II gastric cancer being diagnosed with stage III gastric cancer. In this study, the false negative rate was lower in patients with stage II gastric cancer in the surgeon group; patients shifted from stage II to stage III gastric cancer may accept more radiotherapy and

chemotherapy treatment; therefore, this differential diagnosis may improve the survival of patients with stage II gastric cancer. For stage III patients, we hypothesize that the survival may be improved because of improved quality control in the surgical treatment of gastric cancer. Surgeons may improve lymph node dissection by retrieving the lymph nodes, thereby ensuring the implementation of

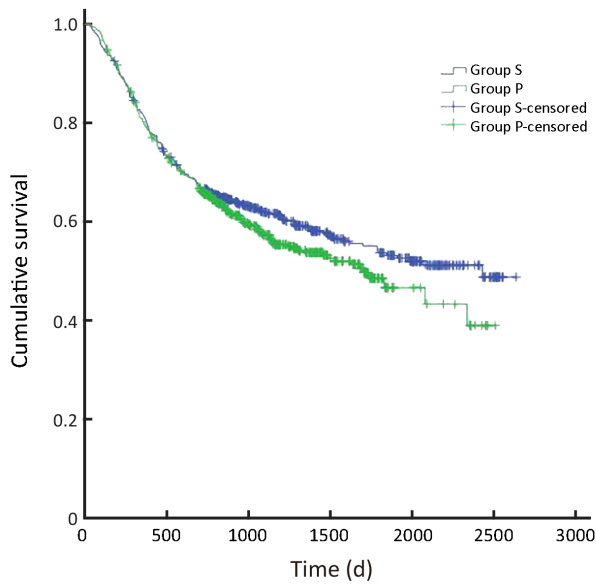


Figure 2 Overall survival of all patients ($P=0.168$). S, surgeon; P, pathologist.

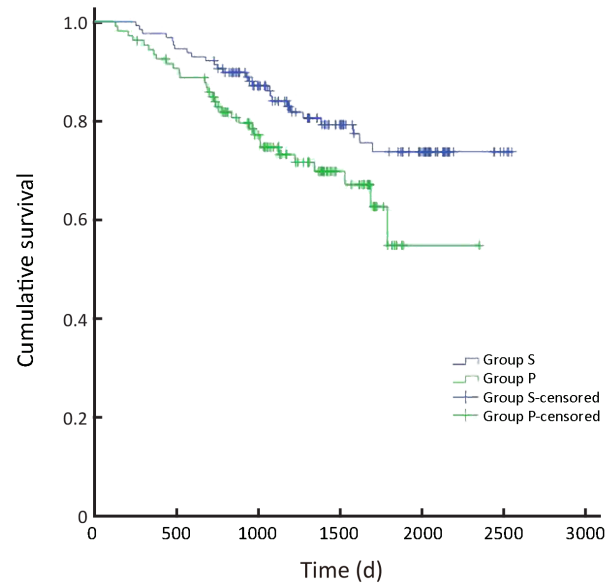


Figure 4 Overall survival of patients with stage II gastric cancer ($P=0.038$). S, surgeon; P, pathologist.

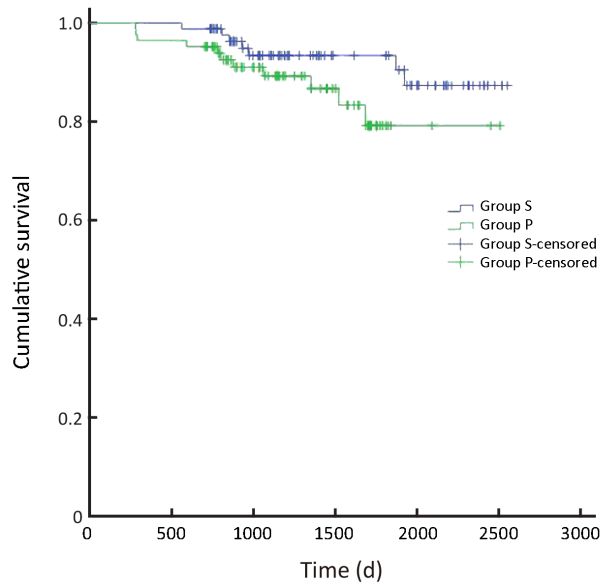


Figure 3 Overall survival of patients with stage I gastric cancer ($P=0.224$). S, surgeon; P, pathologist.

