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Original Research

The retrieval of at least 25 lymph nodes should be essential for advanced gastric cancer patients with lymph node metastasis: A retrospective analysis of single-institution database study design: Cohort study

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ABSTRACT

Background: Recently, increased evidence have shown that the better prognosis of gastric cancer (GC) patients was associated with the larger number of retrieved lymph nodes (RLNs), but the optimal number of RLNs remains controversial. In the present study, we investigated whether adequate LN retrieval (≥15) was necessary to evaluate the prognosis of patients and attempted to propose an appropriate cutoff-point for the number of RLNs.
Methods: We reviewed 2246 GC patients who underwent radical gastrectomy in our research institution between January 1986 and January 2008. All patients were divided into several groups based on the number of RLNs. The prognostic outcomes of different patient groups were compared and clinicopathologic features were analyzed.
Results: In the present study, our results indicated that ≥15 RLNs showed a better survival outcome than inadequate LN retrieval (< 15), regardless of the node-negative or node-positive GC patients ($P < 0.001$). For the more advanced GC patients (T2-T4 stage, N1-N3 stage, and stage II-stage III), the retrieval of 25–29 LNs could provide a better survival benefit compared with < 25 or ≥30 RLNs ($P < 0.05$). In addition, for the patients who underwent proximal or total gastrectomy, the superior prognosis was still observed in the patient group with 25–29 RLNs.
Conclusion: The minimal goal of 15 RLNs may not be enough to accurately evaluate prognosis of all patients and at least 25 RLNs should be necessary for advanced GC patients with lymph node metastasis.

1. Introduction

Gastric cancer (GC) is one of the most common malignancy diseases in the world and remains the main cause of cancer-related death [1]. At present, the curative resection including adequate lymphadenectomy was regarded as the optimum treatment modality for advanced GC patients [2]. However, the prognosis of GC patients was still unsatisfactory due to the high rate of recurrence and metastasis [3,4]. Lymph node metastasis has been considered to be the most important factor associated with the prognosis of GC patients [5,6]. For the advanced GC patients, D2 lymph node dissection was accepted as the standard operative procedure in many countries [7,8]. In addition to the perigastric lymph nodes (LNs), all regional LNs in the N2 station need to be completely dissected. A number of studies have revealed that the N-stage migration may occur if the number of retrieved lymph nodes (RLNs) is inadequate [9,10]. Therefore, the American Joint Commission on Cancer (AJCC) recommended that at least 15 LNs should be retrieved to ensure N-stage reliability [11]. Recently, various studies have shown that the better prognosis of GC patients was correlated with the higher number of RLNs [12–14]. Therefore, the minimal goal of 15 RLNs seems to be insufficient, especially for N2-N3 stage patients [15]. In addition, some studies suggested that the number of RLNs should vary based on the T stage, N stage or TNM stage [15–18]. With regard to other clinicopathologic factors, some studies indicated that the number of RLNs was affected by tumor location, tumor size, the type of surgical resection and the extent of LN dissection [17,19,20].

Considering that the ideal number of RLNs still did not reach an unanimous criterion, it is necessary to set a proper cutoff-point for the LN retrieval and credible survival assessment. In the present study, we reviewed 2246 GC patients who underwent radical gastrectomy in our institution between January 1986 and January 2008. All patients in our cohort were reclassified into several subgroups based on the total number of RLNs. Then, we compared the survival differences between

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Table 1
Clinicopathological characteristics and univariate analysis of prognostic factors in 2246 GC patients who underwent curative gastrectomy.

Factor	Patients (%)	Mean survival (months)	5-year CSS (%)	P value
Age (years)				< 0.001
≤60	589 (26.2%)	161.2 ± 4.6	52.6%	
> 60	1657 (73.8%)	112.1 ± 4.4	44.1%	
Gender				0.819
Male	1265 (56.3%)	148.6 ± 4.1	49.0%	
Female	981 (43.7%)	144.0 ± 7.4	48.9%	
Location				< 0.001
Lower 1/3	1171 (52.1%)	162.0 ± 4.9	54.2%	
Middle 1/3	234 (10.4%)	164.3 ± 9.9	58.9%	
Upper 1/3	280 (12.5%)	107.4 ± 8.9	36.0%	
≥2/3 stomach	561 (25.0%)	124.2 ± 6.6	40.9%	
Tumor size				< 0.001
≤5 cm	1320 (58.8%)	172.2 ± 4.6	56.6%	
> 5 cm, < 10 cm	840 (37.4%)	116.6 ± 5.3	39.6%	
≥10 cm	86 (3.8%)	76.7 ± 12.0	28.3%	
Lauren classification				< 0.001
Intestinal	939 (41.8%)	165.2 ± 5.4	56.5%	
Diffuse	1262 (56.2%)	135.5 ± 4.7	43.7%	
Mixed	45 (2.0%)	94.3 ± 17.3	36.1%	
Resection type				< 0.001
Distal	1613 (71.8%)	168.5 ± 4.2	55.4%	
proximal	285 (12.7%)	112.1 ± 8.9	37.1%	
Total	348 (15.5%)	84.1 ± 7.6	28.8%	
Borrmann type				< 0.001
Borrmann I	70 (3.7%)	166.6 ± 16.0	1.9%	
Borrmann II	364 (19.0%)	165.9 ± 8.0	56.1%	
Borrmann III	1315 (68.5%)	116.8 ± 4.6	39.0%	
Borrmann IV	168 (8.8%)	59.9 ± 8.0	17.9%	
T stage				< 0.001
T1	329 (14.6%)	279.7 ± 5.9	92.7%	
T2	379 (16.9%)	184.4 ± 8.4	65.9%	
T3	955 (42.5%)	120.1 ± 5.3	41.5%	
T4	583 (26.0%)	93.0 ± 5.5	28.5%	
N stage				< 0.001
N0	861 (38.3%)	219.2 ± 5.4	74.5%	
N1	442 (19.8%)	146.6 ± 7.8	50.4%	
N2	448 (19.9%)	108.3 ± 7.4	35.7%	
N3a	355 (15.8%)	60.2 ± 5.2	19.8%	
N3b	140 (6.2%)	29.6 ± 4.1	10.5%	
TNM stage				< 0.001
I	476 (21.2%)	262.8 ± 6.0	88.4%	
II	785 (35.0%)	169.3 ± 6.0	58.9%	
III	985 (43.8%)	77.7 ± 4.2	23.9%	
Retrieved LNs				0.926
< 15	849 (37.8%)	145.8 ± 5.4	48.6%	
≥15	1397 (62.2%)	149.2 ± 4.6	50.2%	
Retrieved LNs				< 0.001
15-19	316 (22.6%)	137.1 ± 9.0	47.2%	
20-24	414 (29.6%)	157.4 ± 8.2	53.3%	
25-29	256 (18.4%)	177.0 ± 10.6	58.9%	
≥30	411 (29.4%)	118.6 ± 8.3	39.2%	
Lymphatic invasion				< 0.001
No	1789 (79.7%)	162.5 ± 4.0	53.9%	
Yes	457 (20.3%)	91.3 ± 6.8	29.8%	
Chemotherapy				0.811
No	1754 (78.1%)	149.1 ± 3.8	49.0%	
Yes	492 (21.9%)	94.4 ± 6.7	46.5%	

various subgroups and assessed impact of the number of RLNs on the long-term survival outcome of GC patients.

2. Materials and methods

2.1. Patients

The inclusion and exclusion criteria of this study were as follows: (1). All of patients were pathologically diagnosed with primary GC via hematoxylin-eosin staining after operation. (2). The gastrectomy with curative intent and LN dissection has been performed. (3). Patients with distant metastasis should be excluded, including liver metastasis, peritoneal metastasis and extraregional LNs metastasis (No.13, No.14, No.15 and No.16 station). (4). GC patients who underwent neo-adjuvant chemotherapy before curative operation and had the history of other malignant tumors were excluded from this study. (5). All cases in which the pathological information of patients were complete and not lost to follow-up.

According to the eligibility criteria mentioned above, this study included 2246 GC patients who underwent curative gastrectomy in our institution. This study was approved by the Ethics Committee of our university, and all patients were provided with written informed consent prior to surgery. Also, our study was carried out in line with the STROCSS criteria [21].