standard D2 radical lymph node dissection. Additionally, the survival of patients in this study was found to be significantly increased, most likely because more positive lymph nodes were harvested.

Conclusions

Compared with retrieval performed by pathologists,

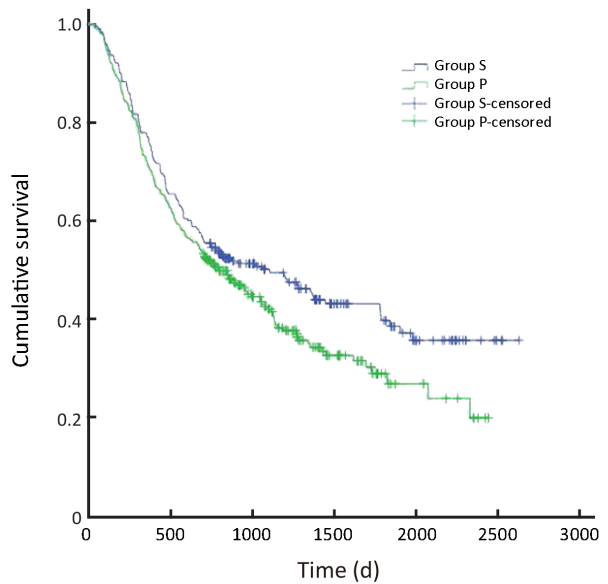


Figure 5 Overall survival of patients with stage III gastric cancer ($P=0.045$). S, surgeon; P, pathologist.

postoperative perigastric lymph node retrieval performed by surgeons was associated with significant increase in the total lymph node number of stage I patients, the numbers of positive and total lymph nodes of stage II and III patients, and the survival of stage II and stage III gastric cancer patients. And we suggest that postoperative gastric cancer lymph nodes should be retrieved not only by stations but also by surgeons and then submitted to the

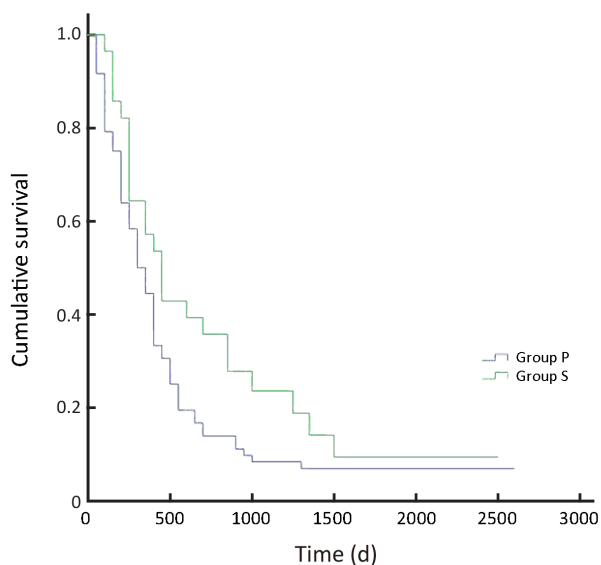


Figure 6 Overall survival of patients with stage IV gastric cancer ($P=0.268$). S, surgeon; P, pathologist.

Department of Pathology for further examination. This method may be helpful not only in accurately staging patients with gastric cancer and facilitating a decision regarding the subsequent use of radiotherapy and chemotherapy treatment but also in improving the survival of patients with gastric cancer significantly.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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